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论文摘要汇编

目　录

Potent Modernization of Traditional Chinese Medicine with Nanotechnology: deer antler extract applications for improvement of sports rehabilitation, anti-COVID-19 fatigue targeting ACE2, and anticancer by MET at nanoscale

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Abstract

Background

Deer antler extract has been shown to enhance immune system, muscle regeneration and anticancer but potential applications in anti-COVID-19 associated and mechanism in anticancer fatigue remains elusive. In addition, chemical compounds and peptides which have been believed to function in many pharmacological processes but extract may exhibit biophysical characteristics at nanoscale acting as intrinsic nanozyme upon processing. We here report our recent research on deer antler in applications for anticancer and infectious diseases.

Methods

We applied a gene set-based network pharmacology and molecular docking analysis with experimental investigation by ACE2 activity inhibition, SEM, TEM, AFM, zeta potential, and cell viability assays.

Results

We found potential targets related to the fatigue, COVID-19 after rehabilitation includes gene sets which are mainly related to B cells, central memory T cells, and activation of the PI3K/AKT, mTOR pathways. Moreover, D-galacturonic acid demonstrated higher affinity against TS2 human serotonin transporter (-12.2038 Kjmol-1), ACE2 (-12.0926 Kjmol-1) and human angiotensin receptor (-10.3093 Kjmol-1). Consistently, antler extract inhibited ACE2 activity by experimental validation. Most importantly, we found that the deer antler extract from Kazakhstan contains nanoscale particles and exhibits nanozyme or co-nanozyme activities of phosphatase, peroxidase with crosstalk of MET thereby inhibiting MET kinase by co-targeting. Finally, the extract can be used for self-embedded complexes including carbon dots, PARP inhibitor and chlorophyll extract from spinach leaves (4-mix). We found light can control PARP inhibitor function in the 4-mix compared with olaparib alone and may also reduce side effects of cytotoxicity of carbon dots materials.

Conclusion

With nanotechnology, deer antler extract might be applied to anti-COVID-19 associated fatigue as a sport medicine by immune enhancement and inhibition targeting of ACE2, and light controlled drug response in anticancer for reducing side effects of nano carriers for potent tumor spatial delivery.

Fraxin regulates the apoptosis of FLs mediated by mitochondrial collapse through PI3K/AKT/HSPA8 pathway to treat RA

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Abstract: Wuweiganlu (WGL) is a classic prescription for the treatment of rheumatoid arthritis (RA). However, knowledge of its active ingredients is limited. Based on this, UPLC-Q-TOF-MS technology and serum untargeted metabolomics were used to analyze the active components in WGL and Fraxin was identified as a key compound in WGL. Thus, the present study was designed to investigate the role and mechanisms of Fraxin in RA. Network pharmacology screening identified heat shock protein family member 8 (HSPA8) as a potential target of Fraxin in RA, confirmed through virtual docking. GO and KEGG enrichment analyses suggested that Fraxin modulates RA progression by regulating cell apoptosis through the PI3K signaling pathway. In vitro, Fraxin significantly reduced inflammation and inhibited the expression of HSPA8 in LPS-exposed fibroblast-like synovial cells (FLs). In vivo, Fraxin significantly inhibited foot swelling, bone deformities, and improved bone volume fraction (BV/TV) in IL1RA$^{-/-}$deficient mice with spontaneous arthritis. Histopathological analysis demonstrated the ability of Fraxin to ameliorate joint inflammation by modulating the inflammatory microenvironment surrounding the joint. Moreover, Fraxin inhibited synovial cell hyperplasia by regulating mitochondrial membrane potential collapse in FLs. Functional studies confirmed that Fraxin regulated mitochondrial collapse in FLs via the PI3K/HSPA8 pathway, thereby inhibiting excessive FLs proliferation and slowing RA progression.

Amplifying hepatic L-aspartate levels suppresses CCl4-induced liver fibrosis by reversing glucocorticoid receptor β-mediated mitochondrial malfunction

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Abstract: Liver fibrosis is a determinant-stage process of many chronic liver diseases and affected over 7.9 billion populations worldwide with increasing demands of ideal therapeutic agents. Discovery of active molecules with anti-hepatic fibrosis efficacies presents the most attacking filed. Here, we revealed that hepatic L-aspartate levels were decreased in CCl_4-induced fibrotic mice. Instead, supplementation of L-aspartate orally alleviated typical manifestations of liver injury and fibrosis. These therapeutic efficacies were alongside improvements of mitochondrial adaptive oxidation. Notably, treatment with L-aspartate rebalanced hepatic cholesterol-steroid metabolism and reduced the levels of liver-impairing metabolites, including corticosterone (CORT). Mechanistically, L-aspartate treatment efficiently reversed CORT-mediated glucocorticoid receptor β (GRβ) signaling activation and subsequent transcriptional suppression of the mitochondrial genome by directly binding to the mitochondrial genome. Knockout of GRβ ameliorated corticosterone-mediated mitochondrial dysfunction and hepatocyte damage which also weakened the improvements of L-aspartate in suppressing GRβ signaling. These data suggest that L-aspartate ameliorates hepatic fibrosis by suppressing GRβ signaling via rebalancing cholesterol-steroid metabolism, would be an ideal candidate for clinical liver fibrosis treatment.

论文题目：Amplifying hepatic L-aspartate levels suppresses CCl4-induced liver fibrosis by reversing glucocorticoid receptor β-mediated mitochondrial malfunction

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Efficacy and Mechanism of Aconiti Lateralis Radix Praeparata in AD Prevention and Treatment

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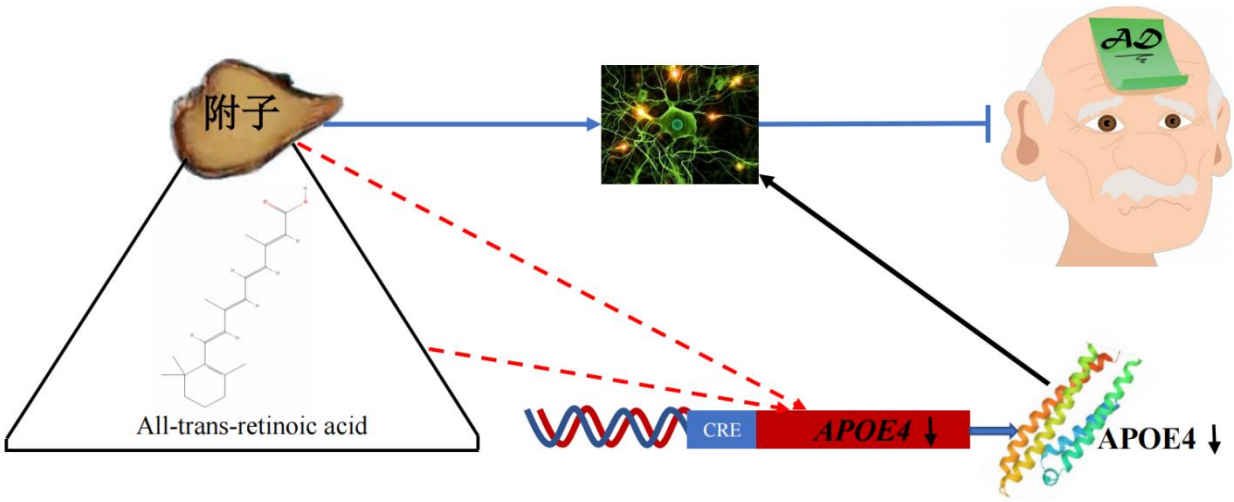
Alzheimer's Disease (AD) is a progressive neurodegenerative disorder projected to affect over 80 million people by 2050. Current treatments cannot reverse neurodegeneration and are ineffective in mild cognitive impairment (MCI), underscoring the need for alternative therapies. **Aconiti Lateralis Radix Praeparata** (FZ), a traditional Chinese medicine, may offer potential in AD prevention and treatment. This study aimed to investigate FZ's efficacy and mechanisms against AD.

A survey of 63 Baoshan residents found that regular FZ consumption significantly reduced the risk of cognitive impairment. In animal studies, FZ treatment (0.064 g/kg) inhibited cognitive decline in aging mice and reversed impairment in MCI models. FZ reduced amyloid-beta (Aβ) deposition, decreased phosphorylated tau (p-tau) levels, and increased synaptophysin (SYN) expression in the hippocampal CA1 region, indicating enhanced synaptic function.

Molecular analyses showed that FZ downregulated Apolipoprotein E (**APOE**) associated with AD risk, and upregulated Tyrosine Kinase(TrkB), a receptor involved in synaptic plasticity. Untargeted metabolomics and network pharmacology identified all-trans retinoic acid (ATRA) as a key FZ component targeting APOE and TrkB, potentially preventing synaptic loss.

These findings suggest FZ can safely and effectively improve cognitive function by reducing Aβ deposition, p-tau levels, and enhancing synaptic integrity. The identification of ATRA as a key bioactive component targeting APOE4 provides insights into FZ's mechanism of action, offering promise for early-stage AD intervention. Further research is needed to validate these findings and explore clinical applications.


附子
All-trans-retinoic acid
AD
CRE
APOE4 ↓
APOE4 ↓

Ultrasensitive Detection of Clinical Pathogens Through a Target-amplification-free Collateral-cleavage-enhancing CRISPR-CasΦ Tool

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Key words: CRISPR-CasΦ, Ultrasensitive Detection, Pathogens, Amplification-free

Introduction:

Clinical pathogen diagnostics detect targets by qPCR (but with low sensitivity) or blood culturing (but time-consuming). Here we leverage a dual-stem-loop DNA amplifier to enhance non-specific collateral enzymatic cleavage of an oligonucleotide linker between a fluophore and its quencher by CRISPR-CasΦ, leading to ultrasensitive target detection. Specifically, the target pathogens are lysed to release DNA, which binds its complementary gRNA in CRISPR-CasΦ to activate the collateral DNA-cleavage capability of CasΦ that cleaves the stem-loops in the amplifier. The cleavage product binds its complementary gRNA in another CRISPR-CasΦ to activate more CasΦ. The activated CasΦ collaterally cleaves the linker, releasing the fluophore to recover its fluorescent signal. The cycle of stem-loop-cleavage/CasΦ-activation/fluorescence-recovery amplifies the detection signal. Our target amplification-free collateral-cleavage-enhancing CRISPR-CasΦ method (TCC), with a detection limit of 0.11 copies/μL, outperforms qPCR in detecting target genes from pathogens. It can detect pathogenic bacteria as low as 1.2 CFU/mL in serum within 40 min.

Materials & Methods: CRISPR-Cas system, MALDI-TOF MS, qPCR, Gel electrophoresis.

Results & Discussion:

Rapid and cost-effective POC diagnostics are crucial for patients with pathogen infections, especially those with BSI. Current blood culture methods can delay treatment for up to 2 days, while detecting pathogens at low concentrations is challenging in hospital settings[1]. In this study, we introduce TCC, a novel diagnostic method for pathogen detection in serum. TCC combines rapid and cost-effective sample processing, enabling rapid, economical, and highly sensitive pathogen detection in serum samples. Compared to gold standard qPCR and blood culture methods, TCC offers superior sensitivity (1.2 CFU/mL) and faster detection time (as low as 40 minutes), making it more effective in diagnosing low pathogen concentrations in BSI samples. We have also developed a portable fluorescence detector for on-site validation of TCC, demonstrating consistent results with the BioTek microplate reader using BSI serum samples. This underscores the clinical potential of TCC for POC diagnosis of BSI. TCC's scalability allows for integration into portable platforms, making it a versatile and widely applicable POC diagnostic tool.

Conclusions:

TCC (Target Amplification-free Collateral-cleavage-enhancing CRISPR-CasΦ method) reached a record-low detection limit of 0.18 aM and took only 40 min. It exhibits exceptional sensitivity, allowing for the detection of pathogen loads as low as 1.2 CFU/mL in clinical samples collected from BSI patients.

References

1. Yagupsky, P. & Nolte, F.S. Quantitative aspects of septicemia. *Clinical Microbiology Reviews* **3**, 269-279 (1990).

Paenibacillus arenilitoris sp. nov., isolated from seashore sand and genome mining revealed the biosynthesis potential as antibiotic producer

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Abstract

Marine environments cover more than 70% of the surface of the earth and are habitats for diverse microorganisms. Marine microorganisms are rich sources for a lot of bioactive natural products. It has become clear that the identification of new antimicrobial compounds is vigorously related to the discovery of novel species. Thus, the mining of microorganisms from various habitats is considered an advantageous approach to discovering novel antibiotics.

In this study, we found that strain IB182493^T, a marine, aerobic, Gram-stain-negative and motile bacterium, was isolated from seashore sand of South China Sea. Cells grew optimally at 25–30°C, pH 7.0–8.0 and in 2–4 % NaCl (w/v). Phylogenetic analysis based on 16S rRNA gene sequence comparison revealed that the strain formed a distinct lineage within the genus *Paenibacillus*, and was most closely related to *Paenibacillus harenae* DSM 16969^T (similarity 96.6%) and *Paenibacillus alkaliterrae* DSM 17040^T (similarity 96.1%). The chemotaxonomic characteristics of strain IB182493^T included MK-7 as the predominant isoprenoid quinone, anteiso-$C_{15:0}$ and iso-$C_{16:0}$ as the major cellular fatty acids and *meso*-diaminopimelic acid as the diagnostic diaminoacid in cell wall peptidoglycan. The polar lipids comprised phosphatidylethanolamine, phosphatidylglycerol, diphosphatidylglycerol and two unidentified phospholipids. The DNA G+C content of

strain IB182493^T was 56.2 mol%. The values of whole genome average nucleotide identity (ANI) and digital DNA-DNA hybridization (dDDH) between the isolate and the closely related type strains were less than 84.7 % and 23.6 %, respectively. In addition, the genome analyses predicted 9 secondary metabolite gene clusters and revealed that this strain has the potential to produce many multifunctional active ingredients, including lasso peptide paeninodin, ectoine, basiliskamide A/B, and staphylobactin, etc. Based on phenotypic and chemotaxonomic properties, phylogenetic distinctiveness and genomic data, we named strain IB182493^T as *Paenibacillus arenilitoris* sp. nov. and proposed that strain IB182493^T (=MCCC 1K04626^T = JCM 34215^T) in the genus *Paenibacillus* represents a novel species.

Keyword

Paenibacillus arenilitoris sp. nov.; 16S rRNA gene; polyphasic taxonomy

NaHS@Cy5@MS@SP nanoparticles improve rheumatoid arthritis by inactivating the Hedgehog signaling pathway through sustained targeted release of H2S into the synovium

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Abstract： Aberrant proliferation and inflammation of fibroblast-like synoviocytes (FLSs) significantly contribute to the joint inflammation and destruction in rheumatoid arthritis (RA). Deficiency of hydrogen sulfide (H2S) is a driving force for the development of RA. Herein, we designed a strategy to achieve slow release of H2S targeted to the synovium, aiming to maintain synovial homeostasis for the management of RA. This was accomplished by synthesizing sodium hydrosulfide (NaHS)-CY5@mesoporous silic@LNP targeted peptide Dil (NaHS@Cy5@MS@SP) nanoparticles. Transmission electron microscopy (TEM) showed that NaHS@Cy5@MS@SP had a spherical structure, with a loading rate of NaHS at approximately 4.2% and an encapsulation rate close to 90%. Our results demonstrated that NaHS@Cy5@MS@SP effectively targets FLSs, upregulates H2S and its-producing enzyme cystathionine-γ-lyase (CSE) in the joints of arthritic mice and LPS-exposed FLSs. Overexpression of CSE inhibited the proliferation, migration, and inflammation of FLSs upon LPS exposure, effects that were mimicked by NaHS@Cy5@MS@SP. In vivo studies showed that the AUCinf of NaHS@Cy5@MS@SP was three times higher than that of free NaHS, significantly improving the bioavailability of NaHS. Further, NaHS@Cy5@MS@SP specifically targeted the joints, and inhibited synovial hyperplasia and reduced bone and cartilage erosion in the DBA/1J mouse model of collagen-induced arthritis (CIA), which was

superior to NaHS. RNA sequencing and molecular studies validated that NaHS@Cy5@MS@SP inactivated the Hedgehog signaling pathway in FLSs, as evidenced by reductions in the protein expression of SHH, SMO, GLI1 and phosphorylated p38/MAPK. Activation of the Hedgehog pathway blocked the anti-arthritic effects of NaHS@Cy5@MS@SP. This study demonstrates the potential of NaHS@Cy5@MS@SP as an effective strategy for slow and targeted delivery of H2S to synoviocytes.

The Nuclear Receptor AaHR78 Mediates 20E Signaling to Influence Larval Development and Adult Reproduction in Aedes aegypti

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Abstract：Nuclear receptors are key factors in signal transduction within insects and constitute essential components of various physiological pathways. Research on HR78 has primarily focused on its role in tracheal and neural development, with limited studies exploring its functions in metamorphosis and reproduction. In this study, we identified the nuclear receptor gene AaHR78 in Aedes aegypti, belonging to the order Diptera, with a full-length sequence of 3117 bp and an open reading frame (ORF) of 1884 bp encoding 628 amino acids. The gene product includes a DNA-binding domain and a ligand-binding domain. Spatiotemporal expression analysis revealed that AaHR78 is highly expressed during the pupal stage, peaking at the white pupae phase, and shows elevated expression in the head, thorax, and ovaries of adult mosquitoes. To investigate the function of AaHR78, RNA interference (RNAi) was performed on both larvae and adult mosquitoes. In larvae, RNAi results indicated that genes in the 20E signaling pathway and its biosynthetic pathway were affected, leading to increased 20E levels and precocious pupation. In adults, AaHR78 knockdown resulted in decreased 20E levels, impaired ovarian development, and reduced egg production. Additionally, we confirmed that AaHR78 is induced by 20E. In conclusion, AaHR78 mediates the influence of 20E on larval metamorphosis and adult mosquito reproduction.

The activation of sulfakinin peptide receptors can inhibit the blood sucking behavior of Aedes aegypti mosquitoes

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Abstract: Although *Aedes aegypti* mosquitoes have been proven to transmit various infectious diseases such as dengue fever, Zika, yellow fever, and chikungunya, little is known about the physiological mechanisms behind their blood-feeding habits. Female *Aedes aegypti* require blood for egg maturation, which is crucial for the transmission of pathogens to humans. In this study, we identified the sulfakinin receptor gene in the *Aedes aegypti* genome and observed its expression activity at different developmental stages and in various tissues of adult mosquitoes three days post-eclosion, particularly in the central nervous system where it exhibits high expression levels. Knocking down the expression of sulfakinin and their receptor genes in female *Aedes aegypti* increases blood meal intake, whereas microinjection of sulfakinins 1 and 2 into the thorax inhibits blood meal intake in a dose-dependent manner and delays the timing of blood intake, a response that can be reversed by receptor antagonists. The ectopic expression of the sulfakinin receptor in CHO-K1 mammalian cells results in sustained calcium spikes in response to sulfakinin stimulation, which can be blocked by receptor antagonists. Collectively, these findings suggest that activating sulfakinin receptors inhibits blood intake in female *Aedes aegypti* mosquitoes, offering potential targets for future strategies to control their reproduction and prevent disease transmission.

Keywords： blood meal intake, Ca^{2+} oscillations, disease transmission, mosquito control, satiety regulation, sulfakinin, sulfakinin receptor

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Extraction, Characterization, and Prebiotic Activity Evaluation of Crude Sphallerocarpus Gracilis Polysaccharides

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Sphallerocarpus gracilis (SG) is a Chinese medicinal and edible plant widely distributed in China, Mongolia, the Russian Far East, and the eastern region of Siberia. The primary functional component of SG is the *Sphallerocarpus gracilis* polysaccharides (SGP), which exhibit various beneficial effects, including immune regulation, antioxidant properties, and hypoglycemic effects. However, the potential application as prebiotics of SGP has not been reported. In this study, the crude SGP was extracted, characterized, and its digestibility was also investigated. Furthermore, the probiotic fermented milk supplemented with 0.5%–1.5% (w/w) crude SGP (YSGP) was prepared. After a 60-day feeding experiment on Wistar rats with YSGP, the levels of inflammatory factors in the rats' serum and the contents of intestinal metabolites were assessed, as well as the changes in the fecal microbiota were analyzed using 16S rRNA high-throughput sequencing. The results demonstrated that the contents of total carbohydrates, reducing sugar, and protein of crude SGP were 72.62 ± 0.32%, 18.56 ± 0.16%, and 0.12 ± 0.01%, respectively. Crude SGP had a lower hydrolysis degree in the simulated gastrointestinal fluid and α-amylase solution (1.52% and 3.04%, respectively) than that of fructooligosaccharides and inulin ($P < 0.05$). When the ratio of crude SGP reached or exceeded 1.0% (w/v), YSGP led to an improved diversity and composition of the intestinal flora by increasing the abundance of *Bacteroidetes*, *Lactobacillaceae*, *Erysipelotrichaceae*, *Prevotella*, and *Turiubacter* ($P < 0.05$), while reducing the abundance of *Firmicutes*, *Ruminococcaceae*, and *Dorea* ($P < 0.05$). The levels of short-chain fatty acids (SCFAs), indole, and serum cytokines (TNF-α, IL-6, IL-8, and IL-1β) were also significantly enhanced ($P < 0.05$). The correlation analysis revealed significant positive correlations between crude SGP and the relative abundance of beneficial gut

microbiota, as well as the levels of SCFAs, indole, and serum cytokines. Therefore, crude SGP exhibited prebiotic activities and could work synergistically with probiotics to regulate the intestinal microecology of rats. These findings suggest promising application prospects for crude SGP in fermented milk.

Keywords: crude *Sphallerocarpus gracilis* polysaccharides, characterization, prebiotic activity, intestinal flora, metabolites

CLIPB9 modulates melanization by activating PPO3, PPO5 and PPO10 in Aedes aegypti

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Abstract

Arthropod melanization is an crucial immune response triggered by catalyzing prophenoloxidases (PPOs) to phenoloxidases (POs), which is mediated by a complicated protease cascade composing of numerous CLIP domain serine proteases (CLIPs). In *Aedes aegypti (Ae. aegypti)*, CLIPB9 has been demonstrated to participate in tissue and immune melanization. Additionally, the PPO gene family in *Ae. Aegypti* has expanded to include 10 members, the specific interaction between CLIPB9 and PPOs has remained unclear. Phylogenetic analysis indicates that CLIPB9 clusters with other four CLIPBs known to function as the PPO activating proteases (PAPs), suggesting a similar role for CLIPB9. To systematically analyze the interaction between CLIPB9 and PPOs, a yeast two-hybrid screen was employed, revealing that CLIPB9 interacts with PPO1, PPO3, PPO5, PPO9, and PPO10. To confirm this finding, the modified proCLIPB9$_{Xa}$ and PPOs were expressed and purified. After incubation, PPO activation assays showed that CLIPB9 is a terminal PAP to directly activate native PPO3, PPO5, and PPO10. Transcriptional analysis showed that *CLIPB9* is expressed in all developmental stages, peaking at pupae followed by adults, and predominantly in the head and hemocytes. *CLIPB9* expression is induced by septic infection and sterile injury, indicating its role in immunity and wound healing in *Ae. aegypti*. RNAi depletion of *CLIPB9* increased adult's sensitivity to pathogens and reduced hemolymph PO activity following bacterial infection. Overall, CLIPB9 is a terminal PAP that regulates melanization by activating certain PPOs, and is a key immune factor in *Ae. aegypti* against pathogen infection.

Keywords: *Aedes aegypti*; melanization; CLIP domain serine proteases; CLIPB9; prophenoloxidase

Rtr1 is required for Rpb1- Rpb2 assembly of RNAPII and prevents their cytoplasmic clump formation

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Abstract:RNA polymerase II (RNAPII) is an essential machinery for catalyzing mRNA synthesis and controlling cell fate in eukaryotes. Although the structure and function of RNAPII have been relatively defined, the molecular mechanism of its assembly process is not clear. The identification and functional analysis of assembly factors will provide new understanding to transcription regulation. In this study, we identify that RTR1, a known transcription regulator, is a new multicopy genetic suppressor of mutants of assembly factors Gpn3, Gpn2, and Rba50. We demonstrate that Rtr1 is directly required to assemble the two largest subunits of RNAPII by coordinating with Gpn3 and Npa3. Deletion of RTR1 leads to cytoplasmic clumping of RNAPII subunit and multiple copies of RTR1 can inhibit the formation of cytoplasmic clump of RNAPII subunit in gpn3-9 mutant, indicating a new layer function of Rtr1 in checking proper assembly of RNAPII. In addition, we find that disrupted activity of Rtr1 phosphatase does not trigger the formation of cytoplasmic clump of RNAPII subunit in a catalytically inactive mutant of RTR1. Based on these results, we conclude that Rtr1 cooperates with Gpn3 and Npa3 to assemble RNAPII core.

Transcranial optogenetic stimulation promotes corticospinal tract axon regeneration to repair spinal cord injury by activating the JAK2/STAT3 pathway

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KEYWORDS

complete spinal cord injury; optogenetic LED device; transcranial optogenetics; axonal regeneration; JAK2/STAT3 pathway

Regeneration of corticospinal tract (CST) axons after a spinal cord injury (SCI) is a key element in rebuilding neuronal connections to restore voluntary motor function. However, it remains challenging owing to limited effective interventions. This study adopted a modified transcranial optogenetic technique to stimulate CST axon regeneration into the injury site of completely transected SCI and explore the underlying molecular mechanisms. A novel optogenetic LED device was used to stimulate the brain motor cortex in ChR2-YFP transgenic mice to observe the regeneration of CST axons in the injury site of a complete SCI. The LED device was also used in vitro to stimulate the motor cortex slices of the transgenic mouse brain for observing the outgrowth of their neurites. After transcranial optogenetic stimulation, the pyramidal neurons of bilateral cerebral motor cortexes in ChR2-YFP transgenic mice were activated, CST axons regenerated into the injury site of the spinal cord, and the motor function of the paralyzed hindlimbs improved. Proteomic analysis revealed that CST axon regeneration was associated with the activation of the JAK2/STAT3 pathway in the cerebral motor cortexes. In vitro LED blue light

illumination enhanced the outgrowth of neurites from the brain slices of transgenic mice. Treatment with FLLL31, a JAK2/STAT3 inhibitor, led to a significant attenuation of neurite outgrowth. The cranial optogenetic stimulation that activates a wide range of cortex by without invading brain parenchyma have significantly enhanced CST regeneration, leading to improved motor function in mice after SCI.In addition, it enhanced the intrinsic growth ability of injured CST axons and promoted CST axon regeneration by activating the JAK2/STAT3 pathway, repairing complete SCI.

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Global, regional, and national burden of maternal disorders, 1990-2021, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021

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ABSTRACT

Background: Maternal disorders have significantly contributed to the disease burden among females, resulting in substantial health loss and mortality. This study provides a comprehensive assessment of the global disease burden attributable to maternal disorders from 1990 to 2021, and includes projections extending to 2050.

Methods: Data were collected from the Global Burden of Diseases, Injuries, and Risk Factors Study 2021 (GBD 2021). Mortality rates and disability-adjusted life years (DALYs) were utilized as indicators to assess the global disease burden and its subtypes for the year 2021. Heat maps were generated to illustrate the geographical distribution of maternal disorders. Additionally, Pearson correlation analysis was conducted to identify the relationship between the sociodemographic index (SDI) and disease burden across various countries and GBD regions. Temporal trends were analyzed using the Age-Period-Cohort Web (APC-Web) tool and Joinpoint regression analysis.

Results: Globally, the age-standardized DALY rate of maternal disorders decreased from 385.79 (350.44-423.74) years per 100,000 population in 1990 to 155.52 (133.70-183.37) years per 100,000 population in 2021, the total percent change from 1990 to 2021 was -0.6 (-0.66--0.52). Among the 204 countries and territories analyzed, Chad experienced the highest disease burden in 2021, with an age-standardized DALY rate of 3067.92 (2006.39- 4391.15) years per 100,000 population, followed by Somalia (2904.07; 1851.20- 2904.07), South Sudan (2565.38; 1567.11- 4039.96), and

Niger (2357.28; 1505.20- 3430.92). Maternal hemorrhage and maternal hypertensive disorders were the main contributors to the disease burden both in 1990 and 2021. Additionally, our study provided evidence that mortality rates were negatively correlated with SDI both in 1990 and 2021. Using APC-Web tool and joinpoint analysis, we found that the disease burden kept decreasing in recent 30 years, and the females aged 50 to 54 showed the highest decreasing trend. The BAPC prediction model exhibited the decreasing trend for disease burden of maternal disorders in the next 25 years. However, the females aged 20 to 24 would still have high risk attributable to maternal disorders.

Conclusion: In conclusion, maternal disorders continued to pose a significant threat to global public health from 1990 to 2021. It is imperative that more targeted and innovative strategies and policies be implemented worldwide to reduce the disease burden among women.

Mechanistic Insights into the Role of 7-Ketodeoxycholic Acid and Its Producing Bacteria in Mitigating Sarcopenia in Type 2 Diabetes Mellitus

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Abstract： **Purpose**: Type 2 diabetes mellitus (T2DM) is a complex systemic chronic disease, the pathogenesis of which is not yet fully understood. T2DM can lead to a variety of complications, and T2DM-related sarcopenia (referred to as sarcopenia) is a common complication of T2DM. With the increasing aging population and the significant rise in the incidence of T2DM, T2DM-related sarcopenia has attracted more and more attention. This study aims to explore the impact of 7-ketodeoxycholic acid (7-KDC) and its producing bacteria on T2DM sarcopenia. **Methods**: A T2DM mouse model was established using a high-fat diet (HFD) combined with intraperitoneal injection of streptozotocin (STZ), and cell viability was measured in C2C12 cells using CCK8 and LDH assays; DHE staining was used to detect cellular oxidative stress; PI staining was used to detect cell apoptosis. Relevant inflammatory factors were detected in C2C12 and muscle tissues using ELISA and qPCR; Western blot was used to detect muscle differentiation markers MyOD, Myf5; GLUT4; protein synthesis markers mTOR, AKT changes. **Results**: After treatment with 7-KDC and its producing bacteria, muscle mass was significantly improved, inflammation was significantly reduced, and muscle differentiation, glucose transport, and protein synthesis markers were upregulated. **Conclusion**: 7-KDC and its producing bacteria alleviate the symptoms of T2DM sarcopenia by improving inflammation, insulin resistance, and upregulating muscle differentiation markers, suggesting that 7-KDC and its

producing bacteria can be effective metabolites for the treatment of T2DM sarcopenia.

Identification of a natural PLA2 inhibitor from the marine fungus Aspergillus sp. c1 for MAFLD treatment that suppressed lipotoxicity by inhibiting the IRE-1α/XBP-1s axis and JNK signaling

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ABSTRACT

Lipotoxicity is a pivotal factor that initiates and exacerbates liver injury and is involved in the development of metabolic-associated fatty liver disease (MAFLD). However, there are few reported lipotoxicity inhibitors. Here, we identified a natural anti-lipotoxicity candidate, HN-001, from the marine fungus *Aspergillus* sp. C1. HN-001 dose- and time- dependently reversed palmitic acid (PA)-induced hepatocyte death. This protection was associated with IRE-1α-mediated XBP-1 splicing inhibition, which resulted in suppression of XBP-1s nuclear translocation and transcriptional regulation. Notably, the ER stress and lipotoxicity amelioration was associated with PLA2. Both HN-001 and the PLA2 inhibitor MAFP inhibited PLA2 activity, reduced lysophosphatidylcholine (LPC) level, subsequently ameliorated lipotoxicity. Additionally, HN-001 treatment suppressed the downstream pro-apoptotic JNK pathway. In vivo, chronic administration of HN-001 (*i.p.*) in mice alleviated all manifestations of MAFLD, including hepatic steatosis, liver injury, inflammation, and fibrogenesis. These effects were correlated with PLA2/IRE-1α/XBP-1s axis and JNK signaling suppression. These data indicate that HN-001 has therapeutic potential for MAFLD because it suppresses lipotoxicity, and provide a natural structural basis for developing anti-MAFLD candidates.

Antiaging effect of Glibenclamide through targeting mitochondrial key enzymes ENO1- ALDOA

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Abstract

Aging is the result of the gradual accumulation of various molecular and cellular damage over time. As individuals age, the prevalence of many chronic diseases associated with aging will significantly increase, greatly impacting the health status of the elderly population. In our initial screening of a marketed drug library for potential senotherapeutic candidates based on the *C. elegans.* lifespan test, glibenclamide (GBM), a sulfonylurea hypoglycemic drug, demonstrated positive effects. Activity-based protein profiling (ABPP) in combination with cellular thermal shift assay (CETSA) was performed to identify the GBM binding target proteins. Our data indicated that several key enzymes in the mitochondrial respiration including ENO1 (Enolase 1), ALDOA (Fructose-Bisphosphate A) were identified as binding targets of GBM, which may improve aging by affecting mitochondrial metabolism. Our findings provide novel insight into underlying mechanisms by which GBM improves aging symptoms, which may help to develop anti-aging drugs based on new targets.

Characterization of Plant Growth Promoting Rhizobacteria for plant development and Soil microenvironment improvement

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Abstract:

Plant growth-promoting rhizobacteria (PGPR) have a specific symbiotic relationship with plants and rhizosphere soil. The purpose of this study was to evaluate the effects of PGPR on blueberry and tea plant growth, rhizospheric soil nutrients and the microbial community. PGPR strains were selected and identified from blueberry and tea plant rhizosphere soil, respectively. PGPR strains chosen for the root irrigation of great plant growth promoting properties.

The plant growth indexes of the treated blueberry group were significantly higher than those of the control group. The rhizospheric soil element contents also increased after PGPR root irrigation. The rhizospheric microbial community structure changed significantly under the PGPR of root irrigation. The dominant phyla in the soil samples， soil element contents and plant growth indexes had the greatest correlation with phosphorus solubilization and auxin production of PGPR strains.

For tea plant root irrigation, the selected PGPR strains treatment groups had a higher plant growth indexes. Irrigation with PGPR strains significantly increased nutrient elements in the rhizosphere soil compared with control. There were significant differences in microbial diversity between the rhizosphere samples collected from tea plants with different treatments as well as metabolite profiles. The contents of nutrients in tea rhizosphere soil were significantly increased by the PGPR. The root metabolites were enhanced by interacting between the PGPR and tea plant.

Plant growth could be promoted by the root irrigation of PGPR to alter plant

root metabplites, improve rhizospheric soil nutrients and the microenvironment. These data may help us to better understand the positive effects of PGPR on plant growth and the rhizosphere soil microenvironment, as well as provide a research about plant and microbial interaction.

The degradation of TYR variants derived from Chinese OCA families is mediated by the ERAD and ERLAD pathway

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Abstract

Oculocutaneous albinism (OCA) is a genetically heterogeneous group of autosomal recessive disorders, which presents with decreased or absent pigmentation in the hair, skin, and eyes. OCA1, as a subtype of OCA, is caused by mutations in the tyrosinase gene (*TYR*). In this study, we performed *in vitro* functional analysis of eight *TYR* variants (one frameshift variant: c.929dupC (p.Arg311Lysfs*7); seven missense variants: c.896G>A (p.Arg299His), c.1234C>A (p.Pro412Thr), c.1169A>G (p.His390Arg), c.937C>A (p.Pro313Thr), c.636A>T (p.Arg212Ser), c.623T>G (p.Leu208Arg), c.1325C>A (p.Ser442Tyr)) identified in Chinese OCA families. TYR plasmids were transfected into HEK 293T cells to explore the effects of TYR variants on their processing, protein expression, activity, and degradation. The results showed that all eight variants caused TYR to be retained in the endoplasmic reticulum (ER), processing was blocked, and TYR activity almost disappeared; the frameshift variant caused the size of the TYR protein to be reduced by about 30KD, and the protein expression of the remaining seven missense variants was reduced; the ER-associated degradation (ERAD) pathway mediates the degradation of TYR variants that occur on the Tyrosinase copper-binding domain, while the degradation of TYR variants that are not located on that domain may be mediated by a new degradation pathway——ER-to-lysosome-associated degradation (ERLAD). In summary, TYR variants affected their protein processing and activity, and may also induce ER stress and trigger degradation through the ERLAD pathway in addition to the ERAD degradation pathway, providing new insights into the potential pathogenic mechanism for OCA1 caused by TYR variants.

Keywords:

TYR, variant, OCA1, ERAD, ERLAD

Brevilin A inhibits VEGF-induced angiogenesis through ROS-dependent mitochondrial dysfunction

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Abstract

Brevilin A (BA), a sesquiterpene lactone isolated from *Centipeda minima* herb, has been identified to exhibit potent anticancer activity. However, the potential pharmacological effect and mechanism of BA in regulating endothelial cell (EC) angiogenesis, a key event in tumor growth, is poorly understood. In this study, BA was shown to significantly prevent vascular endothelial growth factor (VEGF) induced EC angiogenic capacities *in vitro*, *ex vivo* and *in vivo*. Subsequent functional assays revealed that BA dose-dependently inhibited VEGF-stimulated survival, proliferation, migration, and triggered apoptosis activity in human umbilical vein endothelial cells (HUVECs), as well as suppressed the expression of anti-apoptotic protein Bcl-2, and increased the expression of pro-apoptotic protein caspase-3 and Bax, and suppressed PI3K/AKT pathway. Meanwhile, BA was also able to depolarize mitochondrial membranal permeability (MMP), accelerate mitochondrial superoxide accumulation, induce intracellular reactive oxygen species (ROS) production, and decreased intracellular glutathione (GSH) in HUVECs. Furthermore, both mitochondria-specific superoxide scavenger Mito-TEMPOL and broad-spectrum antioxidant N-acetyl-cysteine (NAC) dramatically abolished BA-induced mitochondrial dysfunction and mitochondrial ROS production, causing the reversion of PI3K/AKT pathway and repression of apoptosis, eventually correcting the impaired endothelial behavior in survival, growth, migration, and angiogenesis. Collectively, our data for the first time identified a new mechanism for anti-angiogenic effect of

BA in vascular EC, one that is based on the regulation of mitochondrial-dependent ROS over-production.

De novo design, optimization and mechanism of new AMPs

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This investigation centered on the de novo design of antimicrobial peptides (AMPs), aiming to elucidate the antimicrobial efficacy and underlying mechanisms, as well as to assess the potential applications of liposome encapsulated AMPs for enhanced therapeutic utility. Initially, the length, charge, hydrophobicity and structure of representative AMPs were summarized based on the AMPs database. Using related websites, the antimicrobial activity was predicted and analyzed. Subsequently, AMPs with better predictive data were screened and synthesized. The antibacterial activity assay identified GLK-4 as the most efficacious candidate against *Shigella flexneri* (*S. flexneri*), thereby designating it as the subject of further inquiry. The morphological alterations of bacteria exposed to GLK-4 were meticulously documented using scanning electron microscopy (SEM). Additionally, genomic analyses were conducted to unravel GLK-4's influence on bacterial DNA, uncovering a dual-pronged mechanism involving disruption of both the cell membrane integrity and genetic material. To further enhance the *in vivo* safety of GLK-4, we explored the feasibility of encapsulating AMPs in liposomes. The results emphasized the effective mitigation of cytotoxicity following the encapsulation of AMPs in liposomes, thereby expanding their therapeutic window. Collectively, our research furnished a theoretical and experimental foundation for the advancement and practical implementation of AMPs, while also paving novel avenues for the innovation of next-generation antimicrobial drugs.

Keywords: antimicrobial peptides; GLK-4; de novo design; *Shigella flexneri*

Metabolic Signaling Study of a Small Molecule Tumor Drug

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Using the small molecule drug Palbociclib, we selected appropriate drug concentrations and treatment durations to inhibit tumor cells *in vitro*. After confirming the drug's effects through Western Blot analysis, we collected the cell lysates and performed high-resolution liquid chromatography-mass spectrometry (LC-MS) to detect metabolic molecules. Through metabolomics research, we identified differential metabolites affected by the treatment: cationic PC (14:0e/22:1), Stearamide, and anionic Lithocholic acid and Cys-Gly. This study revealed that the biochemical metabolic signaling pathways of Fatty Acid Biosynthesis and Dopaminergic Synapse could be regulated by the small molecule drug. This study also demonstrates the specific biochemical metabolic changes in tumor cells induced by Palbociclib.

Keywords: Small Molecule Tumor Drug, Signaling Mechanism, Metabolic Research

Development of a Highly Selective Ferroptosis Inducer Targeting GPX4 with 2-ethynylthiazole-4-Carboxamide as Electrophilic warhead

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Abstract

Objective Ferroptosis has been considered an attractive target for cancer therapy, especially for intractable cancers. A highly ferroptosis selective, potent tool compound with drug like properties can significantly advance the research on inducing ferroptosis for anti-cancer purposes. **Methods** In this work, a novel GPX4 inhibitor equipped with more potent ferroptosis-inducing activity and selectivity was rationally designed *via* further structure-based optimization from our previously reported GPX4 inhibitor **26a**. Those compounds were stepwise optimized by structure-based dug design and the SAR of those compounds was exactly revealed. **Results** The preferred compound ***(R)*-9i** exhibited significant GPX4 inhibitory activity (Kd = 20.4 nM) and more highly selective activity to induce ferroptosis in HT1080 cell lines (selectivity index = 2494). At the cellular levels, ***(R)*-9i** could induce the intracellular accumulation of LPO leading to ferroptosis with satisfactory selectivity. The morphological analysis confirmed the ferroptosis induced by ***(R)*-9i**. Furthermore, ***(R)*-9i** significantly restrained tumor growth in a mouse HT1080 xenograft model without obvious toxicity. **Conclusion** Compound ***(R)*-9i** has favorable pharmacokinetic properties which endowed ***(R)*-9i** with potential in anti-tumor research and as a tool drug for further study of ferroptosis.

Keywords: Ferroptosis, GPX4 inhibitor, Structure-based dug design, Synthesis, Anti-tumor

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HSP70A promotes the photosynthetic activity of marine diatom Phaeodactylum tricornutum under high temperature

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Abstract:
With global climate change, the high-temperature environment has severely impacted the community structure and phenotype of marine diatoms. *Phaeodactylum tricornutum*, a model species of marine diatom, is sensitive to high temperature, which grow slowly under high temperature. However, the regulatory mechanism of *P. tricornutum* in response to high-temperature is still unclear. In this study, we found that the expression level of the *HSP70A* in the wild type (WT) increased 28 times when exposed to high temperature (26 °C) for 1 h, indicating that HSP70A plays a role in high temperature in *P. tricornutum*. Furthermore, overexpression and knockdown of HSP70A have great impact on the exponential growth phase of *P. tricornutum* under 26 ℃. Moreover, the results of Co-immunoprecipitation (Co-IP) suggested that HSP70A potentially involved in the correct folding of the photosynthetic system related proteins (D1/D2), preventing aggregation. The photosynthetic activity results demonstrated that overexpression of HSP70A improves non-photochemical quenching (NPQ) activity under high temperature stress. These results reveal that HSP70A regulates the photosynthetic activity of *P. tricornutum* under high temperatures. This study not only helps us to understand the photosynthetic activity of marine diatoms to high temperature, but also provides a molecular mechanism for HSP70A in *P. tricornutum* under high temperature stress.

Melatonin regulates mitochondrial function to alleviate ferroptosis through the MT2/Akt signaling pathway in swine testicular cells

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Abstract: Increasing evidence has shown that many environmental and toxic factors can cause testicular damage, leading to testicular ferroptosis and subsequent male reproductive disorders. Melatonin is a major hormone and plays an vital role in regulating male reproduction. However, there is a lack of research on whether Mel can alleviate testicular cell ferroptosis and its specific mechanism. In this study, the results indicated that Mel could enhance the viability of swine testis cells undergoing ferroptosis, reduce LDH enzyme release, increase mitochondrial membrane potential, and affect the expression of ferroptosis biomarkers. Furthermore, we found that melatonin depended on melatonin receptor 1B to exert these functions. Detection of MMP and ferroptosis biomarker protein expression confirmed that MT2 acted through the downstream Akt signaling pathway. Moreover, inhibition of the Akt signaling pathway can eliminate the protective effect of melatonin on ferroptosis, inhibit AMPK phosphorylation, reduce the expression of mitochondrial gated channel (VDAC2/3), and affect mitochondrial DNA transcription and ATP content. These results suggest that melatonin exerts a beneficial effect on mitochondrial function to mitigate ferroptosis through the MT2/Akt signaling pathway in ST cells.

Keywords: Melatonin, Testicular ferroptosis, Melatonin receptors, Akt signaling pathway

Cross-kingdom transmission of a novel ssDNA Mycovirus in the phytopathogenic fungus Diaporthe pseudophoenicicola

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Abstract: Research on fungal virus cross-kingdom transmission can break barriers in viral spread, providing key insights for the use of attenuated viruses in biological control. In this study, a novel circular ssDNA virus, named Diaporthe pseudophoenicicola DNA virus 1 (DpDV1), was identified in the phytopathogenic fungus *Diaporthe pseudophoenicicola* isolated from an areca palm leaf with leaf spot symptoms. This virus is capable of reducing the pathogenicity of both its host fungus, *D. pseudophoenicicola*, and the non-host fungus *Fusarium oxysporum*, indicating its potential as a biological control agent for areca leaf spot disease and fusarium wilt in bananas. Remarkably, fungal inoculation experiments demonstrated that DpDV1 can be bidirectionally transmitted between *Nicotiana benthamiana* plants and *D. pseudophoenicicola* fungi, with DpDV1 infection causing no phenotypic effects in plants. Moreover, when a virus-infected fungus is directly inoculated onto a plant leaf, the virus can transmit from the fungus to the plant, demonstrating cross-kingdom transmission. Similarly, introducing a virus-free fungus to a virus-infected plant enables the virus to move from the plant to the fungus, further establishing cross-kingdom transmission. Subcellular localization analysis revealed that DpDV1 is systematically localized in the chloroplasts of plant cells. Here, we report a novel ssDNA mycovirus that attenuates the virulence of its fungal host. This study provides evidence of virus transmission between plant and fungus, expanding our understanding of plant-fungus interactions and mycovirus spread, while providing a theoretical foundation for advancing mycovirus biocontrol technology.

Key words: *Diaporthe pseudophoenicicola,* mycovirus, ssDNA virus, cross-kingdom transmission , infectious clone

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Biological function analysis of the secreted protein FoSP1 of Fusarium oxysporum f. sp. Cubense

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Banana Fusarium wilt is a fungal disease which is the most harmful and difficult to control in banana production in China. Due to the influence of banana Fusarium wilt, the banana planting area in China has been decreasing year by year in recent years, which has brought huge economic losses to the subtropical and tropical banana industries in China. The disease occurred because the vascular bundle of banana was invaded by *Fusarium oxysporum* f. sp. *Cubense* (Foc), and its propagation speed was fast, which caused the yellowing of banana leaves and plant wilting. By comparing the genome and transcriptome sequences of Foc race 1 (Foc1, N2) and race 4 (Foc4, B2), a secreted protein FoSP1 located in the lineage-specific (LS) region with high expression was screened out. The results showed that the full length of the *FoSP1* gene sequence was 455 bp, encoding 129 amino acids, and its signal peptide cleavage site was located between the 20th and 21st amino acid residues, and the protein had no known domain and functional site, so it was inferred that FoSP1 was a new secreted protein. In order to study the biological function of the protein in Foc4 strain, the split-marker method was used to knock out the *FoSP1* gene of B2 strain, and the phenotype analysis and pathogenicity determination of the correctly knocked-out mutant were carried out. The results showed that compared with wild-type B2 strain, there was no significant difference in the mycelial morphology and growth rate of the *FoSP1* gene knockout mutant, and it was insensitive to exogenous stresses such as NaCl, D-sorbitol and H_2O_2. The conidial yield and germination rate of knockout mutant were significantly reduced, and its pathogenicity to Brazilian banana was significantly weakened. It is inferred that the secreted protein FoSP1 does not

participate in the nutritional growth of B2 strain, but plays an important role in the process of sporulation and pathogenicity. This result lays a foundation for further study on the pathogenic mechanism of secreted proteins in the genome LS region of Foc4.

The combined toxicity of Nano- and Microplastics with Fusarium oxysporum to Banana

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The structure of nano- and microplastics (NPs/MPs) is intricate and resistant to degradation, resulting in their residues persisting in the soil environment for extended periods while continuously accumulating. When the concentration of accumulation reaches a certain threshold, alterations within the soil ecosystem may exacerbate both the incidence and severity of soil-borne plant diseases.

In this study, Brazilian banana seedlings were exposed to 10 $mg \cdot kg^{-1}$ of NPs/MPs. The findings indicated that the presence of these plastics heightened the occurrence of *Fusarium oxysporum* infections in banana, with varying particle sizes closely correlating with disease severity. Our research demonstrated distinct differences in disease severity caused by polystyrene NPs/MPs after treatment durations of 10 days and 17 days. Specifically, after 10 days, the order influencing disease severity was as follows: 30 nm > 100 nm > 1 μm, whereas after 17 days it shifted to: 100 nm > 30 nm > 1 μm. Utilizing GFP-labeled *Fusarium oxysporum* alongside polystyrene NPs/MPs of differing sizes revealed that treatment with 30 nm Polystyrene nanospheres over a period of 24 days accelerated both distribution and transfer of Fusarium mycelium, notable mycelial distribution was observed within the taproots of banana seedlings under fluorescence microscopy. Furthermore, an investigation into how *Fusarium oxysporum* interacts with various particle sizes of polystyrene NPs/MPs on root vitality and oxidative stress showed that different particle sizes diminished root vitality in banana seedlings to varying extents. However, microplastics alone did not affect root vitality significantly. Notably, under treatment conditions involving *Fusarium oxysporum* at a size threshold below or equal to 1 μm, there was a significant reduction in catalase and peroxidase activities within banana seedling roots, conversely, peroxidase activity increased significantly among groups

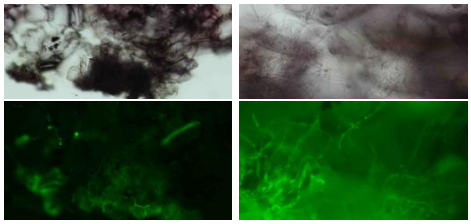
treated with both 30 nm particles as well as those treated at a size threshold below or equal to 1 μm.

Our results offer novel insights into assessing the dual ecological risks posed by interactions between NPs/MPs coupled with *Fusarium oxysporum* towards banana.

Keywords： nano- and microplastics, Oxidative stress, wilt, *Fusarium oxysporu*

Figure 1 Effects of each group on the bulbs of banana seedlings following treatment durations of 10 days and 17 days

Figure 2 The application of 30nm PS in conjunction with the Fusarium after a 24-day treatment significantly enhanced mycelial penetration into the taproot of banana



Reference

[1] Dube E, Okuthe GE. Plastics and Micro/Nano-Plastics (MNPs) in the Environment: Occurrence, Impact, and Toxicity. Int J Environ Res Public Health. 2023 Aug 28;20(17):6667.

[2] Cao X, Wang C, Luo X, et al. Nano- and Microplastics Increase the Occurrence of Bacterial Wilt in Tomato. ACS Nano. 2024 Jul 9;18(27):18071-18084.

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Characterization of a Novel Lectin against OsHV-1 infection in Scapharca broughtonii

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Abstract

As important pattern recognition receptors (PRRs), most C-type lectins (CTLs) are a class of Ca2+-dependent carbohydrate-binding proteins that are found to be involved in non-self-recognition and antiviral process. In this study, a new CTL, named SbCTL, was identified from ark clams, *Scapharca broughtonii*. The amino acid sequence of SbCTL consisted of a predicted CRD structural domain (including 102 amino acid residues). The sequence of SbCTL shared 28%-39% similarity with other CTLs. There were two potential Ca2+ binding sites in SbCTL. The expression of SbCTL mRNA was detected in all selected tissues except muscle, with the highest expression in the gills. After infection with OsHV-1 in ark clams, the expression of SbCTL mRNA was significantly increased at 72 h post infection ($P<0.05$). The binding activities of recombinant SbCTL(rSbCTL) to various PAMPs with or without Ca2+ were analyzed by ELISA, rSbCTL showed especially high binding activity to LPS in a Ca2+-independent manner. rSbCTL also functioned on sheltering ark clams from OsHV-1 infection in vivo, there were less mortality occurred in the rSbCTL treated group than the control. In all, it suggests that SbCTL, could served a critical role in the immune response against intruders in ark clams.

Keywords: Scapharca broughtonii; C-type lectin; PAMP binding; OsHV-1 infection;

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Transcriptomic characterization of neural progenitors in the developing enteric nervous system

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The enteric nervous system (ENS) is the largest and complex automatic nervous system of the peripheral nervous system which contains numerous distinct functional neurons and glial cells. It provides intrinsic innervation of the gastrointestinal tract and regulates the contraction and relaxation of the intestinal muscles. The ENS is derived from enteric neural crest cells (ENCCs) which originate from vagal and sacral neural crest cells (NCCs). ENCCs proliferate, migrate, and differentiate as they traverse long distances to colonize the developing gastrointestinal tract to form the ENS. Defective colonization of NCCs has been ascribed as a possible cause of congenital enteric neuropathies like Hirschsprung's disease (HSCR), characterized by the absence of ganglionated plexuses along varying lengths of the colon. However, the molecular mechanisms governing this long-distance colonization and subsequent cell fate decision of NCCs have not yet been fully understood. In this study, with single-cell transcriptomics, we characterized the cellular profiles of mouse NCCs/ENCCs and mapped their dynamic and molecular landscape during the ENS development. We also dissected the gene expression signatures and compared contributions of NCCs to different cell types of the mouse ENS. Our analysis revealed NCC fate diversification during ENS maturation, where two neuronal types arose through a binary neurogenic branching, with progenitors biased toward neuronal lineages. Overall, our study unveiled the transcriptional and cellular landscapes of

neural crest progenitors, and provide mechanistic insights into the diversification of their cell fates during early ENS development.

The work was supported by the General Research Fund from the Research Grants Council of the Hong Kong Special Administrative Region, China (Ref.: 14120522 and 14118818), and the research fund from Health@InnoHK program launched by Innovation and Technology Commission, the Government of Hong Kong Special Administrative Region, China.

DNA methylation controls cell potency and fate determination during early lung development

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DNA methylation is a reversible epigenetic modification characterized by the addition of a methyl group to cytosine residues within nucleic acids. This mechanism plays a crucial role in regulating cell fate specification during mammalian embryonic development. However, studying human lung development and disease has been challenging due to the lack of biologically relevant in vitro model systems. Consequently, the dynamics and targets of DNA methylation during lung development remain largely unexplored.

In this study, we aim to demonstrate that DNA methylation patterns established during embryonic stages provide epigenetic priming that ensures proper cell commitment during later stages of differentiation. Specifically, we will elucidate the role of DNA methylation in early lung development using a human embryonic stem cell (ESC)-derived lung organoid differentiation model, which offers a unique platform for studying epithelial fate decisions and epithelial-mesenchymal interactions in lung development.

By employing 5-azacytidine, a widely used methylation inhibitor, in combination with genome-wide bulk and single-cell RNA sequencing, chromatin immunoprecipitation, and immunofluorescence staining, we will map the dynamics of methylation patterns and identify key regulatory targets involved in cell specification during early lung development. These findings are expected to uncover novel epigenetic therapeutic targets for lung diseases.

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Effect of Neuropeptide S on a GoStop/StopGo Model of Impulsivity in Wistar and MsP Rats

Abstract:

Impulsivity is a behavior characterized by actions that are poorly conceived, prematurely expressed, risky or inappropriate, with often undesirable consequences. Neuropeptide S (NPS) is a 20-amino acid neurotransmitter characterized by a pro-arousal and anxiolytic physio-pharmacological profile. Previous articles have shown that a variant of the neuropeptide S receptor is associated with impulsivity and alcohol use disorder, so we started to investigate the effect of NPS on impulsive-like traits in Wistar and genetically selected marchigian sardinian alcohol preferring (msP) rats.

First, we developed and validated with atomoxetine a GoStop/StopGo operant model of impulsivity. The model consisted of trials during which rats had access to a lever that when pressed could (or could not) trigger the delivery of a sucrose reward. Each trial consisted of a 3 sec pre-trial period followed by either a 20 sec GoStop or a StopGo trial randomly presented. Rats had to abstain from pressing the lever during pretrials. GoStop trial consisted of 5 sec Go signal followed by 15 sec Stop signal, this schedule was inverted in StopGo trial. Rats had to press the lever when go signal was on and abstain from pressing when the stop signal was on. Correct actions were rewarded with sucrose and followed by a 5 sec inter-trials-interval (ITI) while incorrect action was punished by a 20 sec ITI.

Atomoxetine reduced the number of premature responses and Stop signal errors, demonstrating the predictive validity of the model. Compared to Wistar rats, msP rats showed higher number of Go and Stop errors demonstrating that this strain shows impulsive traits. NPS reduced premature response in both Wistar and msP and incorrect Stop signal response only in Wistars. NPS decreased premature, but increased % total missed go in msP rats. Our results indicates that msP possess impulsive-like traits, suggesting that this might contribute to their alcohol preferring phenotype. In addition, we demonstrated that the neuropeptide S may represent a potential target for treatment of impulsivity.

Title: Effect of Neuropeptide S on a GoStop/StopGo Model of Impulsivity in Wistar and MsP Rats

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Field: Neuroscience

Keywords: Neuropeptide S, Impulsivity, Behaviour, Alcohol, Treatment

Identification, evolution and expression pattern of toll-like receptor genes family in red-spotted grouper (Epinephelus akaara)

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Abstract: Toll-like receptor gene family is a class of conserved pattern recognition receptors, which plays an essential role in innate immunity providing efficient defense against invading microbial pathogens. *Epinephelus akaara* is one of the most important commercial marine fishes, and the main aquaculture industry in China is distributed along the coast of Fujian. The species is also considered a good model for studying immunity. Although *TLRs* have been extensively characterized in both invertebrates and vertebrates, a comprehensive analysis of *TLRs* in *E. akaara* is lacking. This research aims to study the systematic evolution, chromosome distribution, and expression regulation patterns of the Toll-like receptor genes in different tissues of *E. akaara*, based on the published genome and transcriptomic data of *E. akaara*, this study analyzed the phylogenesis, chromosome distribution, and expression regulation patterns of Toll-like receptor gene family in *E. akaara* tissues using bioinformatics methods including BLAST, phylogeny and synteny. The results showed that a total of 17 *TLR* genes were identified in *E. akaara*, which were divided into 5 subfamilies (TLR1, TLR3, TLR5, TLR7 and TLR11) and distributed on 11 of the 24 chromosomes. The 17 *TLRs* showed different expression patterns in different tissues. *EaTLR1-2*, *EaTLR2-2*, and *EaTLR13-2* were mainly highly expressed in the spleen. *EaTLR5M* was highly expressed in the kidney, spleen, gills, and heart, but lowly expressed in other tissues. *EaTLR5S* was highly expressed in the kidney, liver, and spleen, but with low expression in other tissues. *EaTLR18-1* and *EaTLR18-2* were mainly expressed in the heart. *EaTLR8* was highly expressed in all tissues except muscle and liver. *EaTLR1-1*, *EaTLR2-1a*, *EaTLR2-1b*, *EaTLR3*, *EaTLR7*, *EaTLR9*, *EaTLR13-1*, *EaTLR21*, and *EaTLR22* were mainly highly expressed in the brain, spleen, kidney, and gill. In addition, *EaTLR18-1* and *EaTLR18-2* were both located on

chromosome 9 with highly similar expression patterns. *EaTLR2-1a* and *EaTLR2-1b* were located on chromosome 20 and their expression patterns were also highly similar. In addition, *EaTLR5M* and *EaTLR5S*, which had high LRR domain similarity, were located on chromosome 14, and had high similarity in expression levels in different tissues. On the contrary, *EaTLR7* and *EaTLR8*, which were located on chromosome 18, and *EaTLR2-2* and *EaTLR3*, which were located on chromosome 4, had different expression patterns. These suggested that copies of *TLR* genes in the same chromosome may have similar expression patterns or functions. This work provided reference data for studying the evolution of the Toll-like receptor system in fish, and laid a foundation for further research on the function of Toll-like receptor genes in *E. akaara*.

Key words: Red-spotted grouper; Toll-like receptor; Gene family; Expression analysis

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Field:Pharmacology

Osteopontin Promotes VSMC-derived Foam Cells Formation by Inhibiting Cholesterol Efflux in Atherosclerosis

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ABSTRACT

Introduction Atherosclerosis (AS) is the main pathological basis of many cardiovascular diseases in clinical practice, and foam cell formation plays important roles in the development of AS. Increasing evidence shows that a considerable proportion of foam cells derive from vascular smooth muscle cell (VSMC) in atherosclerotic plaques. Osteopontin (OPN) is a cell-secreted phosphorylated glycoprotein that is supposed to promote the development of AS. However, the underlying mechanisms of OPN contributing to the AS progression remain unclear. Therefore, the purpose of the study is to investigate the effects of OPN on VSMC-foaming and AS. **Methods** Mouse AS model was established by feeding ApoE$^{-/-}$ mice with high fat diet (HFD), and the foam cell model of murine aortic vascular smooth muscle cells (MOVAS) were induced with Ox-LDL. During modeling, both ApoE$^{-/-}$ mice and MOVAS were infected with human re-combinant

adenoviruses expressing OPN (Ad-OPN). The ApoE$^{-/-}$ mice were randomly allocated into normal diet(ND)+Vehicle, ND+Ad-OPN, HFD+Vehicle and HFD+Ad-OPN. Similarly, the MOVAS were randomly divided into control(Ctrl)+Vehicle, Ctrl+Ad-OPN, Ox-LDL+Vehicle and Ox-LDL+Ad-OPN, respectively. Eventually, the assays of morphology, function and molecular biology were performed. **Results** All data were presented as mean ± SD. GraphPad Prism 8.0 (GraphPad Software) was used to analyze the data. One-way ANOVA followed by Fisher's LSD post-hoc test was used.Our results show that OPN aggravates vascular smooth muscle dysfunction and AS in the ApoE$^{-/-}$ mice fed with HFD. At the same time, OPN reduces cholesterol efflux and further promotes the formation of VSMC-derived foam cells by decreasing the expression of ABCA1 and ABCG1. Furthermore, OPN inhibits the phosphorylation of p38MAPK through binding to its membrane receptor CD44, thereby reducing the expressions of LXRα, ABCA1 and ABCG1. **Conclusion** Overall, our results demonstrate that OPN reduces the expressions of cholesterol transporters ABCA1 and ABCG1 and promotes the formation of VSMC-derived foam cells, exacerbating the development of AS. The findings would provide a more powerful theoretical support for treating AS with OPN as the target.

This study was supported by the grants from the National Natural Scientific Foundation of China (NSFC, 82260726), the Natural Science Foundation of Jiangxi Province (20232ACB206061) and the Administration of Traditional Chinese Medicine of Jiangxi Province (2023Z018).

Keywords: Osteopontin; Cholesterol efflux; Vascular smooth muscle cells; Foam cell; Atherosclerosis

Deferiprone reduces the qurum sensing related virulence of Burkholderia cenocepacia 162638

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Abstract

The opportunistic pathogen *Burkholderia cenocepacia* poses a significant threat to human health, necessitating the discovery of effective quorum sensing inhibitors (QSIs). In this study, we validate the quorum sensing inhibitory effect of deferiprone (DFP) on *B. cenocepacia* strain 162638. Notably, DFP exhibits pronounced inhibition and disruption of bacterial biofilms in B. cenocepacia 162638, significantly reducing biofilm formation by 44.59% at 1/4 MIC and 24.32% at 1/8 MIC concentrations. The investigation further explores DFP's impact on motility, virulence, and QS signal levels in this strain, revealing inhibitory effects on both protease and lipase activities. LC-MS/MS analysis demonstrates a gradual decrease in the signal content of the QS molecule C6-HSL with increasing DFP concentrations. Additionally, DFP's non-hemolytic property and safety in *Galleria mellonella* infection models verify its biocompatibility. RT-qPCR results indicate that DFP downregulates the expression of QS-related genes, particularly those involved in iron-carrier protein synthesis. Molecular docking studies identify CciR as a key target for DFP's inhibitory action. Collectively, DFP emerges as a promising QS inhibitor with practical applications.

Keywards: Quorum sensing inhibitors; *Burkholderia cenocepacia*; deferiprone；biofilm

Response of growth performance, antioxidant capacity, and gut microbiota to dietary cholesterol and lecithin in the juvenile Redclaw crayfish, Cherax quadricarinatus

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Abstract：

Dietary cholesterol and lecithin are two essential nutrients for the growth and health of crustaceans. A 56-day feeding trial was carried out to evaluate the effects of dietary cholesterol and lecithin on the growth performance, antioxidant capacity, intestinal digestive enzymes, and gut microbiota of the Redclaw crayfish, *Cherax quadricarinatus*. The crayfish (initial average weight 11.39 ± 0.28 g) were fed with six experimental diets formulated with different contents of cholesterol (0.5% and 1%) and lecithin (1%, 2%, and 3%). No additional cholesterol (0%) and lecithin (0%) were added to the diet of the control group. Crayfish fed the diet with 0.5% cholesterol and 2% lecithin improved growth performance, antioxidant capacity, and intestinal digestive enzyme activities than crayfish fed with other diets. Survival, condition

factor, hepatosomatic index, and whole-body proximate composition of crayfish were not significantly affected by different dietary cholesterol and lecithin levels. The Proteobacteria, Firmicutes, and Actinobacteria dominate the gut microbiota community of *C. quadricarinatus*. In diets with 0.5% cholesterol and 2% lecithin, there were more positive connections and a more complex network structure, which may reduce the risk of pathogen infection. Overall, the combination of 0.5% cholesterol and 2% lecithin in *C. quadricarinatus* diets was optimal.

Keywords: *Cherax quadricarinatus*, Cholesterol, Lecithin, Antioxidant capacity, Gut microbiota

Discovery of Novel Triple Targeting G-Quadruplex and Topoisomerase 1/2 Ligands from Natural Products Evodiamine and Rutaecarpine

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ABSTRACT

Inspired by the indolopyridoquinazoline scaffold of natural products evodiamine and rutaecarpine, novel triple G4 and Top1/2 ligands were rationally designed and synthesized. Systematic structure−activity relationship (SAR) studies led to the discovery of compound **15g**, which effectively indueded and stablized G4 and inhibited Top 1/2 with potent antitumor activity. Compound **15g** represents a valuable chemical tool or lead compound for antitumor drug discovery. This proof-of-concept study also validated the feasibility of using planar natural products scaffold as templates to design new G4 ligands.

CBX4 deletion promotes tumorigenesis under KrasG12D background by inducing genomic instability

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Abstract:

Chromobox protein homolog 4 (CBX4) is a component of the Polycomb group (PcG) multiprotein PRC1 complex. CBX4 have been demonstrated having diverse, even opposite functions in different types of tissue and malignancy in previous studies. In this study, we found that CBX4 deletion promoted lung adenocarcinoma (LAUD) in $Kras^{G12D}$ mutated background. In vitro cell experiments, over 50% *Cbx4*$^{L/L}$, *Kras*^{G12D} mouse embryonic fibroblasts (MEFs) underwent apoptosis in the initial period after Adeno-Cre virus treatment, while a small portion of survival cells got increased proliferation and transformation abilities, which we called selected *Cbx4*$^{-/-}$, *Kras*^{G12D} cells. Karyotype analysis and RNA-seq data revealed chromosome instability and genome changes in selected *Cbx4*$^{-/-}$, *Kras*^{G12D} cells compared with *Kras*^{G12D} cells. Further study showed that P15, P16 and other apoptosis-related genes were up-regulated in the primary *Cbx4*$^{-/-}$, *Kras*^{G12D} cells due to chromosome instability, which led to the large population of cell apoptosis. In addition, multiple pathways including Hippo pathway and basal cell cancer-related signatures were altered in selected *Cbx4*$^{-/-}$, *Kras*^{G12D} cells which finally lead to cancer. We also found that low expression of CBX4 in LUAD was associated with poorer prognosis under Kras mutation background from the human clinical data. To sum up, CBX4 deletion causes genomic instability to induce tumorigenesis under $Kras^{G12D}$ background. Our study demonstrates that CBX4 plays an emerging role in tumorigenesis, which is of great importance in guiding the clinical treatment of lung adenocarcinoma.

Self-Assembled TLR7/8 Agonist-Mannose Conjugate as An Effective Vaccine Adjuvant for SARS-CoV-2 RBD Trimer

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Abstract: Small synthetic TLR7/8-agonists can be used as vaccine adjuvants to enhance cell and humoral-mediated immune responses to specific antigens. Despite their potency, after local injection they can be dispersed to undesired body parts causing high reactogenicity, limiting their clinical applications. Here we describe a vaccination strategy that employs the covalent conjugate of a mannose and TLR7/8 agonist as a vaccine adjuvant to take advantage of mannose binding C-type lectins on dendritic cells to enhance the vaccine's immunogenicity. The mannose-TLR7/8 agonist conjugate can self-assemble into nanoparticles with the hydrophilic mannose on the outside and hydrophobic TLR7/8 agonist inside. Although its ability to stimulate HEK-BlueTM hTLR7/8 cells dropped, it can efficiently stimulate mouse bone marrow-derived dendritic cells as indicated by the up-regulation of CD80 and CD86, and higher cytokine expression levels of TNF-α, IL6, and IL-12p70 than the native TLR7/8 agonist. In vivo, vaccination using the SARS-CoV-2 RBD trimer as the antigen and the conjugate as the adjuvant induced a significantly higher amount of IgG2a. These results suggest that the mannose-TLR7/8-agonist conjugate can be used as an effective vaccine adjuvant.

Keywords: adjuvants; mannose; TLR7/8 agonist; immune responses; cytokines; antibody

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Identification and Characterization of Type III Secretion System Effectors in Aeromonas veronii

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Type III secretion system constitutes a trans-membrane injectisome ubiquitous in Gram-negative bacterium, which directly transports effectors (T3SE) to host cells, manipulates host signaling pathways, and thus promotes infection. Specific chaperones (T3SC) are responsible for the recruitment, assembly, and delivery of effectors by binding to the sorting platform. In *Aeromonas veronii*, a pathogen that poses significant threats to aquaculture and human health, T3SS serves as a major virulence factor. Comprehensive analysis of the types and functions of T3SEs in *A. veronii* is essential for elucidating bacterial pathogenicity and its interactions with the host. In this study, bioinformatics analysis reveals four pairs of effectors and their corresponding chaperones from the genome of *A. veronii* C4 strain. On one hand, functional predictions indicate that the effectors possess protease and phospholipase activities, and their 5' UTR regions contain specific binding sites for ExsA, the key T3SS activator. Expression of these effectors in the human colon adenocarcinoma cell line Caco-2 reveals significant effects on cell viability and cytoskeletal integrity. On the other hand, phylogenetic analysis shows that the chaperones belong to the DsfP, ShcO, CesT, and SpcS families, and microscale thermophoresis (MST) assays confirm their direct interactions with the T3SS sorting platform protein AscQ. This study successfully identified novel T3SS effectors and their chaperones in *A. veronii*, providing crucial evidence and a solid foundation for further investigations into the T3SS-mediated pathogenicity in *A. veronii*.

Keywords: *Aeromonas veronii*，Type III secretion system， chaperones， effectors

Construction of biohybrid engineered phage and its application in ultrasensitive detection of Salmonella

With the rapid development of biotechnology, the application of phage gene editing technology in pathogen detection has attracted more and more attention. As a major food safety risk factor, salmonella poses a major threat to public health, and there is an urgent need to develop highly sensitive and rapid detection methods. In our research group, a lysing phage with strong lysing ability was isolated by screening several strains of Salmonella as host, and named PF1. Therefore, we intend to use the highly differentiated properties of the phage as a sensing tool to detect Salmonella pathogens present in the environment. At the same time, this study will develop the phage from the following four aspects to achieve the purpose of ultrasensitive detection of Salmonella typhimurium. Firstly, phage PF1 was modified by biological hybridization, and the signal of phage infection was amplified by internal gene editing and external material hybridization. Genomic analysis was used to screen the gene clusters expressed in the middle and late period of phage, and the highly expressed gene Holin(perforin) was selected, and the promoter of this gene was predicted to be intercepted by analysis about 258bp. The promoter was linked to the eGFP green fluorescence reporter gene by genetic engineering. A progeny recombinant phage with green fluorescent protein eGFP was constructed in BL21(DE3) using CRISPR-Cas9 technology, and the recombinant results were verified by PCR. Fluorescence intensity can be observed by fluorescence microscope and fluorescence enzyme label. Secondly, synthetic up-conversion fluorescent nanomaterials (UCNPs) were used to hybridify phage protein shells by chemical modification, and their optical properties were systematically characterized. The material greatly enhances the strength of the detection signal, improves the detection ability of low concentrations of pathogens, and can obtain results from the fluorescence map. The construction of biohybrid engineered phages and their application in the ultra-sensitive detection of Salmonella can significantly improve the sensitivity and specificity of the detection by optimizing the detection conditions (such as temperature, pH and reaction time). Finally, the feasibility of the system was verified by in vitro test and in vivo mouse experiment.

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Application of machine learning model driven by urine targeted metabolomics data, body movement and sleep recorder to human rhythm disturbance prediction model

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Abstract

Background: The disturbance of circadian rhythm has become a social problem that cannot be ignored. It has been reported that an increased risk of health problems and changes in human hormone levels after shift work can lead to related diseases such as bipolar depression and seasonal affective disorder. Early identification of individuals with biorhythmic disorders is critical for shift workers. The aim of this study is to develop a machine learning model and using this model to output the importance of individual urine metabolites characteristics for whether a subject is staying up late that can help doctors or managers better identify whether the subject has a severe biorhythm disorder and develop a more effective treatment plan or shift schedule.

Methods: 1.Solid phase extraction and the LC MS/MS technique was extensively validated in accordance with relevant guidelines. 2. The Actiwatch Spectrum Activity monitor was used to collect movement ,Illumination information and sleep data from the volunteers in shift work. The Pittsburgh Sleep Scale and Anxiety and Depression Scale were used to measure subjects' sleep and depression scores. The model is evaluated using independent test data and optimized by adjusting XGBoost parameters (such as learning rate, depth of tree, etc.) to improve prediction accuracy and generalization.

Conclusions:1. This LC-MS method was successfully applied to the analysis urine samples and the findings showed a clear correlation between melatonin and cortisol-related metabolites. Longitudinal follow-up of hormone content in morning

urine showed that the levels of cortisol and cortisone showed an increasing trend 1 day after night shift.

2. Multiple hormones in each data were extracted as characteristics and XGBoost algorithm was used to efficiently model urine hormone data. Grid search and K-fold cross-validation were used to verify the accuracy of the model, and the prediction model has an accuracy of more than 80%.

Rapid and highly-efficient intracellular delivery for T-cell genome-editing via a 3D printed microfluidic device

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摘要

The genome editing shown great promise in tumor immunotherapy, yet current existing methods are plagued by laborious viral-based strategies or other approaches that often necessitate lengthy processes and low scalability. Herein, we developed a 3D-printed monolithic electroporation microfluidic device, termed 3D-MED, which allows high-throughput and highly efficient intracellular delivery of functional molecules and cargo/materials into diverse cells with high viability. This method leverages the electroporation effect only by applying low continuous DC voltage (~110V) due to local field amplification with geometric variation. Unlike conventional planar-configured/constructed microfluidic systems, the device design used parallel distribution in three-dimensional space to increase the electroporation scalability of massive flowing cells, reaching up to 10 million cells per minute. The main advantages of electroporation are 2 mL/min throughput, high efficiency (~93%), and cell viability (~90% for primary T cells). Our 3D-MED system demonstrates rapid and efficient electroporation of diverse types of cells including tumor cells and stem cells, as well as T-cells, enabling an alternative microfluidic tool for next-generation genome engineering.

Gestational diabetes mellitus induces neuroinflammation and Anxiety-Depression-Like Behavior in Rat Offspring

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摘要：

BACKGROUND: Gestational diabetes mellitus (GDM) is a common disease during pregnancy with high morbidity, which is associated with a high risk of neurological changes in the offspring. Neuroinflammation plays an important role in the development of anxiety-depression-like behavior. However, the mechanisms involved are unknown. This study aimed to investigate whether GDM induces chronic neuroinflammation in the offspring, resulting in anxiety-depression-like behavior.

METHODS: The gestational diabetes rat model was established by high-fat diets and streptozotocin. 8-week-old offspring were assessed anxiety-depression-like behavior by open field test and modified forced swimming test. Prefrontal cortex (PFC) tissue was observed by H&E staining. The expression level of peripheral and a central inflammation was monitored by ELISA. Differentially expressed genes in the PFC were detected by RNA-sequencing. The results of RNA-sequencing were verified by RT-qPCR, Western blot, and WesTM Automatic Western Blot Quantitative Analysis.

RESULTS: Anxiety-depression-like behavior was observed in the offspring of GDM. It indicated that the PFC neuron was impaired and neuroinflammation was more serious in the GDM offspring, in which the increased concentration of CXCL10 was observed. Moreover, it revealed that the PIK3/AKT pathway was enriched by KEGG analysis. Mechanistically, GDM increased astrocyte activation and facilitated the nuclear translocation of phosphorylated-nuclear factor-κ B (p-NF-κB) p-p65 in the offspring.

CONCLUSION: The study revealed that PFC neuroinflammation might drive anxiety-depression-like behavior in the offspring of GDM rats. These effects may be associated with astrocyte activation and activation of the NF-κB pathway.

sBIPU: Trusted Execution Environments on Brain-inspired Processing Unit

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Brain-inspired Processing Units (BIPU), as a novel computing architecture paradigm, offer advantages such as low power consumption and high compute capability due to computing-in-memory and many-core architecture features. In the era of large language models, BIPU may hold the promise of overcoming the bottlenecks associated with the von Neumann architecture. However, BIPU also introduces new attack surfaces. Sensitive data stored on BIPU can be easily stolen by malicious individuals. Trusted execution environment (TEE) promises strong security guarantee for traditional security-sensitive tasks, e.g., effectively separating hardware resources from untrusted software, ensuring that external attackers cannot access secrets of secure tasks. However, existing TEE systems exhibit inadequate and inefficient support for BIPU. For instance, commercial TEE systems resort to coarse-grained and static protection approaches for BIPU, resulting in notable performance degradation (10%–20%), limited (or no) multitasking capabilities, and sub-optimal resource utilization. In this paper, we present the first comprehensive and secure BIPU architecture, known as sBIPU. Specifically, sBIPU architecture first employs a range-based translation and checking unit (BIPU Guarder), effectively mitigating runtime checking costs while ensuring a strict memory access control. Second, sBIPU defines new attack surfaces for in-BIPU structures, and designs BIPU Isolator to safeguard data on BIPU's scratchpad and ensure the integrity of BIPU's NoC (Network-on-Chip) routing. Third, our system introduces a software module named BIPU Monitor in the secure world, facilitating essential security checks without trusting most software components such as frameworks and drivers. Our prototype, evaluated on FPGA, demonstrates that sBIPU significantly mitigates the runtime costs associated with security checking (from up to 20% to 0%) while incurring less than 1% resource costs.

A network of acetyl phosphate-dependent modification modulates c-di-AMP homeostasis in Actinobacteria

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Cyclic purine nucleotides are important signal transduction molecules across all domains of life. 3′,5′-cyclic di-adenosine monophosphate (c-di-AMP) has roles in both prokaryotes and eukaryotes, while the signals that adjust intracellular c-di-AMP and the molecular machinery enabling a network-wide homeostatic response remain largely unknown. Here, we present evidence for an acetyl phosphate (AcP)-governed network responsible for c-di-AMP homeostasis through two distinct substrates, the diadenylate cyclase DNA integrity scanning protein (DisA) and its newly identified transcriptional repressor, DasR. Correspondingly, we found that AcP-induced acetylation exerts these regulatory actions by disrupting protein multimerization, thus impairing c-di-AMP synthesis via K66 acetylation of DisA. Conversely, the transcriptional inhibition of *disA* was relieved during DasR acetylation at K78. These findings establish a pivotal physiological role for AcP as a mediator to balance c-di-AMP homeostasis. Further studies revealed that acetylated DisA and DasR undergo conformational changes that play crucial roles in differentiation. Considering the broad distribution of AcP-induced acetylation in response to environmental stress, as well as the high conservation of the identified key sites, we propose that this unique regulation of c-di-AMP homeostasis may constitute a fundamental property of central circuits in Actinobacteria and thus the global control of cellular physiology.

Bacillus velezensis HN-2: A Potent Antiviral Agent Against Pepper Veinal Mottle Virus

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Pepper veinal mottle virus (PVMV) belongs to the genus *Potyvirus* within the family Potyviridae and is a major threat to pepper production, causing reduction in yield and fruit quality; however, efficient pesticides and chemical treatments for plant protection against viral infections are lacking. Hence, there is a critical need for discovering highly active and environment-friendly antiviral agents derived from natural sources. *Bacillus spp.* are widely utilized as biocontrol agents for managing fungal, bacterial, and viral plant diseases. Particularly, *Bacillus velezensis* HN-2 exhibits a strong antibiotic activity against plant pathogens and can also induce plant resistance. The experimental subjects employed in this study were *Bacillus velezensis* HN-2, benzothiadiazole, and dufulin, aiming to evaluate their impact on antioxidant activity, levels of reactive oxygen species, activity of defense enzymes, and expression of defense-related genes in *Nicotiana benthamiana*. Furthermore, the colonization ability of *Bacillus velezensis* HN-2 in *Capsicum chinense* was investigated. The results of bioassays revealed the robust colonization capability of

Bacillus velezensis HN-2, particularly in intercellular spaces, leading to delayed infection and enhanced protection against PVMV through multiple plant defense mechanisms, thereby promoting plant growth. Furthermore, *Bacillus velezensis* HN-2 increased the activities of antioxidant enzymes, thereby mitigating the PVMV-induced ROS production in *Nicotiana benthamiana*. Moreover, the application of *Bacillus velezensis* HN-2 at 5 dpi significantly increased the expression of JA-responsive genes, whereas the expression of salicylic acid-responsive genes remained unchanged, implying the activation of the Ja signaling pathway as a crucial mechanism underlying *Bacillus velezensis* HN-2-induced anti-PVMV activity. Immunoblot analysis revealed that HN-2 treatment delayed PVMV infection at 15 dpi, further highlighting its role in inducing plant resistance and promoting growth and development. These findings underscore the potential of *Bacillus velezensis* HN-2 for field application in managing viral plant diseases effectively.

Molecular phylogeny of the Terebellidae (Terebellifomia, Polychaeta) based on the mitochondrial sequences

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Abstract

The mitochondrial genome has been used for phylogenetic analysis of polychaetes, but the classification of polychaetes mostly relies only on morphology, which hinders our understanding of this taxa. Terebellidae is tube worms commonly found in shallow water and deep-sea environment, but our knowledge on its evolutional relationship is limit. In this study, we collected seven species of three subfamilies Terebellinae, Polycirrinae and Thelepinae from Hong Kong and Hainan. Low-coverage sequencing was used to obtain mitochondrial genome and 18S-28S rRNA. The gene order of the two species from the subfamily Thelepinae was different from that of the other five species. Phylogenetic analysis showed that each of the two subfamilies forms a distinct clade, but Polycirrus sp. in Polycirrinae is nested within the Terebellinae group. Additionally, the genus Lanice within Terebellinae is also non-monophyletic. All terebellidae mitochondrial PCGs underwent purification selection, among which atp8 had the smallest purification selection, and cob, cox1, cox2 and cox3 with large purification selection. Codon preference analysis showed that there was a strong preference for GUU、AGU、CUU、GCA、ACA、AGA. PCG nucleotides were used to analyze the genetic distance between the two pairs, and the results showed that cob, cox1, cox2 and cox3 showed lower genetic differences. Overall, our study provides more molecular data for Terebellidae and help us better understand its phylogeny.

High throughput full lifecycle mouse behavior analysis platform

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Abstract: The behavior of mice reflects their physiological and psychological states. The traditional method for analyzing mice behavior is manual observation, which is subjective, time-consuming, and short-term. However, behavioral research requires long-term and high-throughput experiments. The Crop Phenotyping Center of Huazhong Agricultural University has built an intelligent platform for full-life cycle data collection and behavior analysis of mice. Integrating data collection, intelligent management, big data management and analysis, the system can extract about 30 individual and social behaviors of more than 3000 mice throughout their lifecycle. This platform can be used for animal science, neuroscience, pharmacy, and medicine, etc, which provide an efficient platform for them.

The association between dietary habits and phenotypically accelerated aging and the establishment of an accelerated aging interpretable risk prediction model via

SHAP: A cross-sectional study of the NHANES from 2005 to 2018

Author: Houhao Shen,Qidi Zhang, Zhaoyi Bian, Zhengyang Wu

Abstract: Introduction: Few studies have focused on the link between dietary habits, and phenotypically accelerated aging, with limited gender or ethnic diversity in the cohorts studied. Additionally, research on biological aging measurement methods primarily focuses on molecular-level algorithms, hindering practical application of the theory. **Methods:** This study explored the association between diet indices and risk of premature aging using data from the National Health and Nutrition Examination Survey of the United States. Linear regression analysis and machine learning algorithms were employed to construct a model. **Results:** Except for the dietary inflammation index (DII), the other four dietary indicators (AHEI, aMED, HEI-2020, and DASH) were negatively associated with the risk of premature aging. Ten machine learning algorithms was used to establish a risk prediction model, further applying the correlation between dietary habits and premature aging. **Conclusion:** Our study provides theoretical support and an algorithm model for research in the field of factors related to premature aging.

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MiR-1976 inhibits the malignant phenotypes of lung adenocarcinoma by targeting NCAPH 3'-UTR:1627bp-1633bp

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摘要：

Lung adenocarcinoma (LUAD) is a malignancy with an abysmal survival rate. High metastasis is the leading cause of the low survival rate of LUAD. NCAPH, an oncogene, is involved in the carcinogenesis of LUAD. However, the regulation of NCAPH in LUAD remains controversial. In this work, we identified an up-regulation of NCAPH in LUAD tissues. Patients who expressed more NCAPH had shorter overall survival (OS). Furthermore, NCAPH overexpression promoted LUAD cell migration while inhibiting apoptosis. MiR-1976 and miR-133b were predicted to target NCAPH expression by searching TargetScan and Linkedomics databases. Following that, we confirmed that miR-1976 suppressed NCAPH by directly targeting a 7-bp region of NCAPH 3′ untranslated regions (UTR). In addition, increased expression of miR-1976 decreased the proliferation & migration and promoted apoptosis of LUAD cells, and the re-introduction of NCAPH reversed these influences. Furthermore, the xenograft and metastasis mouse models also confirmed that miR-1976 inhibited tumor growth and metastasis in vivo by targeting NCAPH. Finally, we found that MiR-1976 targeting NCAPH blocked the activation of NF-κB. In conclusion, miR-1976 inhibits NCAPH activity in LUAD and acts as a tumor suppressor. The miR-1976/NCAPH/NF-κB axis may, in the future, represent crucial diagnostic and prognostic biomarkers and promising therapeutic options.

Highlights

- MiR-1976 is down-regulated in LUAD tissue and higher miR-1976 is linked to more prolonged OS.
- MiR-1976 impairs cell growth & metastasis, and promotes apoptosis of LUAD by targeting NCAPH.
- MiR-1976, but not mir-133b, targets NCAPH.
- MiR-1976 targets NCAPH 3’-UTR: 1627bp-1633bp.

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Induced Schwann cells/Schwann cell precursors in peripheral nerve regeneration

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Peripheral nerve injury (PNI) is a common and debilitating health problem that affects millions of patients globally. Despite our current understanding of nerve regeneration and advances made in nerve reconstruction, a majority of patients with nerve injury do not regain satisfactory functions after surgical intervention. Hence, new therapeutic strategies are urgently required. Current treatment options for PNI are limited and mostly based on end-to-end suturing (for nerve injuries with a small injury site/gap) and autologous nerve grafting (for nerve injuries with a large gap). However, limitations have been found in autologous nerve grafting such as the restricted supply of donor tissues and the donor-site morbidity. As an alternative approach, artificial nerve guidance conduits (NGCs) in replacement of autologous nerves have been proposed. In this study, we aimed to utilize combinatorial strategies with tissue engineering and cellular induction to develop novel NGCs that provided a biocompatible and favorable microenvironment for peripheral nerve regeneration in large gap injuries. The novel NGCs employed a hybrid hydrogel with micro-patterned surfaces and topographical cues for neurite extension. Additionally, we established stable sources of induced Schwann cells/Schwann cell precursors (collectively termed Schwann cell-like cells) derived from induced pluripotent stem cells (iPSCs), which were embedded to the hydrogel of the NGCs for promoting nerve regeneration. Characterization of these cells and their comparison with primary Schwann cells were performed with single cell RNA sequencing for a comprehensive understanding of

their cellular identities and transcriptomic differences. Furthermore, we also developed an *ex vivo* microfluidic device to assess nerve regeneration after axotomy. With the help of these approaches, our study showed the important roles of Schwann cells, their precursors and different biological and biophysical cues in peripheral nerve regeneration, giving insights into the fabrication of novel NGCs for nerve regeneration in patients with PNI.

The work was supported by the General Research Fund from the Research Grants Council of the Hong Kong Special Administrative Region, China (Ref.: 14120522 and 14118818), and the research fund from Health@InnoHK program launched by Innovation and Technology Commission, the Government of Hong Kong Special Administrative Region, China.

Theaflavine inhibits hepatic stellate cells activation through modulating PKA/LKB1/AMPK/GSK3β cascade and subsequent enhancement of Nrf2 signaling

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Abstract

Activation of hepatic stellate cells (HSCs) constitutes a crucial etiological factor leading to liver fibrosis. Theaflavine (TF) is a characteristic bioactive compound in fermented tea. It is still unclear whether TF suppresses HSCs activation. Here, we found that TF attenuated TGF-β1-induced activation of LX-2 HSCs. TF potentiated Nrf2 signaling in LX-2 HSCs. Knockdown of Nrf2 abrogated TF-mediated resistance to TGF-β1. In addition, TF modulated LKB1/AMPK/GSK3β axis upstream of Nrf2. Inhibition of AMPK or knockdown of LKB1 crippled TF-mediated potentiation of Nrf2. PKA promotes LKB1 phosphorylation. In LX-2 cells, TF increased LKB1/PKA interaction without affecting their contents. Inhibition of PKA abolished TF-mediated potentiation of LKB1/Nrf2 and crippled inhibitory effects of TF on their activation. TF also enhanced direct binding between purified PKA-Cα and LKB1 proteins *in vitro*. Molecular docking indicated that TF showed binding activity with both LKB1 and PKA-Cα proteins. In mouse primary HSCs, TF elevated LKB1/PKA-Cα interaction, boosted LKB1 phosphorylation, potentiated Nrf2 signaling and suppressed their spontaneous activation. Inhibition of PKA or knockdown of LKB1 eliminated TF-mediated induction of Nrf2 signaling and suppression of spontaneous activation of primary HSCs. Furthermore, TF considerably alleviated CCl_4-induced liver fibrosis in mice. In mouse livers, TF increased LKB1/PKA-Cα interaction, upregulated LKB1 phosphorylation and modulated its downstream AMPK/GSK3β/Nrf2 axis. Our findings collectively indicated that TF suppresses HSCs activation. Mechanically, TF elevated LKB1/PKA interaction in HSCs which in

turn upregulated LKB1 phosphorylation and subsequently modulated downstream AMPK/GSK3β/Nrf2 axis.

Key words: Activation of hepatic stellate cells; Theaflavine; PKA; LKB1; Nrf2

Co-infection of Four Novel Mycoviruses from Three Lineages Confers Hypovirulence on Phytopathogenic Fungus Ustilaginoidea virens

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Abstract

Rice false smut caused by *Ustilaginoidea virens* has become one of the most important diseases of rice. Mycoviruses are viruses that can infect fungi with the potential to control fungal diseases. However, little is known about the biocontrol role of hypoviruses in *U. virens*. In this study, we revealed that the hypovirulence-associated *U. virens* strain Uv325 was co-infected by four novel mycoviruses from three lineages, designated Ustilaginoidea virens RNA virus 16 (UvRV16), Ustilaginoidea virens botourmiavirus virus 8 (UvBV8), Ustilaginoidea virens botourmiavirus virus 9 (UvBV9), and Ustilaginoidea virens narnavirus virus 13 (UvNV13), respectively. The *U. virens* strain co-infected by four mycoviruses showed slower growth rates, reduced conidial yield, and attenuated pigmentation. We demonstrated that UvRV16 was not only the major factor responsible for the hypovirulent phenotype in *U. vriens*, but also able to prevent *U. virens* to accumulate more mycotoxin, thereby weakening the inhibitory efects on rice seed germination and seedling growth. Additionally, we indicated that UvRV16 can disrupt the antiviral response of *U. virens* by suppressing the transcriptional expression of multiple genes involved in autophagy and RNA silencing. In conclusion, our study provided new insights into the biological control of rice false smut.

Keywords Mycovirus, Rice false smut, Co-infection, Biocontrol

Research on the correlation between gut microbiota dysbiosis mediated by glyphosate exposure during pregnancy and the developmental abnormalities of ovarian function in offspring

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In recent years, the decline in reproductive capacity among the childbearing population has garnered widespread attention. As the most widely used herbicide globally, the potential impacts of glyphosate cannot be overlooked. Research indicates that glyphosate may negatively affect maternal health and fetal development, particularly during the embryonic period, where environmental exposure could have profound effects on reproductive development. The gut microbiota plays a crucial role in maintaining host health, regulating the immune system, and endocrine functions; its dysregulation can significantly impact the health of both the mother and her offspring. However, the specific effects of glyphosate on reproductive system development remain unclear, and its influence on maternal gut microbiota, as well as the potential mechanisms affecting the reproductive function of female offspring, have yet to be thoroughly explored. Therefore, assessing the specific impacts of glyphosate on reproductive system development and its possible mechanisms has become a cutting-edge topic in current scientific research. Our research indicates that chronic exposure to glyphosate at an environmental dose (5 μg/kg·bw/day) via drinking water can induce maternal intestinal inflammation and gut microbiota dysbiosis. In female offspring, this exposure may lead to abnormalities in ovarian function development, manifesting as abnormal primordial follicle assembly and a reduced number of primordial follicles. Conversely, maternal and female offspring exposed chronically to glyphosate at the same environmental dose (5 μg/kg·bw/day) via subcutaneous injection did not exhibit these phenotypes. This suggests that gut microbiota dysbiosis may mediate the abnormalities in ovarian function development observed in female offspring exposed to glyphosate during pregnancy.

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Inhibitory effect of ginsenoside Rk1 against foam cell formation and atherosclerosis

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Background: Atherosclerotic cardiovascular diseases are prevalent worldwide and are associated with an increased risk of adverse cardiovascular outcomes. Ginseng is a famous traditional Chinese herb medicine and ginsenoside Rk1 is one of its important bioactive ingredients. Our previous study demonstrated that it could improve vascular function by activating peroxisome proliferator-activated receptors in diabetes. Here, we aimed to investigate the potential effect of ginsenoside Rk1 on atherosclerosis.

Methods: ApoE$^{-/-}$ mice were fed by western diet for three months and treated with ginsenoside Rk1 at the dose of 1 mg/kg or 10 mg/kg by tail vein injection every two days during the last 4 weeks. Primary culture of bone marrow-derived macrophages (BMDMs) were obtained from C57BL/6 mice. BMDMs were induced by ox-LDL (50 μg/ml) and co-treated with ginsenoside Rk1 (10 μM or 30 μM) for 24 hours.

Results: Treatment of ginsenoside Rk1 reduced the atherosclerotic plaque in ApoE$^{-/-}$ mice. It also alleviated the plasma levels of triglycerides, total cholesterol, and low-density lipoprotein in mice. Exposure to ox-LDL triggered the transformation of macrophage to foam cell. As shown by Oil Red O staining, co-treatment of ginsenoside Rk1 at 10 μM or 30 μM significantly reversed the change induced by ox-LDL. Meanwhile, the immunofluorescence result indicated that the ginsenoside Rk1 treatment increased the expression levels of Nrf2 and HO-1, which are the markers of special macrophage phenotype Mox in response to oxidative stress. Ginsenoside Rk1 could decrease the levels of inflammatory cytokines such as IFN-γ, MCP-1 and IL-1β in cell supernatant. Lastly, we did the RNA-seq analysis to identify genes involved in the inhibition effect of ginsenoside Rk1 on foam cell formation and atherosclerosis.

Conclusions: The ginsenoside Rk1 could significantly reverse the foam cell formation and atherosclerosis, with reduction of inflammatory cytokines.

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Therapeutic effects of coptisine derivative EHLJ7 on colorectal cancer by inhibiting PI3K/AKT pathway

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摘要：Colorectal cancer (CRC) is the third most common cancer in the world with high mortality rate. EHLJ7 is a quaternary coptisine derivative synthesized by our institute. In this study, the role and mechanism of EHLJ7 on CRC are further elucidated. Using target fishing, colon cancer-associated target screening and molecular docking analysis, PI3K/AKT pathway was selected for the target of EHLJ7 at CRC. Results of Flow cytometry, wound healing assay and transwell migration assay confirmed that EHLJ7 could inhibit migration and apoptosis of colon cancer cells by specifically inhibiting PI3K/AKT pathway in vitro. Xenograft tumor models and a newly established azoxymethane (AOM)/dextran sulfate sodium (DSS)/Peptostreptococcus anaerobiu (P.anaerobius)- induced CRC mouse model are applied to access the anti-cancer action and mechanism of EHLJ7 using westernblot, immunohistochemistry and analysis of exosomes. The key findings in this study are listed as follows: (1) EHLJ7 exerts superior anti-tumor effect with good safety on Xenograft tumor model and CRC model; (2) EHLJ7 exerted its anti-CRC effect by specifically inhibiting PI3K/AKT pathway and apoptosis in vivo and in vitro. In summary, we demonstrated that EHLJ7 exerts therapeutic effect against CRC by PI3K/AKT pathway, which made it possible as a potentially effective compound for the treatment of CRC.

Cooperative and independent functionality of tmRNA and SmpB: A Multifunctional Exploration Beyond Ribosome Rescue

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The trans-translation system, mediated by transfer-messenger RNA (tmRNA, encoded by *ssrA* gene) and its partner SmpB, is responsible for releasing ribosomes stalled on defective mRNA. This study aims to elucidate the cooperative and individual functions of tmRNA and SmpB in pathogenic *Aeromonas veronii*, a serious threat to aquaculture and human health. The results showed that the expression of tmRNA maintains stable throughout the bacterial growth, while *smpB* expression is responsive to nutrient-limited conditions. Both Δ*ssrA* and Δ*smpB* deletions exhibited significantly reduced resistance to multiple environmental stresses compared to the wild type; however, tmRNA individually responded to starvation, and SmpB individually responded to concentration changes of Fe^{2+} and Na^{+} ions. The carbon source utilization of L-asparagine and D-mannitol was consistently reduced in both deletions, while Δ*smpB* showed an independent enhanced ability to utilize β-methylglucoside. Omics analysis revealed that bacteria under nutrient-limited conditions relied more heavily on the trans-translation system. The number of differentially expressed genes in Δ*ssrA* was 1.4 - 2.4 times higher than in Δ*smpB*, while the number of differentially expressed proteins in Δ*smpB* was 14 - 19 times higher than in Δ*ssrA*. KEGG pathway enrichment analysis showed that both strains had altered protein expression in quorum sensing and amino acid metabolism pathways, but SmpB uniquely influenced two-component systems and bacterial

chemotaxis. The findings suggest that the trans-translation system responds to environmental stress by regulating SmpB levels and controls the targets at the protein level. SmpB specifically regulates bacterial chemotaxis at the translational level, and tmRNA controls broader stress responses at the transcriptional level. These results provide important evidence and a key point for further exploration of the multifunction of the trans-translation system, as well as the independent roles of tmRNA and SmpB beyond trans-translation.

Keywords: tmRNA, SmpB, trans-translation, transcriptomics, proteomics, stress response, chemotaxis

Comprehensive Genomic Insights into the Genetic Interrelations of Urological Cancers

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Abstract

Background: Urological cancers, including prostate, testicular, bladder, and kidney cancer, present major health challenges because of their high prevalence and significant impact on patients. Our study aims to assess the causal associations and shared genetic basis among urological cancers.

Methods: Using genome-wide association study (GWAS) summary statistics, we employed Mendelian randomization (MR) and linkage disequilibrium score regression (LDSC) to conduct genetic correlation analysis and causal inference research. Multi-marker analysis of genomic annotation (MAGMA) was utilized to explore single-nucleotide polymorphism (SNP) enrichment at the tissue level. Shared risk SNPs were derived via cross-trait meta-analysis and heritability estimation from

summary statistics (ρ-HESS). We explored the potential risk genes via summary-data-based Mendelian randomization (SMR) and further examined the expression profiles of the risk genes in the tissues.

Results: MR analyses revealed a significant causal relationship in urological cancers such as prostate cancer and testicular cancer (OR=1.91, $P=5.41\times10^{-142}$). LDSC validation confirmed genetic correlations between prostate cancer and testicular cancer ($r_g=0.94$, $P=3.87\times10^{-17}$) and between prostate cancer and kidney cancer ($r_g=0.23$, $P=1.37\times10^{-2}$). ρ-HESS analysis revealed a more evident correlation in local genomic regions between prostate cancer and testicular cancer. Tissue-specific and gene set enrichment analyses revealed common gene expression patterns of prostate cancer and testicular cancer in prostate tissue. Cross-trait meta-analysis revealed 7 shared risk SNPs, with further colocalization and SMR analyses investigating comorbid mechanisms between prostate cancer and testicular cancer and discover 16 potential functional genes in prostate tissue, such as PPP1R14A and CHMP4C.

Conclusion: This investigation elucidates the genetic causality and comorbidity among urological cancers. Our thorough exploration of pleiotropic loci, tissue-specific enrichment, and shared functional genes provides novel insights into their genetic mechanisms' study and future therapeutic advancements.

Keywords: Mendelian randomization; Urological cancer; Linkage disequilibrium score regression; Summary-data-based Mendelian randomization; Colocalization analysis; Comorbidity

Pharmacological intervention increasing hepatic L-aspartate levels counteracts MASLD in mice by targeting ASNS/LKB1/AMPK axis

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Abstract

L-aspartate is a nonessential amino acid involving in tricarboxylic acid cycle (TCA cycle), amplifying hepatic L-aspartate levels is supposed to be a practicable and promising therapeutic approach in treating Metabolic dysfunction-associated steatotic liver disease (MASLD) and liver injury-induced liver fibrosis. However, few compounds have been reported to increase hepatic L-aspartate levels for ameliorating MASLD *in vivo*. Asparagine synthetase (ASNS) catalyzes the conversion of L-aspartate into asparagine, here, we identified a natural molecule, from the compound library (~7133 compounds) using the free energy perturbation (FEP)-based virtual screening strategy. The compound showed strong binding affinity (K_D: 8.8 μM) against recombinant human ASNS and inhibited its enzymatic activity (IC_{50}: 7.1 μM), subsequently increasing cellular L-aspartate levels, thus activating the LKB1/AMPK central metabolic axis and enhancing lipid oxidation, resulted in suppression of lipid accumulation in hepatocytes. Correspondingly, treating compound (20 mg/kg/per 2 days, *i. p.*) in mice for 6 weeks efficiently corrected high-fat and high-cholesterol diet (HFC) induced bodyweight gained, glucose tolerance impairment, insulin resistance, and all the typical manifestations of MASLD, including hepatic steatosis, liver injury, and inflammation. These therapeutics were associated with decreases in ASNS expression levels in livers, leading to increases in hepatic L-aspartate levels, activation of LKB1-AMPK axis, and improvement of mitochondrial oxidation. These data indicate that increasing hepatic L-aspartate level would be a promising

therapeutic strategy in treating MASLD-associated metabolic disease and ASNS would be a novel target for developing anti-MASLD agents.

Nobiletin Ameliorates Endothelial Dysfunction and Oxidative Stress in Diabetes

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Nobiletin is one of the main components of tangerine peel. The aim of this study was to investigate the protective effect of nobiletin on vascular endothelium in diabetes and the underlying mechanisms. For *in vitro* experiments, primary rat aortic endothelial cells (RAECs) were isolated from Sprague Dawley (SD) rats and cultured. C57BL/6J mouse aortas were isolated for *ex vivo* organ culture experiments. Hyperglycemic model was established by stimulation of high glucose (30 mM) for 48 h. Different concentrations of nobiletin were co-cultured with high glucose. In the *in vivo* study, C57BL/6J mice were fed with a high-fat diet (HFD, 60% kcal) for three months to establish diet-induced obesity (DIO) diabetic model. Nobiletin (50 mg/kg/day) was orally administered in the treatment group for 8 weeks. Exposure to high glucose increased oxidative stress, and decreased the protein expressions of phosphorylation of AMPK and eNOS, as well as Nrf2 and HO-1 in RAECs. These led to reduced nitric oxide (NO) generation and elevation of oxidative stress, and thereby impaired the endothelium-dependent relaxations (EDRs) in mouse aortas. The DIO-induced diabetic animal model showed imbalance of glucolipid metabolism, impaired EDRs and elevated oxidative stress in mouse aortas. AMPK/eNOS and Nrf2/HO-1 pathways were downregulated in aortas from DIO mice. Oral administration of nobiletin could at least partially reverse the above damages. In conclusion, the present study demonstrates that nobiletin has a protective effect on endothelial function for the first time and may be a promising agent for the treatment of endothelial dysfunction associated with type 2 diabetes.

Funding: Young Talent Support Project of Guangzhou Association for Science and Technology, QT2024-048

Keywords: Nobiletin; endothelial function; diabetes; oxidative stress

A Compiler for Hybrid Near-Memory and In-Memory Many-Core Architecture

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文章摘要：
Building hybrid systems that incorporate various processing-in-memory (PIM) devices and processing near-memory (PNM) technologies can offer complementary advantages in both efficiency and flexibility, while many-core architectures show great potential in deploying data-centric parallel applications with high performance. Compilers for the hybrid PN/IM architecture are critical for enabling such computing systems to be put into practical use. However, most of the existing neural network compilers for PIM or PNM are optimized from the perspective of an operator, and cannot effectively take advantage of a decentralized core-level dataflow with large on-chip memory access bandwidth. Here, we propose a fullstack System-on-graph Compiler (SongC) framework for many-core architecture, which optimizes the efficiency of the PIM devices and leverages the flexibility of the PNM architectures. SongC establishes multi-level graph abstractions to clarify the critical deployment challenges at different levels and generalizes the standard optimizations, decoupling versatile algorithms and diverse types of hardware. To handle the complexity of many-core resource utilization, we also establish a simulation-compilation interaction flow, including a just-in-time evaluator to boost the scheduling search and an extended Roofline model, referred to as the Palace model, to guide the search. Experiments demonstrate the various optimizations and overall performance of SongC and reveal the capability of strategy exploration.

Study on the flexibility of shoulder joints in people who exercise regularly

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Fitness includes bodybuilding, aerobics, self-resistance and external resistance movements, etc. In recent years, with the development of economy and the enhancement of mass sports awareness, fitness has gradually entered the public field. People who have been engaged in strength training in the gym for a long time often have limited shoulder joint movement, and healthy people think that this is the inevitable consequence of the excessive volume of shoulder muscles. It can be observed that weightlifters also do strength training for a long time, and such movements also require flexibility of shoulder joint, which shows that strength, volume and flexibility can co-exist. Therefore, this paper attempts to add functional training commonly used in weightlifting training as an intervention.

附：

论文题目：长期健身人群肩关节灵活度的研究

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Association of dietary inflammatory potential, systemic immune-inflammation index and ovarian cancer

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Abstract:

OBJECTIVE: The diet inflammatory index (DII) and the systemic immune-inflammation index (SII) are novel inflammatory indicators, which have been reported to be associated with prognosis value in many tumors. However, the relationship between the SII and the prognosis of ovarian cancer is still unclear. Our study aimed to explore the associations of inflammatory factors with the development and prognosis of ovarian cancer from different perspectives.

METHODS: All data in this study were obtained from the NHANES, TCGA and IEU-OpenGWAS project. Weighted logistic regression was used to analyze the associations between inflammatory factors and ovarian cancer incidence. Piecewise linear regression, subgroup and sensitivity analyses were also applied. Three machine learning algorithms were used to predict ovarian cancer. The internal dataset was randomly split into an internal training set (70%) and test set (30%). Training was performed by applying fivefold cross-validation and SMOTE. Subsequently, a MR study was performed using the genome-wide association study (GWAS) summary statistics to identify the causal associations between inflammatory factors and ovarian cancer genes that were highly associated. Primary inverse variance weighted (IVW) and sensitivity analyses were conducted to confirm the robustness of the results. Finally, we used Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO) analyses and constructed a TF-miRNA-hub gene network to present underlying molecular mechanisms.

RESULTS: The highest SII group had higher odds ratios (ORs) for the incidence of ovarian cancer in adjusted models. There was a 162% (156%) increased risk of ovarian cancer incidence per one-unit increment when analyzing DII (SII) as categorical variable (quartiles). Consistent results were also observed when DII was examined as a continuous variable. The results were robust in subgroup and sensitivity analyses. We employed advanced machine learning algorithms to construct an ovarian cancer risk prediction model incorporating the SII index. The area under the curve (AUC) values for the models based on decision tree regression (DT), random forest (RF), and the Catboost algorithm were 0.765, 0.774, and 0.783, respectively. Using GWAS data of 41 inflammatory factors and 20 types of ovarian cancer, a total of 11 inflammatory factors were identified as having causal relationship with the risk of ovarian cancer by IVW. Subsequent GO and KEGG enrichment analysis revealed that cytokine mediated signaling pathways were highly

enriched. Furthermore, 40 related transcription factors and 117 related miRNAs were identified, and a key gene-transcription factor- mi-RNAs regulatory network was established.

CONCLUSIONS: Our study is the first to demonstrate the relationship between SII or DII and ovarian cancer incidence in a large population in the US and further explored the potential regulatory mechanisms at the molecular level.

Key Words: Systemic immune-inflammation index; Ovarian cancer; Diet inflammatory index; Mendelian randomization analysis; Cytokine; mi-RNAs

Development of a PEI-coated SWNTs Nanocarrier for Efficient Delivery of CRISPR/Cas9 in Early Embryos of Litopenaeus vannamei

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摘要：

Cultivation of superior varieties is the key to maintaining the sustainable development of the *Litopenaeus vannamei* (*L. vannamei*) industry. CRISPR/Cas9 technology represents a generation of genetic breeding technology based on gene editing. However, the conventional delivery strategy of CRISPR/Cas9 components could not be used due to the particular physiological traits and practical difficulties of *L. vannamei* embryos. We designed and established polyethylenimine (PEI)-coated nanoparticles with carboxylated SNWTs core to safely deliver CRISPR/Cas9 plasmids into early embryos for target gene editing. The results showed that the transfection efficiency of this strategy was 36%, which was approximately 4-fold higher than the efficiency of the classical lipid transfection method. The transcription factor *Pax6*, which has notable effects on early embryonic eye development, provides clear phenotypic proof for this strategy. Unnatural base alterations were found in up to 25% of transfected embryos. This study establishes a foundation for the application of CRISPR technology in *L. vannamei* and provides an innovative approach for large-scale gene function studies in aquaculture.

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Study on the mechanism of Astragaloside A from Bupleurum on osteoporosis using network pharmacology and molecular docking technology

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Abstract： Osteoporosis (OP) is a global disease characterized by the loss of bone mass and the deterioration of bone microstructure. The main clinical manifestations include bone pain, height reduction, kyphosis, fractures, and mob ility impairment, which significantly increase the morbidity and mortality rates among middle-aged and elderly women,posing a serious threat to their health a nd quality of life.**Objective:**This study explores the potential mechanisms of Sa ikosaponin A (SA) in the treatment of osteoporosis through a combination of n etwork pharmacology and molecular docking techniques.**Methods**: The targets c orresponding to SA were obtained from the SwissTargetPrediction database, wh ile relevant targets for osteoporosis (OP) were acquired from the GeneCards da tabase. A comparison of the protein-protein interactions (PPI) between SA and OP revealed that these interactions play a crucial role in the occurrence, devel opment, and prevention of OP. A common target network was constructed usin g the STRING database, and visualized with Cytoscape 3.10.1 software. Additi onally, GO functional and KEGG pathway enrichment analyses of the intersecti ng targets were performed using R 4.3.1 software. The molecular docking soft ware AutoDockTools 1.5.7 was used to dock the three-dimensional structure of SA (MOL004635) with the STAT3 and IL-6 proteins.**Results:** A total of 100 targets for Saikosaponin A (SA) and 5,741 targets for osteoporosis (OP) were screened, resulting in 63 common targets. The common targets were analyzed using R 4.3.1 software, leading to preliminary enrichment in pathways such a s the Rap1 signaling pathway, Ras signaling pathway, and MAPK signaling pat hway. The potential target pathways were primarily enriched in inflammation, metabolism, environment, cellular processes, biological systems, and diseases.Pro tein-protein interaction (PPI) analysis indicated that STAT3, EGFR, HIF1A, JU

N, BCL2, KDR, PTGS2, IL2, FGF2, and GSK3B play significant roles in protein interactions. Molecular docking was employed for theoretical validation of the network pharmacology findings. After docking SA with STAT3 and IL-6 proteins, it was found that SA exhibited good binding activity with both proteins, suggesting.**Conclusion:**Saikosaponin A (SA) can alleviate osteoporosis by regulating various signaling pathways, including the Rap1 signaling pathway, Ras signaling pathway, and MAPK signaling pathway, as well as influencing biochemical reactions related to inflammation and metabolism, and targeting relevant proteins such as STAT3, EGFR, and HIF1A.

Keywords:Osteoporosis, Saikosaponin A, network pharmacology, signaling pathways, molecular docking, targets.

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KIN supports esophageal cancer progression via resolving noncanonical STING activation induced by R-loop

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Abstract

Targeting DNA damage response is of high efficacy to induce immune activation and improve patient prognosis. However, not all patients get benefit for complexity of DNA damage response compensatory in certain cancer. Here, we report that high expression of DNA damage response genes supports esophageal squamous cancer progress and suppress immune microenvironment. Enriched DNA damage response protein KIN in esophageal squamous cell carcinoma (ESCC) tissues supports DNA damage clearance and escape from apoptosis. Mechanistically, KIN supports R-loop regulator DHX9 recruitment at R-loop site, dealing with DNA damage associated R-loop. KIN deficiency activates STING pathway via NFκB induced by accumulated R-loop and initiates innate immune response. Together, our study identifies KIN as a new R-loop binding protein recruiting R-loop resolute complex and repressing tumor-intrinsic innate immunity.

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Effects of SLC4A4 Overexpression on the Proliferation and Migration of Gastric Carcinoma Cells

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Abstract

Objective: To investigate the effects of SLC4A4 overexpression on the proliferation and migration of gastric carcinoma cells. **Methods:** The BGC-823 cells that had been transfected with SLC4A4 overexpression viral vector were designated as the 'OE' group, those that had been transfected with empty viral vectors were designated as the 'NC' group, and the untransfected BGC-823 cells were designated as the 'Ctrl' group. The impacts of SLC4A4 overexpression on gastric carcinoma cell proliferation and migration were substantiated through the utilisation of CCK-8, EdU, scratch assay, and plate cloning assay. **Results:** A lentiviral vector overexpressing SLC4A4 was constructed and transfected into BGC-823 at a multiplicity of infection (MOI) = 80. After 48 hours, full-field green fluorescent protein expression was observed. qPCR and Western blot confirmed that the expression of SLC4A4 was significantly higher in the OE group than in the Ctrl and NC groups ($P < 0.05$). The CCK-8 and EdU assays demonstrated that the proliferation rate of cells in the OE group was markedly lower than that observed in the Ctrl and NC groups ($P < 0.05$). The scratch assay further confirmed that the migration rate of cells in the OE group was also significantly lower than that in the Ctrl and NC groups ($P < 0.05$). Additionally, the plate cloning assay revealed that the colony formation rate in the OE group was markedly lower than that observed in the Ctrl and NC groups ($P < 0.05$). **Conclusion:**

It has been demonstrated that the overexpression of SLC4A4 inhibits the proliferation and migration of gastric carcinoma cells.

Keywords: SLC4A4, Proliferation, Migration, Gastric Carcinoma

Fund Projects: Guizhou Provincial College Student Innovation and Entrepreneurship Training Program (S202310661037), Project of Postgraduate Research Fund of Zunyi Medical University (ZYK240).

The Relationship between SLC4A4 and the Occurrence and Development of Gastric Carcinoma

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Abstract

Objective: To investigate the expression of SLC4A4 in the development of gastric carcinoma and to provide a theoretical basis for whether SLC4A4 may become a new therapeutic target for treatment. **Methods:** The relationship between SLC4A4 and the development of gastric carcinoma was examined through immunohistochemical (IHC) analysis. The expression of SLC4A4 in adjacent non-carcinomatous tissues and gastric carcinoma tissues, as well as in human gastric carcinoma cells (BGC-823 and SGC-7901) and normal human gastric epithelial cells (GES-1), was evaluated through quantitative polymerase chain reaction (qPCR) and Western blot. **Results:** The IHC results demonstrated that SLC4A4 was markedly expressed in normal gastric mucosal epithelium, with a gradual decline observed in low-grade intraepithelial neoplasia, high-grade intraepithelial neoplasia, early gastric carcinoma, and advanced gastric carcinoma ($P < 0.05$). qPCR and Western blot analyses revealed that the expression of SLC4A4 in adjacent non-carcinomatous tissues was higher than that in gastric carcinoma tissues. Furthermore, its expression was observed to be higher in GES-1 than in BGC-823 and SGC-7901 ($P < 0.05$). **Conclusion:** SLC4A4 exhibits significant differential expression between normal gastric mucosal epithelium and gastric carcinoma. It is highly expressed in normal gastric mucosal epithelium but

shows low expression in gastric carcinoma. Therefore, SLC4A4 can be further studied as a specific target for the diagnosis of gastric carcinoma.

Keywords: SLC4A4, Gastric Carcinoma, Normal Gastric Mucosal Epithelium.

Fund Projects: Guizhou Provincial College Student Innovation and Entrepreneurship Training Program (S202310661037), Project of Postgraduate Research Fund of Zunyi Medical University (ZYK240).

Expression of Nm23 and EMT-Related Proteins in Gastric Carcinoma Tissues

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Abstract

Objective: To determine the expression of Nm23 and epithelial-mesenchymal transition (EMT)-related proteins E-cadherin and N-cadherin in normal gastric mucosal epithelium, intraepithelial neoplasia, highly-to-moderately differentiated gastric carcinoma and poorly differentiated gastric carcinoma. **Methods:** The expression of Nm23, E-cadherin and N-cadherin was evaluated using immunohistochemistry in 20 cases of normal gastric mucosal epithelium, 20 cases of intraepithelial neoplasia, 20 cases of highly-to-moderately differentiated and 20 cases of poorly differentiated gastric carcinoma. **Results:** The expression of Nm23 was significantly decreased in highly-to-moderately differentiated and poorly differentiated gastric carcinoma compared with that in intraepithelial neoplasia and normal gastric mucosal epithelium. Furthermore, the lowest expression was observed in poorly differentiated gastric carcinoma ($P < 0.05$). The expression of E-cadherin was found to be considerably reduced in both highly-to-moderately differentiated and poorly differentiated gastric carcinoma when compared with that detected in intraepithelial neoplasia and normal gastric mucosal epithelium. In addition, the lowest expression was observed in poorly differentiated gastric carcinoma ($P < 0.05$). In contrast, the expression of N-cadherin was markedly higher in highly-to-moderately differentiated and poorly differentiated gastric carcinoma than in intraepithelial neoplasia and normal gastric mucosal epithelium. Moreover, the highest expression was noticed in poorly differentiated gastric carcinoma ($P < 0.05$).

Conclusion: The expression of Nm23 and E-cadherin was found to be notably lower in both highly-to-moderately differentiated and poorly differentiated gastric carcinoma than in intraepithelial neoplasia and normal gastric mucosal epithelium. The expression of N-cadherin was significantly higher in both highly-to-moderately differentiated and poorly differentiated gastric carcinoma than in intraepithelial neoplasia and normal gastric mucosal epithelium, indicating a potential correlation between these proteins and the development of gastric carcinoma.

Keywords: Nm23, E-cadherin, N-cadherin, Gastric Carcinoma.

Fund Projects: Guizhou Provincial College Student Innovation and Entrepreneurship Training Program (S202210661231).

Blended Glial Cell's Spiking Neural Network

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ABSTRACT :

Spiking Neural Networks (SNNs), the third generation of artificial neural networks, have been widely employed. However, the realization of advanced artificial intelligence is challenging due to the dearth of efficient spatiotemporal information integration models. Inspired by brain neuroscientists, this paper proposes a novel spiking neural network - Blended Glial Cell's Spiking Neural Network (BGSNN). BGSNN introduces glial cells as spatiotemporal information processing units based on neurons and synapses, and also provides four new network dynamics connection models which extend the information processing dimension, enhance the network global information integration in the spatiotemporal domain, as well as the plasticity of neurons and synapses. In this paper, a BGSNN application - Sudoku solver is designed and implemented on the "WenTian" neuromorphic prototype. On the Easybrain dataset, the BGSNN solver achieves 100% accuracy, outperforming the same structure SNN solver by 97% at the Evil difficulty level, and has faster converges speed compared with the SOTA Sudoku solver LSGA. On the kaggle dataset, the BGSNN solver achieves over 99.99% accuracy, outperforming the publicly available optimal DNN solver under this dataset by 3.82%. In addition, BGSNN exhibits good parallelism and sparsity, decreasing computation by at least 92.9% compared to serial solvers and reducing sparsity by 88% compared to the equal fully dense DNN. BGSNN improves the expression, feedback, and regulation

capabilities of neural networks while maintaining the advantages of SNN parallel sparsity, making it simpler to implement advanced artificial intelligence.

Choline transporters are required for oligodendrocyte differentiation and myelin sheath formation in postnatal brains

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ABSTRACT: Insufficient oligodendrocyte (OL) myelination has been demonstrated as a factor causing neurodysfunctions in postnatal and adult brains. In principle, upon the onset of differentiation, each oligodendrocyte precursor cell (OPC) must produce more than a 3000-fold membrane to form myelin sheaths within hours. However, the mechanisms underlying the cell membrane synthesis remain largely unknown. Choline is an essential nutrient for lipid metabolism, which is required for cell membrane synthesis and extension. Choline transporters (ChTs) are responsible for choline uptake from extracellular environments. Here, we reported that SLC44A1 and SLC44A5 are the major ChTs specifically expressed in oligodendrocyte lineage cells by single-cell sequencing and analysis. We hypothesized that these ChTs are required for OPC differentiation and myelination. As expected, conditional knockout (cKO) of SLC44A1 or SLC44A5 in OPC inhibited oligodendrocyte (OL) differentiation and myelination in neonatal mice. Further, hypomyelination persists into adulthood in the SLC44A1 cKO but not SLC44A5 cKO brains, which is probably due to vanishing SLC44A5 expression in adult OPCs. Of note, tracing and calculating newly-formed myelin sheaths revealed that the total length of myelin sheaths produced by individual OL was significantly decreased upon SLC44A1 deletion in adult brains. These findings indicate that OL differentiation and myelin sheath formation necessite choline uptake. Consequently, the SLC44A1 conditional knockout mice performed

poorly in the cognition test with anxiety-like behaviors in adulthood compared to the littermate controls. These findings together revealed that choline transport is required for oligodendrocyte myelination and white matter integrity in postnatal brains, implying SLC44A1 and SLC44A5 as potential targets for pro-myelination strategies.

Keywords: choline; choline transporters; myeline; oligodendrocyte; OPC; SLC44A1/5

Decorating Probiotics with A Triggerable and Catalytic Shell for Synergistically Enhanced Colitis Biotherapy

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论文内容

论文题目：Decorating Probiotics with A Triggerable and Catalytic Shell for Synergistically Enhanced Colitis Biotherapy

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摘要:Decorating probiotics with a triggerable and catalytic shell for precise on-demand reactivation in the inflamed colon is crucial for treating colitis.

Here, we developed a simple double-layer coating strategy that endows probiotics with on-demand reactivation and extrinsic catalytic capacity by coating probiotics with a metal-phenolic shell, embedding enzymes in situ within the shell, and applying an external pH-triggerable enteric coating. The functional shell formed rapidly, showed excellent biocompatibility, and protected probiotics from environmental stress. Additionally, the shell innovatively enables the on-demand reactivation of ingested probiotics through sequential degradation in inflamed colon, responding to pH and reactive oxygen species (ROS). This is highly beneficial for both preventing and treating colitis, as it simultaneously addresses its underlying causes by enabling targeted probiotic delivery, scavenging excessive ROS, and modulating gut microbiota. This research established a solid foundation for developing probiotics that can be reactivated on demand while also providing extracellular catalytic functions, representing a powerful strategy for colitis therapy.

精彩节选:In this study, we established a platform capable of on-demand reactivation of probiotics in the inflamed colon while simultaneously eliminating excessive ROS and regulating gut microbiota homeostasis. Probiotics Escherichia coli Nissle 1917 GDMCC 1.3181 (EcN), Lactobacillus paracasei CGMCC 1.2744 (LP), and Bifidobacterium bifidum CGMCC 1.5091 (BB) were sequentially mixed with Fe^{3+} and tannic acid (TA), creating a film on their surface (probiotic@T). The remarkable adhesive peculiarity of TA provided by its pyrogallol and catechol groups can enhance the colonization capacity of probiotics in the intestine. Subsequently, catalase (CAT) and superoxide dismutase (SOD) were embedded into the straticulate shell (probiotic@Te), empowered shell with capabilities of ROS scavenging and inflammation alleviation. To improve the oral probiotic delivery to the colon for reinforcing bacteriotherapy, we further encapsulated probiotic@Te with Eudragit L100-55 (probiotic@TeL), which is a clinically used enteric coating that precipitates in acidic environments and dissolves in the intestine (pH > 6). This coating protects probiotics from acid attacks in the stomach and enables probiotics targeted release in the intestine. Our strategy endows probiotics with triggerable and catalytic nanoshells, which can separate probiotics from

the hash gastric environment and trigger the release of EcN@Te upon delivery to the intestine; then the CAT and SOD embedded within the shells can scavenge excess ROS and simultaneously release probiotics with negligible damage. Dissociated polyphenols can be decomposed and metabolized by microbiota into more active metabolites, representing prebiotic-like characteristics. The therapeutic effect on colitis is further enhanced by the synergistic effect of catalytic therapy, intestinal immunomodulation, and microbiota remodeling (Fig. 1B). Our research demonstrated that EcN@TeL could resist the hostile environment in the digestive tract and target the formation of intestinal ecological niche, effectively preventing and alleviating DSS-induced UC symptoms including weight loss, DAI elevating, colon shortening, ROS overproduction, and restoring the intestinal barrier. Furthermore, the dysbiosis of intestinal flora and the short-chain fatty acids (SCFAs) were rebuilt in the treated mice. This strategy is applicable to different strains such as gut microbes and therapeutic bacteria, and is suitable for implanting with diverse enzymes. We foresee that encapsulating probiotics with responsive and catalytic shells will serve as a versatile method for creating biologically functional probiotics that offer improved bioavailability and enhanced treatment efficacy. We believe that these shell-coated probiotics represent a distinctive tool for various biomedical applications.

The Dynamic Changes in Fecal Microbiota and Sex-Specific Effects in Aged Mice Transplantated with Adipose-Derived Stem Cell

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Abstract

Aging-related obesity has become a global concern, primarily due to declining metabolic levels and chronic inflammation. Research indicates that part of obesity in the elderly is attributed to dysbiosis of the gut microbiota, which affects the integrity of the gut barrier. Adipose-derived stem cells (ASCs) have garnered attention for their tissue repair and immune-modulating properties, and preliminary studies show that ASC transplantation can significantly reduce body weight in aged mice. However, the trends in gut microbiota changes at different time points during transplantation and the impact of sex differences on transplantation responses remain unclear. This study aims to utilize 16S rRNA sequencing to investigate the dynamic changes in gut microbiota composition in mice receiving ASC transplantation at various time points and to analyze the differences in transplantation responses between male and female mice.

USP1 inhibits influenza A and B virus replication in MDCK cells by mediating RIG-I deubiquitination

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Abstract: The post-translational modification and stability regulation of RIG-I play critical roles in promoting IFN-I production and maintaining immune homeostasis. In this study, we found that ubiquitin-specific peptidase 1 (USP1) promotes RIG-I protein stability through deubiquitination, which in turn enhances antiviral immunity through the production of inflammatory cytokines, and inhibits the replication of influenza virus in MDCK cells. In contrast, USP1 knockdown inhibited the deubiquitination of RIG-I, decreased the RIG-I protein level, and significantly increased the influenza virus titer. Meanwhile, inhibition of USP1 expression did not have a significant effect on the proliferation of MDCK cells, suggesting that USP1 could be used as a target gene to establish a vaccine-producing MDCK cell line. The above results provide a more comprehensive understanding of the function of USP1

and the antiviral response mechanism, and provide a theoretical and methodological basis for the screening of target genes for the artificial establishment of high-yield MDCK cell lines for vaccine production.

miR-175 Targets CLDN1 to Inhibit MDCK Cell Adhesion

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Abstract: The Madin–Darby canine kidney (MDCK) cell line constitutes a key component of influenza vaccine production, but its dependence on adherent growth limits cell culture density and hinders vaccine yield. There is evidence that the use of gene editing techniques to inhibit cell adhesion and establish an easily suspended cell line can improve vaccine yield; however, the mechanisms underlying MDCK cell adhesion are unclear. In this study, we used transcriptomics to analyse differentially expressed mRNAs and miRNAs in adherent and suspension cultures of MDCK cells. We found that claudin-1 (CLDN1) expression was downregulated in suspension MDCK cells and that CLDN1 promotes MDCK cell–extracellular matrix adhesion. Additionally, microRNA (miR)-175 expression was upregulated in suspension MDCK cells. Importantly, we demonstrated that miR-175 inhibits MDCK cell adhesion by targeting the CLDN1 3'-untranslated region (UTR). These findings contribute to a more comprehensive understanding of the regulatory mechanisms modulating cell adhesion and provide a basis for establishing suspension-adapted

genetically engineered cell lines. Our work could also facilitate the identification of targets for tumour therapy.

Keywords: MDCK; cell adhesion; CLDN1; miR-175; suspension

SDP: SPIKING DIFFUSION POLICY FOR ROBOTIC MANIPULATION WITH LEARNABLE CHANNEL-WISE MEMBRANE THRESHOLDS

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This work introduces a Spiking Diffusion Policy (SDP) learning method for robotic manipulation by integrating Spiking Neurons and Learnable Channel-wise Membrane Thresholds (LCMT) into the diffusion policy model, thereby enhancing computational efficiency and achieving high performance in evaluated tasks. Specifically, the proposed SDP model employs the U-Net architecture as the backbone for diffusion learning within the Spiking Neural Network (SNN). It strategically places residual connections between the spike convolution operations and the Leaky Integrate-and-Fire (LIF) nodes, thereby preventing disruptions to the spiking states. Additionally, we introduce a temporal encoding block and a temporal decoding block to transform static and dynamic data with timestep T_S into each other, enabling the transmission of data within the SNN in spike format. Furthermore, we propose LCMT to enable the adaptive acquisition of membrane potential thresholds, thereby matching the conditions of varying membrane potentials and firing rates across channels and avoiding the cumbersome process of manually setting and tuning hyperparameters. Evaluating the SDP model on seven distinct tasks with SNN timestep $T_S = 4$, we achieve results comparable to those of the ANN counterparts, along with faster convergence speeds than the baseline SNN method. This improvement is accompanied by a reduction of 94.3% in dynamic energy consumption estimated on 45nm hardware.

Optimization of self-microemulsifying drug delivery system for honokiol by central composite design combined with response surface method

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Abstract: Objective To prepare and optimize honokiol self-microemulsion drug delivery system (HN-SMEDDS) and evaluate its quality. **Methods** Pseudo-ternary Phase Diagrams was used to screen excipients of HN-SMEDDS. On the basis of solubility test and pseudo ternary phase diagram, the particle size of microemulsion was used as the evaluation index, and the HN-SMEDDS prepared under the optimal formulation was optimized by central design-response surface methodology. The structure of the HN-SMEDDS prepared under the optimal formulation was characterized by electrical conductivity method, and the HN-SMEDDS were evaluated in vitro. **Results** The optimal formulation of HN-SMEDDS was: Tween-80 71.54%, PEG200 14.62%, peanut oil 10.56%, castor oil 3.28%. The drug loading capacity is 60 mg/mL. In this system, HN-SMEDDS has good dilution stability between 5 and 400 times, and the dilution of different dispersion media has no significant effect on the particle size of the microemulsion; the average particle size after become dilution in HN microemulsion is (16.83±0.3521) nm, The PDI zeta is 0.189±0.021, and the zeta potential is (-15.53±0.205) mV; it can still form a stable self-microemulsion after being stored for 15 days at -20℃ and room temperature; the structure characterization results show that an O/W microemulsion is formed under this system HN-SMEDDS needs to be diluted more than 3 times; in vitro drug release experiments show that the self-microemulsion prolongs the release time of honokiol

in artificial gastric juice and improves its release in artificial intestinal juice. **Conclusion** The screened HN-SMEDDS have simple preparation process, small particle size and good stability, which can effectively improve the solubility of honokiol in wate and its release in artificial intestinal juice.

Key words: Honokiol；Self-microemusifying drug delivery system；Pseudo-ternary phase diagrams； Central composite design- response surface methodology； Vitro evaluation

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Phycosphere bacterial disturbance of *Saccharina japonica* caused by white rot disease relates to seawater nutrients

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Abstract

In mid-November 2021, there were large areas of white rot disease on cultivated *Saccharina japonica* in Rongcheng City, China, and diseases were undetected on *Sargassum horneri* and *Porphyra yezoensis*. The disturbance direction of bacterial community in the phycosphere after disease outbreak and the relationship with seawater nutrients remain unclear. Here, in situ studies of bacterial community in the non-diseased and diseased areas (Shawo and Dongchu islands) and seawater nutrient levels were carried out. 16S rRNA sequencing showed that the bacterial richness of the studied seaweeds increased in the diseased area. Only in *S. japonica*, *Algitalea* outcompeted abundant primary bacteria with probiotic relationships to the host of the non-diseased area, and dominated in the diseased area (17.6% of the total abundance). Nitrogen and phosphorus levels in seawater were 57.8% and 19.6% higher in the non-diseased area than those in the diseased area, respectively, and were strongly correlated with the phycosphere bacteria at the family level of *S. japonica*. There was no difference in potential pathogenicity between the two areas, while positive signal communications decreased, and nitrogen cycle, chemoheterotrophy, and cellulolysis increased in the diseased area compared to the non-diseased area. Overall, white rot disease caused a structural disturbance in phycosphere bacterial community of *S. japonica* that related to seawater nutrient levels. Enriched degraders and altered bacterial community functions may exacerbate the disease. This evaluation will

provide information for white rot disease management to prevent and mitigate the occurrence of *S. japonica* outbreaks.

Keywords *Algitalea*; *Saccharina japonica*; Seawater nutrient; White rot; 16S rRNA sequencing

Intestine proteomic and metabolomic alterations in dogs infected with Toxocara canis

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Abstract Toxocariasis is an important zoonotic parasitic disease. *Toxocaris canis* adults live and reproduce in the intestinal tract of dogs and other canine hosts, and the infectious eggs are continuously excreted in feces, which causes environmental contamination and has an important public health significance. In this study, TMT proteomic and untargeted metabolomic methods were used to explore the physiological and pathological effects on the intestinal tract of dogs which infected with *T. canis*, and a series of bioinformatics analyses were conducted to identify differentially expressed proteins (DEPs) and differentially expressed metabolites (DEMs). The proteomics results showed that 198 DEPs were mainly enriched in the immune system and signal transduction pathway, and involved in the regulation of the occurrence and development of cancer and infectious diseases. *T. canis* could disrupt intestinal permeability by increasing the expression of proteins such as zinc finger protein DZIP1L and myosin heavy chain 10. Additionally, *T. canis* infection could also inhibit the host immune response by decreasing the expression of MHC-II, NF-κB, DLA and other immune-related molecules. While, the metabolomics results revealed that the expression of oxoglutaric acid, glutamate, d-aspartate, arginine, taurochenodeoxycholic acid and taurocholic acid which participated in tricarboxylic acid (TCA) cycle, glycolysis/gluconeogenesis, bile secretion, biosynthesis of amino acids pathway were significantly decreased. The correlation results of proteomics and metabolomics showed that DEPs and DEMs were mainly co-enriched in bile secretion pathway to regulate intestinal peristalsis. Analyzing DEPs and DEMs will not only provide insights into the mechanisms of host parasite interaction, but also aid in identifying potential targets for therapy and diagnosis, thus setting the groundwork for effectively preventing and managing toxocariasis.

High-throughput and Specific Detection of Microorganisms by Intelligent Modular Fluorescent Photoelectric Microbe Detector

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投稿论文摘要：
It is fundamental to the protection of human health and the improvement of quality of life that food safety is ensured. Governments and consumers around the world are increasingly concerned about food safety, which has emerged as a major global issue. Detecting foodborne pathogenic microorganisms and controlling them is the key to prevent and control foodborne diseases caused by microorganisms. The IMFP (Intelligent Modular Fluorescent Photoelectric Microbe, IMFP) automatic microbial growth monitoring system, in which the photoelectric detection, temperature control, fluorescent probe, and bioinformatics screen are integrated into one platform, was developed and employed into the detection of pathogenic microorganisms. Moreover, a specific medium was also developed that match the use of this system for Coliform bacteria and Salmonella typhi. Together with such system, a limit of detection of 1 CFU/mL achieved for both bacteria, while the specificity can reach 99%. In addition, the IMFP system can detect 256 samples at the same time, which can meet the high-throughput needs of fields for microbial identification and related research, such as the development of pathogenic microbial diagnostic reagents, medical animal husbandry, aquatic drug susceptibility tests, antibacterial sterilization
performance tests and microbial growth kinetics research in fermentation and many fields. In general, thisIMFP system has the merits of high specificity and sensitivity, high-throughput, as well as simplicity to-operate compared to conventional testing, and it has a high potential as a tool for the application of food safety control and many other fields.

Comparative analysis of midgut bacterial communities among three different pathogen infected and non-infected of Aedes aegypti

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Abstract:

The midgut microbiota of the yellow fever mosquito, *Aedes aegypti*, plays a crucial role in the insect's survives, facilitating host digestion, nutrition, and development. The mosquito midgut microbiota can also interfere with pathogen development, impacting susceptibility and transmission of diseases such as yellow fever and *dengue*. In this study, we utilized bacterial soaking to introduce *Escherichia coli*, *Staphylococcus aureus*, and *Beauveria bassiana* into mosquitoes. The midguts of 4th instar larvae and female adult mosquitoes were dissected for high-throughput 16S rDNA sequencing to assess bacterial load and microbiota composition. Our results indicate significant variation in midgut microbial composition depending on the pathogen. Notably, we identified 20 unique genus in the CO_4W group, including *Pedomicrobium* and *Novosphingobium*, *Veillonellaceae*, *Fenollaria* and 7 other families were found in the CO_CW group, while the S_CW group infected with *S. aureus* showed a marked reduction to 14 unique bacterial families. OTUs from S_4W group microbiota were assigned to 194 bacterial, with one mapping to the genus *Elizabethkingia*, which decreased with *S. aureus* injection. Furthermore, at the species level, *B. bassiana* infection assays revealed that bacterial community samples from CK_4W group larval midguts contained a significantly higher proportion of *Elizabethkingia_meningoseptica* (42.9% vs. 0.9%) compared to those from B_4W group larval midguts. Functional content prediction was performed using PICRUSt to infer metabolic capabilities from 16S rDNA data. Our analysis revealed that infections led to significant enrichment in pathways related to Carbohydrate metabolism, Amino acid metabolism and Metabolism of cofactors and vitamins

pathways, suggesting specific adaptations of the microbiota to pathogen presence. Taken together, our study demonstrates that the midgut microbiome composition of *Aedes aegypti* is volatile, influenced by different pathogens infections, and can impact the growth and development of the host.

HSP90 enhances mitophagy to improve the resistance of cardiomyocytes to heat stress in Wenchang chickens

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Abstract: Global warming threatens the survival of humans and animals worldwide, with acute myocardial injury being key factor to heat stress (HS) mortality. As a typical tropical species, Wenchang chickens (WCC) are known for their heat resistance, but the mechanisms by which their cardiomyocytes resist damage are not well understood. Therefore, we are dedicated to elucidating the key mechanisms of WCCs' resistance to HS-induced myocardial injury. The WCCs were divided into the HS survival group (HSS) and the HS death group (HSD) based on whether they survived after exposure to HS. HS caused significant damage in the hearts of WCC and the degree of damage in HSS was lower than that in HSD. Heat stress-induced sudden death is associated with apoptosis, and heat shock response (HSR) and mitochondrial function contribute to variations in heat stress resistance. Additionally, we established the heat-stressed primary cardiomyocytes from Wenchang chickens (PCWs). As a key regulator of the HSR, HSP90 mRNA and protein levels are significantly upregulated in heat-stressed cardiomyocytes. We further confirmed structural and functional damage in mitochondria of heat-stressed cardiomyocytes, as well as the occurrence of mitophagy. Finally, we demonstrated that HSP90 overexpression enhances its interaction with Beclin-1, thereby increasing PINK1/Parkin-mediated mitophagy, and ultimately inhibit the apoptosis of heat-stressed PCWs. However, these changes were reversed by Geldanamycin (GA). This discovery provides new insights and therapeutic strategies for reducing mortality in humans and animals in high-temperature regions around the world, by improving their resistance to heat stress through artificial intervention.

Keywords: HSP90, Mitophagy, Heat stress damage, Cardiomyocytes, Wenchang chicken

Qilong Capsule Regulates Microglia Function and Inhibits Platelet Activation after Multiple Cerebral Infarction by Regulating P2Y12/AC/cAMP Signaling Pathway

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Background Multiple cerebral infarction (MCI) is a common type of ischemic stroke. It can affect people's life or endanger their lives. Qilong capsule (QLC), a Chinese patent medicine made from Buyang Huanwu Decoction (BYHWD), has the effect of "tonifying Qi and promoting blood circulation, removing blood stasis and clearing collateralization", which is suitable for the sequelae of ischemic stroke, such as

multi-infarct dementia (MID). However, its potential mechanism in the analysis of biology has not been fully explored, which will be further explored in this study.

Purpose The aim of this study was to explore the potential mechanism of QLC in MCI and its sequelae.

Methods Male SD rats aged 7-8 weeks weighing 210-230 g were used to MCI model, and QLC and Clopidogrel (CL) were used to intervene. The neurobehavioral effects of QLC on MCI model rats were evaluated by observing body weight, neurological function score, forelimb grip and water maze test. The effects of QLC on neurons and microglia were observed by hematoxylin-eosin (HE) staining, silver staining, transmission electron microscopy and positron emission tomography / computed tomography (PET/CT). The effects of QLC on platelets were observed by platelet aggregation rate and flow cytometry (FCM). Finally, the mechanism was verified by Elisa, immunofluorescence staining and Western blot.

Results Studies have found that QLC improves neurobehavior, forelimb grip, and spatial memory in rats after MCI because QLC improves brain tissue and neuronal damage. QLC can also effectively inhibit the inflammatory response after MCI in rats, we found that QLC can improve microglia and reduce the expression of translocator protein 18 kDa (TSPO). QLC can improve platelet aggregation and reduce the expression of CD62p and CD61, indicating that QLC has a significant anti-platelet aggregation function. At the molecular level, we found that QLC affects the content of cyclic adenosine monophosphate (cAMP) and cyclic guanosinc monophosphate (cGMP), reduces the expression of recombinant purinergic receptor P2Y, G protein coupled 12 (P2Y12) in microglia, and regulates the P2Y12/adenylate cyclase (AC) /cAMP signaling pathway.

Conclusions QLC can ameliorate neuronal necrosis and MID induced by MCI models and has an antiplatelet aggregation effect. QLC has potential application to MID by regulating P2Y12/AC/cAMP.

Halophilic microalga-based circular economy producing functional food by reclaiming high-salinity seafood processing sewage

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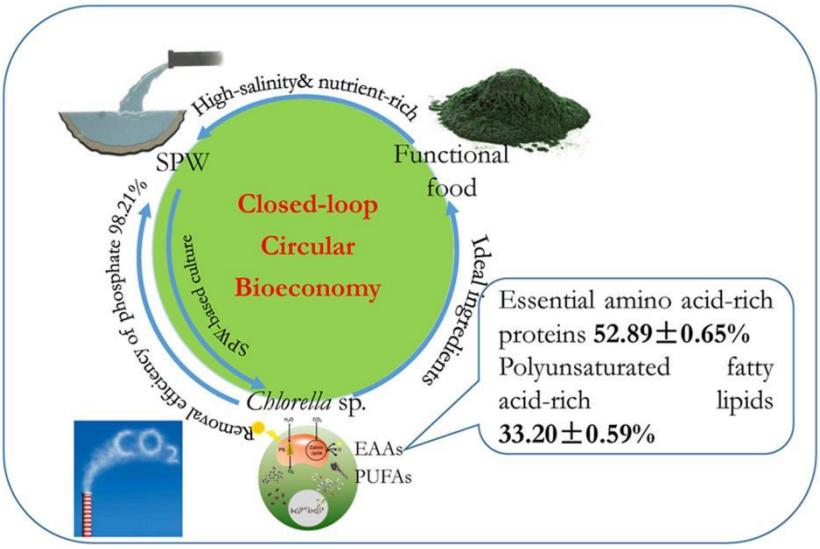
The high-salinity and nutrient-rich feature of seafood processing wastewater (SPW) challenges current treatment technologies. Microalgae-based circular economies offer promising solutions to reduce environmental pollution and increase bioproducts production. In this study, we employed industrial capacity demonstrated halophilic microalga Chlorella MEM25 as a model to demonstrate a closed-loop circular bioeconomy. The approach mutually achieves clean water via the reclamation of high-salinity SPW and the production of valuable bioproducts suitable for functional food. With experimentally and computationally optimized parameters, MEM25 grows robustly in SPW-based culture and produces high amounts of essential amino-acid-rich proteins (52.89 ±0.65%) and polyunsaturated fatty acid-rich lipids (33.20 ±0.59%), which are ideal ingredients for functional food. Moreover, the removal efficiency of phosphate was as high as 98.21%, further demonstrating the advantages of using microalgae to produce functional food and reclaim SPW as an eco-friendly circular model.



Target-based synthesis and activity evaluation of anti-aging compounds

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Ageing and associated diseases are a serious threat to human health and quality of life. Anti-aging drugs are the most effective interventions to improve bodily functions and prolong healthy life span. Currently, a variety of anti-aging mechanisms and compounds have been reported, but the lack of specific anti-aging intervention targets and target-activity-oriented compound structure optimization has severely limited the development of original new anti-aging drugs. The group has long been committed to the discovery of phenotype-based anti-aging active molecules, identification and validation of anti-aging targets, optimisation of compound structures and discovery of new drug candidates. In our previous study, we found that LW18402, a PDE4 inhibitor, had significant in vitro and ex vivo anti-aging activity with glibenclamide, an old glucose-lowering drug, and confirmed that PDE4 and MDH2 are potential anti-aging targets. Accordingly, we carried out the design, synthesis and evaluation of anti-aging compounds targeting PDE4 and MDH2 by bioelectronic isoform substitution, backbone transition and structural biology-guided rational drug design using LW18402 and GBM as lead compounds, respectively, to obtain preferred compounds with well-defined ex vivo and in vivo anti-aging efficacy and good ADME/T properties.

References

[1] Mao Z, Liu W, Huang Y, et al. Anti-aging effects of chlorpropamide depend on mitochondrial complex-II and the production of mitochondrial reactive oxygen species. Acta Pharm Sin B. 2022, 12(2): 665-677.

Continuous high temperature impacts female largemouth bass more: effects on gonadal development and apoptosis

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Abstract:

With the continuously expanding scale of largemouth bass breeding in China, the demand for seedlings continues to increase. World average temperature are increasing, we must study the effects of high temperature on gonad development in largemouth bass and its regulatory mechanisms. Therefore, we simulated the water temperature in Hainan (28℃) to treat largemouth bass, this study observed growth, reproduction, metabolism, apoptosis, and methylation markers in largemouth bass exposed to high-temperature conditions for 28 days. Growth was not affected in male or female largemouth bass. However, the high-temperature exposed females had reduced Growth hormone (GH) and Estradiol (E2) levels and elevated cortisol levels. They also showed upregulated expression of *AR*, *cyp19a*, *igf*, *fshβ*, and *lhβ* in ovarian tissue. The continuous high temperatures increased oxidative stress in females, which corresponded with increases in SOD, CAT, and GSH-Px, likely to counteract the excess reactive oxygen species. Additionally, continuous high temperatures triggered both branches of endoplasmic reticulum stress, indicated by increases in *IRE1* and *ATF6*, leading to upregulation of apoptosis-related genes and subsequent apoptosis of ovarian cells. In summary, sustained high temperature affected ovarian development by altering the expression of hormone and gonad related genes and inducing endoplasmic reticulum stress leading to ovarian cell apoptosis. However, we also found low demethylase activity in the testis, while the whole genome methylation level was high. This result indirectly indicated that sustained high temperature may affect the expression of key genes through methylation, thereby affecting the development of testis and potentially affecting offspring production.

Keywords: High temperature, *Micropterus salmoides*, Gonad, Apoptosis, Methylation

Antifungal Mechanism of Thiolutin Produced by Streptomyces luteireticuli ASG80 Against Phytophthora nicotianae

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Phytophthora nicotianae is a significant pathogen that causes severe damage to a wide range of host crops, infecting more than 255 plant species. Prolonged use of chemical agents not only leads to the development of resistance in pathogens but also contributes to environmental pollution. Therefore, it is essential to explore new approaches to reduce or replace the use of fungicides to effectively prevent agricultural losses caused by *P. nicotianae*. In this study, a novel anti-*Phytophthora* disulfide pyrrolone compound, Thiolutin, was obtained from *Streptomyces luteireticuli* ASG80. Both in vitro and in vivo assays demonstrated that Thiolutin exhibits strong inhibitory activity against *P. nicotianae*, with an EC_{50} value of 0.8266 μg/mL. Transcriptome sequencing (RNA-Seq) analysis revealed that thiolutin treatment significantly downregulated antioxidant activity and energy metabolism in *P. nicotianae*, including antioxidant enzymes and ATP production. Proteomic analysis indicated that the affected pathways primarily involve carbohydrate metabolism, energy metabolism, amino acid metabolism, and ABC transporters. Biophysical and biochemical experiments showed that Thiolutin induces oxidative stress in *P. nicotianae*, inhibits antioxidant enzyme and ATPase activities, and increases cell membrane permeability. Therefore, thiolutin has the potential to serve as a novel eco-friendly fungicide for the control of Phytophthora diseases.

Key words: *Phytophthora nicotianae*; Thiolutin; Fungicide; Proteomics; Transcriptomics

Hexavalent chromium affected eyes development in zebrafish larvae

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Abstract：Hexavalent chromium (Cr(VI)) is an environmental pollutant produced by human activities and industrial production, and its toxicity is an environmental and health problem that needs serious attention. Cr(VI), which is soluble in water, affects the morphology and functional changes of a variety of tissues and organs in fish in the aquatic environment, thus inhibiting normal growth and development of fish, and embryos and larvae are more sensitive to Cr(VI) than adult fish. The visual system is one of the sensitive targets to environmental pollutants in the aquatic environment, and if the visual function is impaired as a result, it will prevent the animal from foraging for food and escaping from danger, which will affect the normal survival of the animal, and there are limited studies on the effect of Cr(VI) on the development of the eye. In this study, we explored the overall effect of Cr(VI) on the zebrafish embryos by investigating the developmental toxicity, eye morphology, reactive oxygen species(ROS) production, apoptosis, histopathology, and gene expression. The results showed that exposure to Cr(VI) led to the reduction of the length and surface area of the eye axis of zebrafish embryos, and induced the production of ROS and apoptosis in the eyes. In addition, histopathological analysis showed that Cr(VI) could cause the pyknosis of retinal cells and the widening of the space between the lens and the retina, which resulted in the damage to the eyes of zebrafish embryos. The qPCR analysis revealed that, in comparison to the control group, the expression levels of genes associated with antioxidative enzymes, apoptosis, retinal cell-specific functions, opsins, and crystallins in zebrafish exposed to Cr(VI) exhibited variable disturbances. Our results demonstrate for the first time that the exposure of Cr(VI) leads to oxidative stress damage and apoptosis as well as abnormal expression of crystallin genes, thereby adversely affecting eye development and individual development.

Keywords：Hexavalent chromium, eyes development, reactive oxygen species, apoptosis

Investigation of the Molecular Mechanisms Underlying the Efficacy of Scheduled Yoga Interventions in Alleviating Insomnia Among Shift Workers

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Abstract:
Shift work disrupts the natural circadian rhythm, leading to sleep disturbances among those working irregular hours. Prolonged insomnia not only precipitates cognitive decline but also triggers negative emotional states, including depression and anxiety. The sedative hypnotics currently administered in clinical settings exert inhibitory effects on the central nervous system, posing addiction risks and significant adverse reactions upon long-term usage.
In recent years, a mounting body of clinical trials and empirical research has endorsed yoga as an adjunct therapy for insomnia relief. Nevertheless, the underlying molecular mechanisms that facilitate yoga's beneficial effects on sleep remain elusive. This study enrolled 60 female volunteers, aged 25 to 45, in a regular 7-day yoga exercise. Participants wore smart monitoring devices to track their exercise and sleep patterns, while completing the PSQI, SDS, and SAS questionnaires. Blood samples were procured from the subjects before and after yoga sessions for high-throughput sequencing analysis.
After yoga intervention, the PSQI scores of shift personnel decreased by 40%, and the depression and anxiety levels of insomnia subjects decreased by 21% and 28%, respectively.Transcriptome sequencing of shift workers with insomnia revealed a significant association between differentially expressed genes pre- and post-yoga intervention and conditions such as non-alcoholic fatty liver disease, coronavirus, and neurodegenerative disorders. We corroborated these sequencing findings at the gene level through in vitro cellular experiments.

Systemic inflammation index partially mediates the association between serum vitamin C and premature aging: a cross-sectional study

This study explores the association between serum vitamin C levels and premature aging, with a focus on the mediating role of the Systemic Inflammation Index (SII). Using data from the NHANES 2003-2006 survey, premature aging was defined as a dichotomous variable, while serum vitamin C was treated as continuous. Multiple covariates, such as age, sex, and BMI, were controlled for. Statistical analyses, including multivariate logistic regression, restricted cubic spline modeling, and mediation analysis, revealed a significant negative correlation between higher serum vitamin C and reduced premature aging risk (OR = 0.50, 95% CI: 0.42-0.58, $P < 0.001$). An L-shaped nonlinear relationship was observed, with higher concentrations of vitamin C providing a protective effect. Subgroup analyses showed the consistency of this relationship across different populations. Additionally, mediation analysis confirmed that SII significantly mediated the effect of vitamin C on premature aging ($P < 0.001$). These findings suggest that serum vitamin C can reduce the risk of premature aging, with SII playing a key mediating role.

题目：Systemic inflammation index partially mediates the association between serum vitamin C and premature aging: a cross-sectional study

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The role of exosomal microRNAs in ovarian cancer progression

Author：Qidi Zhang, Zhaoyi Bian, Houhao Shen

Abstract: Ovarian cancer (OC) is one of the most common gynecological tumors with a high mortality rate, strongly impairing women's health. Identification of new biomarkers and effective targets is important for the diagnosis and precision treatment of OC. Exosomes are a type of cell-derived vesicle that loads proteins, DNA, and RNA and are closely related to cancer onset and progression. microRNAs (miRNAs), a class of noncoding RNAs, can be delivered via exosomes. Exosomal miRNAs function as cancer promoters or cancer suppressors in a variety of cancers. In recent years, an increasing number of studies have investigated the relationship between exosomal miRNAs and OC. In this review, we summarize the roles of exosomal miRNAs in OC proliferation, metastasis, angiogenesis, apoptosis, and the microenvironment, revealing exosomal miRNAs as potential targets for OC treatment.

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Molecular mechanism of virulence regulation in Aeromonas Dhakensis by the two-component system envZ/ompR

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Abstart

Aeromonas dhakensis (*A. dhakensis*) is a ubiquitous pathogen that can infect a variety of freshwater fish, leading to septicemia. Biofilm formation was one of the primary virulence factors in *A. dhakensis*, playing a crucial role in both pathogenicity and adherence to the host. This study aimed to elucidate the role of the *env*Z/*omp*R genes in pathogenicity of *A.dhakensis*. Results demonstrate that deletion of *env*Z/*omp*R genes leads to reduced growth rate and attenuated virulence in animal models. Additionally, the *env*Z/*omp*R genes mutant had decreased growth, motility, ECPase activity, and hemolytic capacity.The LD_{50} value of the mutant was higher than that of the wild-type strain (7.7×10^5 CFU/ml). These data reveal for the first time that *env*Z/*omp*R is associated with the virulence of *A. dhakensis*.

In vivo optical imaging study on the regulation of liver Kupffer cells phagocytosis by exercise training

Authors: Jing Ai, Xiang Yu, Zhihong Zhang*

Abstract: Exercise training pose significant effects to maintaining physical health and balance. Recently, there has been increasing recognition of the detrimental impacts of sedentary behavior and the therapeutic potential of exercise, particularly in cancer treatment. Kupffer cells, which play a crucial role in early tumor clearance and late immune suppression within the immune microenvironment of liver metastasis, have not received sufficient interest and attention in the field of exercise research. In vivo optical imaging, a large-field, long-term, and high-quality imaging methods, which can simultaneously observe the structure of blood vessels and movement activities of immunocyte in abdominal organs without invasive operations, has made great progress and applications in the field of life sciences. Our study unveils a novel mechanism by which exercise regulates and enhances the phagocytosis of Kupffer cells in liver. Using our specific non-invasive in vivo abdominal window optical imaging, we observed the real-time process of Kupffer cells contacting, engulfing, and partially degrading bacterial clusters in the hepatic sinusoids after the fluorescent bacteria entered the bloodstream through a blood borne E. coli infection model. Notably, Kupffer cells in exercised mice exhibited a higher proportion of bacterial contact and phagocytosis. Ex vivo experiments further confirmed these findings, showing that exercise promotes bacterial clearance in both the liver and kidneys. Additionally, using a liver metastasis model, we found that, long-term in vivo imaging revealed that exercise enhances Kupffer cell contact, infiltration, and phagocytosis of metastatic tumor cells during the early stages of metastasis. This phenomenon was consistently observed across three time points and was further validated in ex vivo experiments. Our research findings suggest that exercise training enhances the phagocytic activity of Kupffer cells and plays a pivotal role in early tumor clearance in liver metastasis. This discovery highlights the potential for integrating exercise therapy into clinical treatment of diseases such as cancer in China in the near future.

Keywords: Exercise, Kupffer cells, in vivo Optical Imaging, Phagocytosis, Bacteria, Liver Metastasis.

Preferred presentation (either/oral/poster): Poster

Abstract theme: In vivo optical imaging study on the regulation of exercise training-mediated effects on bacteria infection and liver metastasis

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Genome-wide Association Analysis and Transcriptome Data of Resistant and Susceptible Varieties to Screen Genes Related to Cassava Bacterial Blight

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Abstract

Cassava (2n=36, *Manihot esculenta* Crantz) is the main source of dietary calories for more than 800 million people worldwide. One of the most serious bacterial diseases of cassava is cassava bacterial blight (CBB) caused by *Xanthomonas phaseoli* pv. *Manihotis* (*Xpm*). 266 germplasm were selected for *Xpm* infection and genome-wide association analysis (GWAS). The results showed that a total of 104,395 high-quality SNPs were obtained to create a BLINK model and 25 significant sites were identified through the BLINK model. The resistant and susceptible varieties were screened and the transcriptome expression levels were measured. There were 7764 differential genes among the susceptible varieties before *Xpm* infection, 4258 and 6497 differential genes after 3 and 6 days of *Xpm* infection, respectively. The different expression genes (DEGs) were mainly enriched in biosynthesis of secondary metabolites. The transcription factors with the greatest difference in expression were from ARR-B, AP2-EREBP, bHLH, NAC, and WRKY. Combined with the results of GWAS and transcriptome, the genes that maybe involved in responding to CBB were selected for verification. The function of three *RLCK* genes and *bHLH* transcription factors were proved. After *Xpm* infection, the expression levels of the three *RLCKs* in resistant varieties were significantly higher than those in susceptible varieties. The result of VIGS showed *bHLH66* positively regulates cassava disease resistance, while *bHLH105* negatively regulates cassava disease resistance.

Revealing the Interactions between Tumor Microenvironment-Associated Stromal Cells and Colon Cancer Cells through Single-Cell RNA Sequencing

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Abstract

Background: Colon cancer is one of the most common malignant tumors in the digestive tract. According to World Health Organization statistics, colorectal cancer is the third most prevalent malignant tumor, accounting for about 10% of all cancer cases. It is also the second leading cause of cancer-related deaths globally, with the proportion of colon cancer increasing year by year. The development of new treatment strategies for colon cancer requires a thorough understanding of the cancer cells and microenvironment of colon cancer.

Methods: We conducted single-cell RNA sequencing (scRNA-seq) on three primary colon cancer tissues from three untreated colon cancer patients and two adjacent normal tissues. Characterization of the transcriptomic landscape of single cells and ligand-receptor-based intercellular communication networks was conducted.

Results: Ultimately, we identified a total of 46,528 single-cell transcriptomes, with 18,867 (40.5%) derived from tumor tissues and 27,661 (59.5%) from adjacent normal tissues. Considering that colon cancer often originates from epithelial cells, we subdivided them and observed significant heterogeneity. After annotating cancer cells, we analyzed their potential evolutionary trajectories. Additionally, by comparing differences between tumor and normal groups, we found a significant increase in the proportions of fibroblasts, endothelial cells, and mural cells in the tumor group, indicating heterogeneity. Further analysis of the relationship between these three types of stromal cells and tumors revealed that the key interaction APP_SORL1 may be crucial for stromal cells to influence processes such as tumor cell proliferation.

Conclusions: In conclusion, our research provides valuable resources for uncovering the heterogeneity of colon cancer and the functions of stromal cells in the tumor microenvironment, which will aid in clinical diagnosis and the development of new treatment strategies.

Vagus nerve stimulation delays allograft immune rejection

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Vagus nerve stimulation (VNS) is a neuromodulation therapy that stimulates the vagus nerve through modalities such as electrical stimulation. VNS has been reported to inhibit the development of inflammatory and autoimmune diseases such as inflammatory bowel disease and arthritis. However, the role of VNS on immune rejection has not been fully explored. Allogeneic transplantation is a crucial treatment for organ failure, but the long- term survival of allografts is challenging due to immune rejection. Thus, we investigated the impact of VNS on allograft immune rejection.

We first verified the effectiveness of VNS by a reduction in heart rate. Next, we assessed the role of VNS in a mouse allograft model. Mice in the VNS group underwent electrical stimulation, and mice in the Sham group underwent sham surgery as a control. We found that VNS significantly prolonged the median survival time of grafts compared with Sham. Next, H&E and immunofluorescence staining were used to detect histopathologic changes at the graft sites. Sham had graft necrosis and massive inflammatory cell infiltration, while VNS had less inflammatory cell infiltration. Further, VNS reduced the number of T cells and macrophages at the graft site compared with Sham.

In summary, VNS delayed allograft rejection, which may be related to the reduced number of T cells and macrophages at the graft site. This study extends the potential applications of VNS while providing new therapeutic strategies for allograft rejection.

Effects of Personal Exercise Intervention on the Plasma Glucose of Prediabetic Subjects

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Abstract: Objective To investigate the different effects of personal exercise and group exercise intervention on the plasma glucose of prediabetic subjects and provide practice and theoretical basis for prevention diabetes by exercise. Methods 90 prediabetic subjects were randomly divided into 3 groups, the control group (CG), the group exercise intervention (GI) and the personal exercise intervention (PI), 60～70% HRmax, 3/week, 50 min. The indexes related to plasma glucose were measured before exercise, exercise for 12 weeks, and exercise after 24 weeks. Results (1) Compared with the CG, the plasma glucose, triglyceride (TG) and HDL were significantly decreased after 12-week exercise ($P < 0.01$). (2)The total cholesterol of the personal exercise intervention (PI) were significantly decreased compared with that of the group exercise intervention (GI) ($P < 0.01$). (3) The personal exercise intervention is more helpful to formation exercise habits than the group exercise intervention. Conclusions The plasma glucose could be decreased in prediabetic subjects by exercise. Compared with the group intervention, the subjects could formation exercise habits after the personal exercise intervention. Therefore, the abnormal glycometabolism could be improved by the personal exercise intervention.

TLR8 in the Trigeminal Ganglion Contributes to the Maintenance of Trigeminal Neuropathic Pain in Mice

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Abstract

Trigeminal neuropathic pain (TNP) is a significant health problem but the involved mechanism has not been completely elucidated. Toll-like receptors (TLRs) have recently been demonstrated to be expressed in the dorsal root ganglion and involved in chronic pain. Here, we show that TLR8 was persistently increased in the trigeminal ganglion (TG) neurons in model of TNP induced by partial infraorbital nerve ligation (pIONL). In addition, deletion or knockdown of Tlr8 in the TG attenuated pIONL-induced mechanical allodynia, reduced the activation of ERK and p38-MAPK, and decreased the expression of pro-inflammatory cytokines in the TG. Furthermore, intra-TG injection of the TLR8 agonist VTX-2337 induced pain hypersensitivity. VTX-2337 also increased the intracellular Ca^{2+} concentration, induced the activation of ERK and p38, and increased the expression of pro-inflammatory cytokines in the TG. These data indicate that TLR8 contributes to the maintenance of TNP through increasing MAPK-mediated neuroinflammation. Targeting TLR8 signaling may be effective for the treatment of TNP.

论文题目：TLR8 in the Trigeminal Ganglion Contributes to the Maintenance of Trigeminal Neuropathic Pain in Mice

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Matrine disrupts Nrf2/GPX4 antioxidant system and promotes hepatocyte ferroptosis

Matrine (MT) is an alkaloid isolated from Sophora flavescens with various bioactivities and is widely used clinically. However, the broader its clinical use, the greater its toxicity concerns. We investigate the role of ferroptosis in MT-induced liver injury caused by an imbalance in the antioxidant pathway. Our results showed that MT could cause pathological changes in liver tissues and lead to a significant reduction in L02 cell viability. MT also reduced superoxide dismutase (SOD) and glutathione (GSH), increased malondialdehyde (MDA), reactive oxygen species (ROS), and lipid peroxidation levels, and disrupted iron homeostasis, leading to ferroptosis. In addition, MT decreased the protein levels of FTH, Nrf2, xCT, GPX4, HO-1 and ferroptosis suppressor protein 1 (FSP1) and increased the protein levels of TRF1 and DMT1, characteristic indicators of ferroptosis. Interestingly, the cytotoxic effects of MT were alleviated by ferroptosis inhibitor, Nrf2 agonist, or selenium supplementation. These results revealed that MT triggers hepatocyte ferroptosis by inhibiting the Nrf2/GPX4 antioxidant system.

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Biomimetic Antithrombotic Tissue-Engineered Vascular Grafts for Converting Cholesterol and Free Radicals into Nitric Oxide

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Key words: tissue-engineered vascular grafts, cholesterol oxidase, L-Arginine, nitric oxide, antithrombotic

Introduction: Small-diameter tissue-engineered vascular grafts (sdTEVGs) are essential materials used in bypass or replacement surgery.[1] However, their application efficacy is limited because of patency rates, especially under hyperlipidemia. In such cases, a practical and reliable strategy for transforming "harmful" substances into "beneficial" factor at early transplantation stages is presented, that have good antiplatelet and antithrombotic functions after transplantation in hyperlipidemic model.

Materials & Methods: AuNPs were modified on the collagen-containing acellular blood vessels by biomineralization.[2] Dithiobis -N-succinimidyl-propionate (DTSP) was then used to efficiently immobilize ChOX and Arg via covalent bonding. After the modification, AuNP-ChOX-Arg coated sdTEVGs were then grafted into the left common carotid arteries of hyperlipidemic rats through the vascular anastomosis.

Results & Discussion:

The cholesterol oxidase modified on the surface of blood vessels can effectively convert cholesterol into H_2O_2, which then reacts with L-Arg to generate NO (Fig. 1).[3] In vitro experiments have found that modified sdTEVGs with cascade reactions can generate NO and inhibit platelet adhesion, thereby inhibiting the formation of thrombosis. In vivo studies have shown that the blood flow velocity and patency rate of sdTEVGs modified with cascade reactions are significantly higher than those of the control group after grafting for 60 days, and the vascular endothelialization can be observed.

Conclusions: The study describes a biomimetic antithrombotic sdTEVG developed by incorporating cholesterol oxidase and arginine into biomineralized collagen–gold hydrogels on an sdTEVG surface. The results showed that strategy converts cholesterol into nitric oxide through a cascade reaction with good antiplatelet and antithrombotic functions,[4] thus providing a new method for constructing sdTEVGs in clinical transplantable vascular replacements that will simultaneously inhibit thrombosis whilst promoting endothelialization.

References

Activation of $GABA_BR$ attenuates intestinal injury by modulating polarization and autophagy of Enteric glial cells

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Abstract

Enteric glial cells (EGCs) exhibit plasticity to maintain intestinal homeostasis by regulating cellular functions in pathological conditions such as inflammation or bacterial infection, but the exact mechanisms remain to be further elucidated. The γ-aminobutyric acid (GABA) signaling system attenuates brain damage by regulating glial cell funtion. However, little is known about the roles of GABA signaling in intestinal injury. The present study aimed to investigate the effects and mechanisms of EGCs polarization and autophagy mediated by GABAB receptor ($GABA_BR$) in intestine inflammation. We established lipopolysaccharide (LPS)- or Enterotoxigenic *Escherichia coli* K88 (ETECK88)-induced inflammation models in mice intestine and EGCs to explore the role of EGCs in the regulation of intestinal homeostasis. The results showed that the application of GABA significantly repressed the shedding of intestinal mucosal epithelial cells and inflammatory cell infiltration, inhibited the expressions of proinflammatory factors, including granulocyte colony-stimulating factor and granulocyte-macrophage colony stimulating factor, and enhanced the levels of anti-inflammatory cytokines IL-4 and IL-10, indicating that GABA could alleviate enteritis in mice. This observation was further supported by transcriptome sequencing, revealing a total of 271 differentially expressed genes, which exhibited a marked enrichment of inflammatory and immune-related pathways, alongside a prominent enhancement of $GABA_BR$ signaling following GABA administration. EGCs exposed to LPS acted as E1 phenotype expressing immune-related molecules including CD80, MHC II, and iNOS, whereas $GABA_BR$ activation strongly promoted EGCs polarization into E2 phenotype, mainly expressing Arg1 and CD206. Notably, activation of $GABA_BR$ mitigated intestinal damage through facilitating EGCs to

transform into E2 phenotype and inhibiting NF-κB pathway in LPS-induced mice. Next, we observed alterations of EGCs phenotype and autophagy in both mice intestine and EGCs infected with ETECK88. Interestingly, $GABA_BR$ activation notably increased Beclin 1 and LC3 levels, thus promoting autophagy activation and enhancing antimicrobial responses for EGCs against ETECK88 infection. Furthermore, myeloid differentiation factor 88 (MyD88) was indispensable for the activation of EGCs autophagy, which was proved on the base of inhibition or overexpression of MyD88. These data indicate that $GABA_BR$ could mitigate intestinal injury by modulating EGCs polarization and autophagy pathways to attenuate the inflammatory response and resistance to bacterial infection, which offer important targets for developing new treatments of intestinal diseases.

Keywords: Intestinal inflammation, Enteric glial cells, $GABA_BR$, Polarization, Autophagy

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Neuromorphic Computing Platform "WenTian I" and Engneering Applications

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Abstract—AI applications tend to have high demands on computation and energy. However, the benefits obtained from advanced semiconductors to achieve high performance are no longer sufficient. There are trends to develop neuromorphic computing platforms to overcome these challenges. However, progress in this direction has been sluggish due to the lack of superior engineering applications powered by spiking neural networks. Here, this paper proposes and demonstrates a general region traffic lights self-adaptive control neuromorphic system to address this issue. First, this paper integrates spatial topological parallels between traffic networks and spiking neural networks, as well as temporal pattern similarities between traffic flows and spike trains, to develop a regional traffic self-adaptive control spiking neural network, which is distinguished by being training-free and possessing short-term memory and prediction abilities. Second, this paper fabricates a regional traffic lights control system based on the neuromorphic platform 'WenTian I'. In a real-world urban traffic scenario involving 774 traffic lights, the proposed system outperforms other GPU-driven neural network systems in terms of traffic performance, memory occupation, and energy efficiency. This work demonstrates that spiking neural networks, leveraging specialized topologies, can surpass the performance of existing methods even under sparse network connections, and the integrated system

with neuromorphic computing platforms holds immense cost-effective potential for engineering applications.

Index Terms—Neuromophic Computing Platforms; Self-Adapative Traffic Control; Cost-Effective; Engineering Applications;

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Haematococcus Pluvialis Improves Renal Fibrosis Caused by Urinary Tract Obstruction by Restoring Mitochondrial Dysfunction

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Renal fibrosis resulting from urinary tract obstruction is a crucial pathological manifestation in chronic kidney disease, accompanied by EMT and abnormal mitochondrial function HP is a type of freshwater unicellular green algae that is abundant in natural antioxidants, including astaxanthin, unsaturated fatty acids, etc. Recent studies have demonstrated that HP has multiple biological activities, such as anti - inflammation, anti - oxidation, and immune regulation. The aim of this paper is to explore whether HP can ameliorate renal fibrosis caused by urinary tract obstruction by rectifying mitochondrial dysfunction and improving the EMT process. Through in vivo experiments, we observed that HP can reduce ECM deposition and alleviate renal cortical injury in a rat renal fibrosis model induced by UUO. In vitro experiments showed that HP can improve the EMT process and mitochondrial dysfunction induced by TGF - β1 in HK - 2. Moreover, HP can restore mitophagy by regulating the PINK1/Parkin signaling pathway, thereby reversing HK - 2 fibrosis induced by TGF - β1. Additionally, in this paper, a rat and HK - 2 renal fibrosis model with AST intervention was used, and it was found that HP had a better effect than AST at the same dose. In conclusion, we found that HP inhibits the pathological process of renal fibrosis caused by urinary tract obstruction by improving ECM deposition, renal cortical injury, the EMT process, and mitochondrial dysfunction. These results imply that HP can be developed into a functional food for improving renal fibrosis.

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Infection with SARS-CoV-2 can cause pancreatic impairment .

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ABSTRACT

Evidence suggests associations between COVID-19 patients or vaccines and glycometabolic dysfunction and an even higher risk of the occurrence of diabetes. Herein, we retrospectively analyzed pancreatic lesions in autopsy tissues from 67 SARS-CoV-2 infected non-human primates (NHPs) models and 121 vaccinated and infected NHPs from 2020 to 2023 and COVID-19 patients. Multi-label immunofluorescence revealed direct infection of both exocrine and endocrine pancreatic cells by the virus in NHPs and humans.Minor and limited phenotypic and histopathological changes were observed in adult models. Systemic proteomics and metabolomics results indicated metabolic disorders, mainly enriched in insulin resistance pathways, in infected adult NHPs, along with elevated fasting C-peptide and C-peptide/glucose ratio levels. Furthermore, in elder COVID-19 NHPs, SARS-CoV-2 infection causes loss of beta (β) cells and lower expressed-insulin in situ characterized by islet amyloidosis and necrosis, activation of α-SMA and aggravated fibrosis consisting of lower collagen in serum, an increase of pancreatic inflammation and stress markers, ICAM-1 and G3BP1, along with more severe glycometabolic dysfunction. In contrast, vaccination maintained glucose homeostasis by activating insulin receptor α and insulin receptor β. Overall, the cumulative risk of

diabetes post-COVID-19 is closely tied to age, suggesting more attention should be paid to blood sugar management in elderly COVID-19 patients. The article was highly praised by Professor Alexander Kleger, an international expert in the field of pancreas, as "This study represents a significant milestone in understanding th interplay between COVID-19 and metabolic disorders such as diabetes."

Electroacupuncture improves symptoms of depression with gastric dysfunction by modulating cellular autophagy via BNST GABA neurons

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Gastric dysfunction is very common in depressed patients, and the coupling mechanism between the brain and the stomach is a key point in its occurrence. Electroacupuncture (EA) can act on ‘form’ (i.e., physical level) and ‘spirit’ (i.e., mental-emotional level) at the same time in the treatment of negative emotions and gastrointestinal co-morbidities, realising the therapeutic effect of ‘form-spirit co-medication’. However, the neural mechanism is still unclear.

In this study, we established a mouse model of depression through chronic unpredictable stress (CUMS), focusing on the potential impact of the specific modulation of gamma-aminobutyric acid (GABA)ergic neurons in the bed nucleus of the stria terminalis (BNST) on depressive-like behaviours and concomitant gastric dysfunction. To further reveal the specific role of BNST GABAergic neurons in regulating stress responses and depressive pathology, we employed chemical genetics techniques to achieve specific activation or inhibition of these neurons. Subsequently, transcriptomics gene sequencing, a high-throughput technique, was integrated to comprehensively resolve the dynamics of gene expression in the stomach of the CUMS mouse model after receiving electroacupuncture (EA) intervention. Electrophysiological techniques were also incorporated to directly monitor the changes in the electrical activity of BNST GABAergic neurons in response to EA and how these changes affected the overall behavioural phenotype of the mice, particularly depression-like behaviour and gastric function. The experimental results showed that EA reduced depression in CUMS mice by activating BNST GABA neurons, and inhibited excessive autophagy in gastric cells, possibly through the modulation of BNST, thus improving the gastric dysfunction induced by depression. This may be one of the ways for EA to realise the ‘form-spirit co-management’.

This finding not only enriches our understanding of the therapeutic mechanisms of EA, but also deepens our understanding of the mechanisms that regulate the neural-gastrointestinal axis.

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Haematococcus pluvialis regulates mitochondrial inflammation cGAS-STING pathway to improve stomatitis

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Oral mucositis (OM) is a chronic inflammatory disease that seriously affects the oral function and quality of life of patients. In the present study we examined the protective effects of *Haematococcus pluvialis* (*H.pluvialis*) on oral mucositis induced by lipopolysaccharide (LPS) in Human Oral Keratinocytes cells (HOKs) and 5-fluorouracil (5-FU) in Male Sprague–Dawley rats, aimed to investigate whether *H.pluvialis* could ameliorate the pathological progression of OM by changining the permeability of mitochondrial membran, and activating the cGAS-STING signaling, which is a pivotal mitochondrial inflammatory system, to strengthen mitochondrial function and diminish levels of inflammatory factors. The effect of *H.pluvialis* on oral were investigated by observing the histopathological morphological changes of oral mucosa, the level of inflammatory factors in rats, detecting the changes of Tight junction protein (Occludin, ZO-1) and signaling pathway proteins (cGAS, STING, TBK1). To evaluate epithelial leakage, mitochondrial morphology, mitochondrial permeability, mitochondrial membrane potential (MMP) and mitochondrial reactive oxygen species (mtROS) of HOKs induced by LPS. The results showed that compared with the control group, nail spikes in the oral mucosal tissue of rats in the model group gradually flattened or even disappeared, epithelial atrophy, lamina propria thickening, inflammatory factor levels significantly increased, mitochondrial inflammatory cGAS-STING signaling pathway was activated and tight connections were destroyed. Compared with the model group, *H.pluvialis* treatment group significantly recovered the epithelial spike process and improved the reduction of excess ROS, MitoSOX,

MMP and the increase of MPTP in LPS-induced HOKs. Further research results showed that *H.pluvialis* group decreased the level of inflammatory factors, up-regulated the expression of Occludin and ZO-1 proteins, and promoted the distribution of Occludin and ZO-1 proteins on cell membrane.The study found that *H.pluvialis* may ameliorate OM damage by improving mitochondrial dysfunction, reducing oxidative stress levels, and reducing the release of inflammatory cytokines, suggesting that *H.pluvialis* could be developed for a functional food for oral mucosal barrier repair.

Identification of two transcriptional regulators underlying aroma and the increase of rice fragrance without yield penalty

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Aromatic rice is globally favored for its distinctive scent, not only increasing nutritional value but also enhancing economic importance. However, apart from 2-acetyl-1-pyrroline (2-AP), the metabolic basis of aroma remains elusive, and the genetic underlying of the accumulation of fragrance metabolites are largely unknown. Here, we revealed 2-AP and fatty acid-derived volatiles (FAVs) as key contributors to rice aroma. In addition, we identified two regulatory genes in determining the natural variation of these fragrance metabolites. We demonstrated that OsAROMA1, a WRKY transcription factor that negatively regulated *OsBADH2*, which enhanced both 2-AP content and superior agronomic performance. We also revealed OsAROMA2, a NAC transcription factor that negatively regulated FAVs through LOX pathway, and the knockout of it resulted in the over-accumulation of grain FAVs without yield penalty. Our findings provide a compelling example of deciphering the genetic regulatory mechanisms underlying rice fragrance and pave the way for the creation of aromatic rice varieties.

Keywords: aromatic rice; volatilome; natural variation; metabolic regulation

A decellularized optic nerve scaffold grafting combined with electroacupuncture enhances the repair of the long segment median nerve defect in rats.

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Long segmental nerve defect is the most serious type of Peripheral Nerve Injury (PNI). Although the autologous nerve transplantation is regarded as the “gold standard” to repair such injury, its application is limited due to the limited source of donor nerves and the loss of nerve function in the donor area. In this study, we first prepared a porcine decellularized optic nerve (DON) scaffold, which contains many naturally straight oriented channels and molecules facilitating nerve regeneration. And then the DON bridged the defected median nerve and combined with electroacupuncture treatment to explore the efficacy and potential mechanism. The results showed that the combination therapy of DON graft and electroacupuncture could significantly promote the survival of damaged neurons and the long-distance regeneration and myelination of the defected median nerve fibers along the straight channel of DON, together with the regenerated nerve fibers re-innervating the distal target muscle, and thus further promote the recovery of motor sensory function in the injured forelimb. We also preliminarily found that the activating of NT3/TrkC signal pathway was one of the molecular mechanisms how electroacupuncture promote the regeneration of peripheral nerve. Therefore, this study suggests that the combination of traditional electroacupuncture therapy and novel biomaterial transplantation provides a new therapeutic strategy for long segment defect of PIN.

Glutathione S-transferase regulates oxidative stress in *Megalurothrips usitatus* in response to environmental stress

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Abstract

The escalating environmental pollution, coupled with the degradation of the ozone layer, has led to an increase in ultraviolet radiation (UV) at the Earth's surface. There is also a growing accumulation of pesticide residues in the environment. These stressors are exerting a profound impact on insect populations. When insects are subjected to adverse environmental stressors, their antioxidant enzymes can quickly respond with appropriate feedback adjustments, facilitating their adaptation to environmental changes. Glutathione S-transferases (GST), integral members of a multifunctional supergene family in insects, are pivotal in countering environmental stress and detoxifying chemical agents. Through transcriptomic screening and RT-qPCR, this investigation identified *MuGSTs1* as a gene whose expression is significantly altered under UV stress. The application of RNAi confirmed the gene's function in managing oxidative stress induced by UV and lambda-cyhalothrin. The research demonstrated that *Megalurothrips usitatus*, the *M. usitatus* caterpillar, adapts to these stressors by modulating the activity of antioxidant enzymes, thereby exhibiting a robust adaptability to UV light and lambda-cyhalothrin exposure.

Experimental silencing of *MuGSTs1* has been shown to impair the *M. usitatus'*s oxidative stress management, resulting in accelerated cellular apoptosis and an increased susceptibility to lambda-cyhalothrin, with sensitivity being augmented by a factor of 2.89. These findings provide a theoretical framework for understanding the adaptive mechanisms of insects to environmental stress.

Key words: *Megalurothrips usitatus*; Glutathione-s-transferase; Ultraviolet radiation; lambda-cyhalothrin; Antioxidant enzymes; Oxidative stress

ACACA reduces lipid accumulation through dual regulation of lipid metabolism and mitochondrial function via AMPK-PPARα-CPT1A axis

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Abstract

Non-alcoholic fatty liver disease (NAFLD) is a multifaceted metabolic disorder, whose global prevalence is rapidly increasing. Acetyl CoA carboxylases 1 (ACACA) is the key enzyme that controls the rate of fatty acid synthesis. Hence, it is crucial to investigate the function of ACACA in regulating lipid metabolism during the progress of NAFLD.Here, we induced models of NAFLD in mice at different time points (2W, 12W, and 20W), and dynamically analyzed RNA-seq data to attempt to accurately identify genes involved in the occurrence and development of NAFLD. In addition, this study characterizes that the effects of ACACA in vitro. Based on a PAOA-induced lipid accumulation cell model, the expression of ACACA was inhibited using siRNA or CMS-121 inhibitors to examine its effects on mitochondrial dysfunction, oxidative stress and lipid metabolism.

Conclusion

1. Studies both in vivo and in vitro revealed that the expression levels of ACACA protein and mRNA were increased in the model of lipid accumulation.

2. Targeting ACACA can reduce lipid accumulation by mediating the AMPK-PPARα- CPT1A pathway, which regulates lipid metabolism and alleviates mitochondrial dysfunction.

†Jian Dong and Muzi Li contributed equally to this work.

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Assessing mercury exposure and its ecological risks to an endangered primate via individual behavior observation in Karst region, SW China

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Abstract

The White-Headed Langur (*Trachypithecus leucocephalus*) is one of the most endangered primate species in the world, exclusively found in the karst areas, Southwest China. The extensive agricultural activities (such as sugarcane cultivation) and mining operations within their foraging areas are highly likely to lead to environmental mercury (Hg) pollution, potentially posing health risks to the White-Headed Langur. This study utilizes habituated groups of langurs, estimating their daily foraging intake based on individual observation and assessing ecological risks through Hg content in biological samples. The results show that the White-Headed Langurs' daily foraging intake is 251.54±130.43 g/d, with Hg content in plant samples at 28.89±36.98 μg/kg, and fecal samples at 74.02±34.68 μg/kg. Seasonally, there is no significant difference in daily foraging intake of food plants

(GLMM: χ^2=3.5244, df=1, p=0.0605), while significant differences were observed in Hg levels in both fecal and plant samples (Fecal: GLMM, χ^2=93.902, df=1, p<0.001; Plant: GLMM, χ^2=47.049, df=1, p<0.001). The mercury pollution risk (HQ) in the dry season is significantly higher than in the rainy season (Plant pathway: GLMM, χ2=45.444, df=1, p<0.001; Fecal pathway: GLMM, χ^2=63.693, df=1, p<0.001). The White-Headed Langurs are more susceptible to Hg pollution during the dry season, suggesting that mercury biomonitoring should be intensified during this period.

Keywords: White-Headed Langur; Mercury; Karst habitat; Exposure risk; Individual Observation.

Investigation of food borne parasites infection in common freshwater fish in Songhua River Basin of Jilin City

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Abstract： In order to understand the infection of food borne parasites in common freshwater fish in Songhua River Basin of Jilin City, 2259 samples of 19 common freshwater fish were collected in this city. The morphological identification was carried out by artificial digestion, muscle compression and other methods. The infection rate and infection intensity were calculated, and the parasitic infection of different fish species in different sections of Songhua River Basin of Jilin city was analyzed. The results showed that seven kinds of parasites were found, which were *Clonorchis sinensis, Clonorchis sinensis, Clonorchis formosanus, Clonorchis orientalis, Capillaria, uterine nematode* and *Dactylogyrus*. The total infection rate of freshwater fish was 15.36%. The fish species with the highest infection rate was *Perca Pueraria* (44.23%), and the insect species with the highest infection rate was *Clonorchis sinensis* (6.55%). The investigation showed that the parasite infection of freshwater fish in Songhua River Basin of Jilin city was relatively common. *Clonorchis sinensis*, *Clonorchis orientalis* and *Clonorchis formosanus* were the dominant species in this region. Further investigation and control of food borne parasites of freshwater fish in this region should be strengthened.

Key words: Songhua River Basin in Jilin City; Freshwater fish; Food borne parasites; Epidemiological survey

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Conservation Law of Cell Bioelectricity Membrane Area and Ion Inequality Equation Based on Potassium Channel "Origami Windmill" Model

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Abstrac: At present, there are misunderstandings and even subversive errors in the understanding of cellular bioelectricity phenomena. The theory explaining the mechanism of bioelectricity generation is the ionic theory, and the ionic theory is based on the membrane theory. The membrane theory maybe the correct part, and the ionic theory does not give a definite affirmation; the membrane theory may be the wrong part, and ionic theory does not give a clear negative, instead, has been further strengthened in the later period. Whether it is membrane theory or ionic theory, the author has ignored the structure and characteristics of ion channels, and has not found the essence and law of ion exchange inside and outside the cell membrane. Therefore, the GHK equation and the H-H equation based on the ionic theory have congenital deficiencies. Therefore, it is necessary to put forward a new doctrine on this basis and establish a new mathematical model based on the new doctrine to re-explain the mechanism of bioelectricity generation scientifically and rationally.

This paper is based on the principle of K+ channel "origami windmill" model, the conservation law of membrane area of cell action potential ion exchange was proposed, and establishes a new mathematical model of cell action potential based on the conservation law ofmembrane area—ion inequality equation. The expression of conservation law of membrane area: SA (t) + SB (t) = S0, the expression of the ion inequality equation: resting potential N = N0 + Vt; action potential N = N0 + 170t -90t2.

The conservation law of membrane area holds that bioelectrical activity is a process in which

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different cations replace each other on the inner surface of the cell membrane. Cl is already surrounded by the cell membrane at the beginning of cell membrane formation, which determines the “positive” and “negative” of the cell action potential; The cations such as Na+, K+, etc., the amount of mutual replacement on the inner surface of the cell membrane determines the amplitude of the action potential, and the ratio of mutual replacement complies with the principle that the membrane area is equal and the ions are not equal.

The ion inequality equation, cited the kinematics principle, can not only reflect the nature and rule of cation exchange on the inner surface of cell membrane,but also can reasonable avoid cell membrane expansion force and ionic driving force, completed the bioelectricity generation mechanism from the qualitative to the quantitative expression, supports the preexistence of membrane theory, to verify the theory of brain cell activation, the theory of dove-likeparticles and “origami windmill” model, has opened up a scientific and quantitative description cell action potential new ways and means.

Keywords: K+ channel “origami windmill” model; ionic theory; GHK equation; H-H equation; conservation law of membrane area; ion inequality equation

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Early postnatal whisker deprivation cross-modally modulates prefrontal cortex myelination and leads to social novelty deficit

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Sensory experience affects not only the corresponding primary sensory cortex, but also synaptic and neural circuit functions in other brain regions in a cross-modal manner. However, it remains unclear whether oligodendrocyte (OL) generation and myelination can also undergo cross-modal modulation. Here, we report that while early life short-term whisker deprivation from birth significantly reduces in the number of mature of Ols and the degree of myelination in the primary somatosensory cortex(S1) at postnatal day 14 (P14), it also simultaneously affects the primary visual cortex (V1), but not the medial prefrontal cortex (mPFC) with a similar reduction. Interestingly, when mice were subjected to long-term early whisker deprivation from birth (P0) to P35, they exhibited dramatically impaired myelination and a deduced number of differentiated OLs in regions including the S1, V1, and mPFC, as detected at P60. Meanwhile, the process complexity of OL precursor cells(OPCs) was also rduced, as detected in the mPFC. However, when whisker deprivation occurred during the mid-late postnatal period (P35 to P50), myelination was unaffected in both V1 and mPFC brain regions at P60. In addition to impaired OL and myelin development in the mPFC, long-term early whisker-deprived mice also showed deficits in social novelty, accompanied by abnormal activation of c-Fos in the mPFC. Thus, our results reveal a novel form of cross-modal modulation of myelination by sensory experience that can lead to abnormalities in social behavioral, suggesting a possible similar mechanism underlying brain pathological conditions that suffer from both sensory and social behavioral deficits, such as autism spectrum disorders.

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Arylalkalamine N-acetyltransferase-1 affects blood feeding behavior by affecting various coagulation pathways of the host，*Aedes aegypti*

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Abstract Arylalkalamine N-acetyltransferase-1 (aaNAT1) exhibits high expression levels in the salivary glands of *Aedes aegypti*. Previous studies have demonstrated that the salivary glands of aaNAT1 mutant strains fail to effectively prevent coagulation of the host's blood. Through integrated transcriptome, proteome, and metabolome analysis, key metabolites and proteins interacting with aaNAT1 were identified. ITC analysis further confirmed that aaNAT1 interacts with norepinephrine to attenuate host platelet aggregation. Additionally, Coagulation Four experiments revealed that aaNAT1 inhibits activation of host thrombin. Knockdown of aaNAT1 in *Aedes aegypti* resulted in suppressed blood feeding behavior and reduced blood intake volume due to inhibition of its anticoagulant effect.

Hybrid Neural Networks for Continual Learning Inspired by Cortico-Hippocampal Circuits

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Current artificial systems suffer from catastrophic forgetting during continual learning, a limitation absent in biological systems. Biological mechanisms leverage dual representation of specific and generalized memories within cortico-hippocampal circuits to facilitate lifelong learning. Inspired by this, we develop a cortico-hippocampal circuits-based hybrid neural network (CH-HNN) that emulates these dual representations, significantly mitigating catastrophic forgetting in both task-incremental and class-incremental learning scenarios. Our CH-HNNs incorporate artificial neural networks and spiking neural networks, leveraging prior knowledge to facilitate new concept learning through episode inference, and offering insights into the neural functions of both feedforward and feedback loops within cortico-hippocampal circuits. Crucially, CH-HNN operates as a task-agnostic system without increasing memory demands, demonstrating adaptability and robustness in real-world applications. Coupled with the low power consumption inherent to SNNs, our model represents the potential for energy-efficient, continual learning in dynamic environments.

A Novel Biomineralized Collagen Liquid Crystal Hydrogel Possessing Bone-like Nanostructures by Complete In Vitro Fabrication

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摘 要： The microstructure of bone consists of nano-hydroxyapatite (nano-HA) crystals aligned within the interspaces of collagen fibrils. To emulate this unique microstructure of bone, this work applied two biomimetic techniques to obtain bone-like microstructures in vitro, that is, combining the construction of collagen liquid crystal hydrogel (CLCH) with the application of a polymerinduced liquid precursor (PILP) mineralization process. Upon the elevation of pH, the collagen macromolecules within the collagen liquid crystal (CLC) were activated to self-assemble into CLCH, whose fibrils packed into a long and dense fiber bundle in high orientation, emulating the densepacked matrix of bone. We demonstrated that the fibrillar mineralization of CLCH, leading to a bonelike nanostructured inorganic material part, can be achieved using the PILP crystallization process to pre-mineralize the dense collagen substrates of CLCH with CaCO3 , immediately followed by the in situ mineral phase transformation of CaCO3 into weak-crystalline nano-HA. The combination of CLCH with the biomineralization process of PILP, together with the mineral phase transformation, achieved the in vitro simulation of the nanostructures of both the organic extracellular matrix (ECM) and inorganic ECM of bone. This design would constitute a novel idea for the design of threedimension biomimetic bone-like material blocks for clinical needs.

The Impact of Acupuncture at Acupoint Zhongwan and Zusanli on Intestinal Microbiota, Serum Neurological Related Cytokines, and Therapeutic Efficacy in Chronic Atrophic Gastritis

Abstract

Background: Chronic atrophic gastritis (CAG) was a prevalent gastrointestinal disorder associated with an increased risk of gastric adenocarcinoma. While conventional Western medicine (WM) was a mainstay in CAG management, complementary therapies such as acupuncture have gained attention for their potential adjunctive role. However, the specific effects of acupuncture on intestinal microbiota, serum neurological-related cytokines, and therapeutic efficacy in CAG remain under investigation.

Methods: Patients diagnosed with CAG and admitted to our hospital between January 2023 and June 2023 were categorized into four groups based on the different treatment modalities they received: WM group (n=64), WM combined with acupuncture at Zhongwan acupoint group (n=65), WM combined with acupuncture at Zusanli acupoint group (n=67), and WM combined with acupuncture at both Zhongwan and Zusanli acupoints group (n=66). Intestinal microbiota analysis, serum neurological-related cytokine measurement, and therapeutic efficacy assessment were conducted to evaluate the impact of acupuncture on these parameters.

Results: Intestinal microbiota analysis revealed significant differences in Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, and p-Proteobacteria levels between the groups ($p < 0.05$). Serum neurological-related cytokines showed significant reductions in TNF-α, IL-6, BDNF, NGF, and NSE levels in the acupuncture groups ($p < 0.05$). The combined acupuncture group demonstrated the highest therapeutic efficacy in terms of remission and response rates ($p < 0.05$).

Conclusion: Acupuncture at Acupoint ZW and ZSL may modulate the intestinal microbiota, serum neurological-related cytokines, and enhance the therapeutic outcomes of patients with CAG undergoing conventional WM treatment.

Keywords

Acupuncture; Acupoint Zhongwan; Acupoint Zusanli; Intestinal Microbiota; Serum Neurological Related Cytokines; Therapeutic Efficacy; Chronic Atrophic Gastritis

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Shenlian extract protects against ultrafine particulate matter-aggravated myocardial ischemic injury by inhibiting inflammation and cell apoptosis

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Emerging evidence suggests that exposure to ultrafine particulate matter (UPM, aerodynamic diameter < 0.1 μm) is associated with adverse cardiovascular events.Previous studies have found that Shenlian (SL) extract possesses anti-inflammatory and antiapoptotic properties and has a promising protective effect at all stages of the atherosclerotic disease process. In this study, we aimed to investigated whether SL improves UPM-aggravated myocardial ischemic injury by inhibiting inflammation and cell apoptosis.

We established a mouse model of MI+UPM. Echocardiographic measurement, measurement of myocardialinfarct size, biochemical analysis, ELISA, histopathological analysis, TUNEL, WB , PCR and so on were used to explore the anti-inflammatory and anti-apoptotic effects of SL in vivo and in vitro.

SL treatment can attenuate UPM-induced cardiac dysfunction by improving left ventricular ejection fraction, fractional shortening, and decreasing cardiac infarction area. SL significantly reduced the levels of myocardial enzymes and attenuated UPM-induced morphological alterations. Moreover, SL significantly reduced expression levels of the inflammatory cytokines IL-6, TNF-α, and MCP-1. UPM

further increased the infiltration of macrophages in myocardial tissue, whereas SL intervention reversed this phenomenon. UPM also triggered myocardial apoptosis, which was markedly attenuated by SL treatment. The results of in vitro experiments revealed that SL prevented cell damage caused by exposure to UPM combined with hypoxia by reducing the expression of the inflammatory factor NF-κB and inhibiting apoptosis in H9c2 cells.

The establishment of prognostic model of uterine corpus endometrial carcinoma based on antigen presentation-related genes

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Background: Uterine corpus endometrial carcinoma (UCEC) is the major gynecologic tumor in most countries around the world with a poor prognostic in the late stages. The down-regulation of the antigen presentation level serves a pivotal strategy employed by tumor cells to evade the immune system, leading to diminished neoantigen presentation. However, the function of antigen presentation-related genes (APGs) in UCEC is still unknown, and a prognostic model for UCEC with high accuracy is urgently needed.

Methods: RNA-seq data and the clinical information on UCEC patients are provided from the Cancer Genome Atlas database (TCGA) and normal samples are provided from TCGA and Genotype-Tissue Expression (GTEx). Then we obtained the differentially expressed genes (DEGs) and prognostic genes and chose the antigen presentation-related DEGs. We performed the Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis and identified molecular subtypes by consensus clustering analysis. APGs were also used to create a prognostic model for UCEC with machine learning algorithms. In addition, by using Cox regression analysis and two-sample Mendelian randomization analysis, we selected a single gene from the key APGs and performed the single gene analyses to explore its key role of progress in UCEC.

Results: UCEC was divided into two subtypes according to APGs, each of which has unique clinicopathologic characteristics, prognostic indicators, tumor microenvironment characteristics, and microsatellite instability. On a whole, the higher level of somatic mutations and the complexity of the immune

microenvironment contribute to the poor prognosis of the antigen presentation-low subtype. Additionally, we created a prognostic model based on APGs with a strong prognosis evaluation capability. The best prognostic model was established based on Random Survival Forest (RSF) algorithm (1-, 3- and 5-year AUCs are 0.80, 0.84 and 0.87). The single gene analysis also revealed a strong association between the expression of *ASB2* and UCEC.

Conclusion: We identified molecular subtypes based on APGs and compared specific clinical features between two subtypes. Besides, a prediction model with accurate prediction ability was developed.

Keywords: UCEC, antigen presentation-related genes, prognostic model, machine learning

Social Enhancement Facilitates Fear Extinction in Group Exposure Therapy for PTSD via the Oxytocinergic System

摘要：

Psychiatric disorders pose a significant threat to public health and quality of life, with many linked to emotional memory processes. Once formed, negative emotional memories, such as fear memories, are difficult to extinguish. Under natural conditions, the body counteracts fear memories through extinction, a process that forms new memories to inhibit fear. When fear becomes overwhelming and extinction mechanisms are impaired, conditions like post-traumatic stress disorder (PTSD) and anxiety disorders emerge. Exposure therapy, rooted in fear extinction, remains the most effective intervention for PTSD, yet patients often report unmet social and emotional needs during treatment. The underlying neural mechanisms governing extinction within social contexts remain poorly understood. We developed an "extinction together" rodent model to simulate group exposure therapy for PTSD incorporating social components. Unexpectedly, extinction together did not enhance fear extinction but instead led to social impairments. Through targeted recombination in active populations (TRAP) technology and c-fos staining, we identified the paraventricular nucleus (PVN) as the key region responsible for these social deficits. Using optogenetic inhibition of oxytocin (OXT) neurons in the PVN, we were able to promote fear extinction and rescue social impairments. Notably, through the translationally promising approach of intranasal oxytocin administration, we found that it not only facilitated fear extinction learning but also rescued the associated social impairments in the extinction together paradigm. These findings illuminate the complex interplay between social behavior and fear extinction, offering new perspectives on improving PTSD treatments by addressing the social limitations of current therapeutic approaches.

关键词：PTSD | extinction together | social impairments | paraventricular nucleus | oxytocin

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Interleukin-33 facilitates efferocytosis of microglia in epileptogenesis

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[Objectives]

The failure of anti-seizure medications (ASMs) in preventing occurs and development of epilepsy triggers the need to investigate pathological process during epileptogenesis. Neuroinflammation takes an important role in epileptogenesis and cytokines like IL-1β and TNF-α are recognized as risk factors lead to tissue damage and spontaneous seizures. Interleukin-33 (IL-33), another IL-1 family cytokine highly expressed in nervous system, has proven to be a necessary factor to maintain normal neural circuit via promoting phagocytosis of microglia upon neurodevelopment. Thus, deficit of IL-33 or its specific receptor IL1RL1 increases susceptibility of seizures. However, the dynamic and role of IL-33 in acquired epilepsy are still unknown.

[Methods]

The mouse model of intrahippocampus kainic acid (KA) injection was used to investigate dynamic and the role of IL-33 in epileptogenesis. At first, we detected the protein level and cellular source of IL-33 by immunoblotting and immunofluorescence. Then we used ST2 gene knock out mice to explore the effect of the increasing IL-33 during epileptgenesis on ST2 positive expression cells. To work on that, Microglial morphology analysis, CD68 immunofluorescence together with TUNEL staining and phagocytic capacity assay were utilized to evaluate the effect of IL-33 on microglial efferocytosis. At last, in order to estimate whether IL-33 impacted on spontaneous seizures, we monitored the electrocorticography and video of mice 2 weeks after KA injection.

[Results]

We found the protein level of interleukin-33 in hippocampus is elevated through the latency period of epilepsy, with a short diminishment in cerebral spinal fluid upon early phase. Astrocytes and oligodendrocytes are the primary cellular source of interleukin-33, while neuron may also transiently express high level of interleukin-33

before severe neuronal death occurs. In addition, IL1RL1 positive cells are mainly microglia. ST2 deficiency results in decreased phagocytosis of apoptotic cells by microglia. Furthermore, ST2 deficiency aggravates granule cell dispersion and spontaneous seizures.

[Conclusions]

Interleukin-33 effects on efferocytosis of microglia while the ST2 loss of function causes poorer outcomes in epileptogenesis.

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Research progress on antidepressants of traditional Chinese medicine preparations based on multi-source data-driven

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[ABSTRACT] With the accelerated pace of life, people are facing increasing social pressure, resulting in an increasing incidence of depression year by year, which seriously affects global public health security. As one of the important means of clinical depression treatment, traditional Chinese medicine preparations play a key role in antidepressant treatment. However, in the process of clinical treatment of depression, the cause of depression is unknown, and the choice of drugs is faced with difficulties. Therefore, the importance of how to choose antidepressants in the treatment of depression is self-evident. In recent years, with the rapid development of genomics, proteomics, metabolomics and other multi-omics, it is possible for clinicians to use big data mining to find more efficient and accurate drug screening methods. Based on this, this study constructed an antidepressant knowledge network of traditional Chinese medicine preparations based on the knowledge of traditional Chinese medicine preparations and depression in multi-source databases published at home and abroad. This review focuses on how to accurately treat depression based on multi-source data-driven Chinese medicine preparations, and to explore the future development prospects in this field, so as to open up a new theoretical basis for the research direction of antidepressant treatment.

[Key words]Multi-source data driven; Chinese medicine; antidepressant treatment

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The structure and diversity of bacterial and fungal in roots and rhizosphere soil of three different species of *Geodorum*

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Abstract: *Geodorum* is a kind of protected orchid plant with important medicinal and ornamental value. *Geodorum eulophioides* (GE) is an endangered and narrowly distributed species, and *Geodorum densiflorum* (GD) and *Geodorum attenuatum* (GA) are widespread species. Growth of Orchidaceae plants depend on microorganisms. However, there are few studies on microorganisms structure in *Geodorum* and the roles of microorganisms in the endangered mechanism of *G. eulophioides* is little known. In this study, the structure and composition of bacterial and fungal communities in roots and rhizosphere soil of GE, GD and GA were analyzed. The results showed that Delftia, Bordetella and norank_f_Xanthobacteraceae were the dominant bacteria in roots, while norank_f_Xanthobacteraceae, Gaiella and norank_f_norank_o_Gaiellales are the dominant bacteria in rhizosphere soil of

Geodorum. As well, rhizosphere soil of *Geodorum* growing in understory and roadside mainly differ in the abundance of Bordetalla. Compared with GD_underatory, the roots of GD_roadside had lower microbial diversity. As an endangered species, the main fungus in the roots and rhizosphere soil of GE is Russula, and its fungal diversity was lower than that of widespread species. Among the widespread species, the dominant fungal genus in roots and rhizosphere soil were g__unclassified_f__Geoglossaceae, g__Neocosmospora, g__Fusarium and g__Coprinopsis. This study is important for better understanding of the microbial composition and diversity and their effects on the growth and protection of *Geodorum*.

Key words: *Geodorum*; Orchidaceae; roots; rhizosphere soil; bacterial; fungal

Neurons Can Generate Electromagnetic Waves

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Abstract: Based on the potassium channel "origami windmill" model, and the conservation law of cell membrane area and ion inequality equation of based on the potassium channel "origami windmill" model, and Maxwell's electromagnetic theory, it is theoretically proved that neurons can generate electromagnetic waves. The electromagnetic wave is an energy wave, never disappear. Neurons are equivalent to engineering antennas, and information between neurons can be transmitted through electromagnetic waves. The material basis for neurons to generate electromagnetic waves is the result of the exchange of cations on the inner surface of the cell membrane, especially Na+ and K+ ; The essence of consciousness should be electromagnetic wave. The conclusion that "neurons can generate electromagnetic waves" provides theoretical support for human beings to finally solve the mystery of the brain. At the same time, the author gives seven falsification schemes. The brain is a huge gold mine, and it is too important to crack the mystery of the brain. It should be a joint operation of "multiple arms". It should not only be the work of brain scientists,but also the participation of physicists, chemists and mathematicians.

Keywords: neuron; electromagnetic wave; accelerated motion charge; antenna; the nature of consciousness

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Microbial metabolite EEM alleviates Ulcerative Colitis in micevia enhancing efferocytosis

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Macrophage efferocytosis plays a vital role in regulating inflammatory responses and facilitating tissue repair, yet insufficient efferocytosis often occurs at inflammatory sites. Enhancing macrophage efferocytosis has emerged as a promising strategy for treating inflammatory diseases such as inflammatory bowel disease and non-healing wounds associated with diabetes. In this study, we identified a group of spontaneous Ulcerative Colitis (UC) monkeys from a large population, all of which exhibited inadequate efferocytosis alongside clinical histological changes characteristic of UC. Serum metabolomics analysis revealed a sharp decrease in the microbial metabolite EEM in these UC monkeys compared to normal conditions. Further microbial metagenomics confirmed a reduction in the EEM-producing microbe, Limosilactobacillus__t__SGB7095, within the colons of the UC monkeys. To investigate whether EEM can modulate macrophage efferocytosis, we performed *in vitro* efferocytosis assays, which demonstrated that EEM significantly enhances efferocytosis, particularly by promoting the acidification of apoptotic cells. Additionally, treatment with EEM led to a marked increase in the efferocytosis-mediated production of pro-inflammatory resolution cytokines, including IL-10 and TGF-β. Overall, these findings highlight EEM's important role as a microbial-derived modulator of efferocytosis, contributing to the maintenance of tissue homeostasis.

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Characterisation of antigens genes of *Clonorchis sinensis*

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Abstract：To study the localization and characteristics of the recombinant antigens of *Clonorchis sinensis*, two amino acids highly repetitive sequences were obtained by construction and screening of a cDNA expression libraries of *C. sinensis* etacercaria and adult worms. Then we synthesized peptides with highly repetitive gene sequences and coupling with the carrier protein. Animals were immunized and sera was collected. Then antibodies were purified by ammonium sulfate precipitation and affinity chromatography. At last antigenic genes were located by immunofluorescence technique. In results， recombinant antigens CsSQ1 and CsSQ2 of *C.sinensis* mainly distributed in oral sucker and ventral suckers， respectively. The localization of the recombinant antigens of *C.sinensis* was confirmed. We speculate that the recombinant antigens may be related to the immune adhesion of *C. sinensis*. It provided the reference for the applied research in diagnosis and immunological characteristics of antigens of *C.sinensis* in the future.

Key words：*Clonorchis sinensis*; antigen genes; immunolocalization;

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Genotyping of *Toxoplasma gondii* from pig in jilin city

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Abstract： As a globally distributed obligate intracellular protozoan, *Toxoplasma gondii* causes serious harms to humans and animals. In this study, one *Toxoplasma gondii* (JLpig1) strain was isolated from the hilar lymph node of a sick pig in our laboratory in jilin city. The JLpig1 strain was genotyped by PCR-RFLP at the SAG3, GRA6 and L358.The results showed that: JLpig1 had type II alleles at three sites, type I allele at two site, which are the same as Chinese 1 strain except at the L358 locus. This study is the first to study the situation of pig-derived toxoplasma infection and genotyping in jilin province, so as to supplement the genetic diversity database of toxoplasma in jilin province and even China, and provide theoretical reference for the prevention and control of toxoplasmosis in China and the response to public health problems.

Keywords: *Toxoplasma gondii*; Genotyping; PCR-RFLP; Isolates; Pig

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Interpretation of Action Potential Generation Mechanism in Cells by Potassium Channel "Origami Windmill" Model

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Abstract:
The mechanism of cell action potential was explained by using the principle of potassium channel "origami windmill" model. It is inferred that ion channels should include at least two categories: One kind of channel is "special ion channel", its structure is like an origami windmill model. All cations passing through this channel rotate into the interior from one-way, only in and no out. Compared with K^+, they have two states of "open" and "closed", When they are "open", their aperture is not less than K^+ diameter. When "closed", their aperture is smaller than K^+ diameter, but not smaller than Na^+ diameter. The other channel is the "universal ion channel". All Ions passing through this channel unidirectional flow too, only out and no in. Compared with K^+, they have two states of "open" and "closed", When they are "open", their aperture is not less than K^+ diameter. When "closed", their aperture is smaller than K^+ diameter, but not smaller than Na^+ diameter. This model reasonably explains the whole process of action potential occurrence, and supports Hodgkin, Huxley 's experimental the results of action potential. This model does not support their explanation of the mechanism of action potential generation in cells and the core ideas of "membrane theory" and "ion theory". It negates the selective filter atomic model and the propeller model established by MacKinnon et al. It is tiped that the main role of "sodium-potassium pump" or "ATPase" is not responsible for the transport of Na^+ and K^+ from the inside and outside of the cell and maintaining cell membrane potential. The channels through which ions enter and escape cells are independent. This suggests that most channels may be sharing in the same direction by other inorganic ions and organic molecules.
Key words: Potassium channel; Origami windmill; Model; Resting potential; Action potential; Sodium-potassium pump

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Brain-inspired Multicore Interconnect Architecture Based on Adaptive Routing and Information Optimization

Abstract: In traditional Network on Chip (NoC) designs for multicore systems, Spiking Neural Networks (SNNs) exhibit distinct communication patterns characterized by high concurrency, large data transmission volumes, and uneven spike transmission. These features result in significant communication delays and low throughput. To address these issues, we optimized the communication architecture for SNNs and proposed a NoC design based on a Spiking Router (SR). This router architecture incorporates two main innovations. First, to tackle the intensity and immediacy of spike data in SNNs, we employed a dynamic ODD-EVEN routing algorithm, which dynamically adjusts data transmission paths according to the actual traffic conditions in the network. This optimization reduces global buffer usage and avoids communication congestion. Additionally, a multicast strategy is introduced to reduce the communication processing time for spike data, further improving system throughput. Second, we propose a spike-based information exchange mechanism that assigns different communication priorities based on the importance of the transmitted information. Experimental results demonstrate that the proposed NoC architecture, based on the Spiking Router, significantly enhances communication performance in neuromorphic hardware systems.

中文题目：《基于自适应路由和信息优化的类脑多核互连架构》

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Metabolomic-proteomic combination analysis reveals the targets and molecular pathways associated with high-fat diet induced brain dysfunction and cognitive impairment

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Objectives: Diabetes and obesity have been shown to significantly affect brain functions and metabolism, subsequently causing cerebral atrophy and cognitive impairment. However, it remains to be determined whether brain dysfunction induced by obesogenic diets results from brain metabolic alterations.

Methods: C57BL/6 mice were fed with normal chow diet or high fat diet (HFD) for a total 24 weeks. The combination analysis of metabolomics and proteomics of brain tissues was performed to discover the candidate targets and potential molecular pathways involved in HFD-induced brain dysfunction and metabolism.

Results: Mice fed the HFD developed obesity, glucose intolerance, insulin resistance as well as impaired memory in object recognition tasks and spatial memory as evaluated by Morris water maze. By comparing the differences in metabolites and proteins in the brains from HFD treated and control mice, we discovered 133 differential metabolites between comparative analysis of HFD vs Control on brain metabolomics. Moreover, a total of 245 proteins were obtained whose changes were significantly differed between HFD and Control mice brains. A combined analysis of brain metabolomics and proteomics was then conducted, revealing 22 shared molecular pathways, as well as the enrichment of purine metabolism, beta-alanine metabolism, lysosome, butanoate metabolism and neuroactive ligand-receptor interaction.

Conclusions: We performed the first study combining metabolomics and proteomics to explore the mechanisms behind the HFD-induced cognitive impairment. Our

results reveals possible molecular mechanisms as well as preventive and therapeutic targets for HFD-induced brain dysfunction.

Key words: High-fat; Cognitive impairment; Metabolics; Proteomics

ASO Efficacy Prediction Using a Pretraining Paradigm Based on Multi-scale RNA Information

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Abstract: Antisense oligonucleotides (ASO) are a promising class of small molecule therapeutics. Their development requires screening numerous candidate sequences, leading to repetitive testing, high costs, and long development cycles. This creates a demand for reliable tools to predict therapeutic efficacy. However, limited data and complex interaction factors hinder existing models, resulting in poor precision and generalization, failing industry needs. To address these challenges, this thesis proposes an ASO efficacy prediction framework using a pretrained paradigm with large foundation models. Its core innovation combines upstream mixture-of-experts feature extraction with downstream multi-task learning. By integrating patented and open-source datasets, it sets metrics for accuracy, generalization, and efficiency. Comprehensive validation shows the model's high recall and AUC, with generalizability across datasets and tasks, offering potential as a tool for drug development and clinical trials, advancing ASO therapeutics.

Phase separation promotes Atg8 lipidation for autophagy progression

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SUMMARY

Upon starvation, the autophagy-initiating Atg1 complex undergoes phase separation to organize the pre-autophagosomal structure (PAS) in yeast, from which autophagosome formation is considered to proceed. However, the physiological roles of the PAS as a liquid droplet remain unclear. Here we show that core Atg proteins are recruited into early PAS droplets that are formed by phase separation of the Atg1 complex with different efficiencies in vitro. The Atg12–Atg5–Atg16 E3 ligase complex for Atg8 lipidation is the most efficiently condensed in the droplets via specific Atg12–Atg17 interaction, which is also important for the PAS targeting of the E3 complex in vivo. In vitro reconstitution experiments reveal that E3-enriched early PAS droplets promote Atg8 lipidation and incorporate Atg8-coated vesicles to the interior, thereby protecting them from Atg4-mediated delipidation. These data suggest that the PAS utilizes its liquid-like property to function as an efficient production site for lipidated Atg8 and pool membrane seeds to drive autophagosome formation.

Hippocampal Network and Continuous Learning

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Abstract

The problem of continual learning is a challenge that has yet to be overcome in artificial intelligence. A significant challenge currently faced is how agents can learn new knowledge without forgetting old knowledge. Research indicates that the hippocampus plays a crucial role in humans' ability to complete continual learning tasks. This study aims to achieve breakthroughs in the continual learning problem through the research and simulation of the hippocampal network.

General and Stable Emulation of Finite State Machines with Spiking Neural Networks

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Finite state machines (FSMs) are fundamental computational models extensively utilized across various domains including natural language processing, digital circuit design, control systems, and so on. Despite their wide applicability, FSMs face challenges in modeling complex, dynamic systems due to state explosion and limitations in handling continuous states. Neural networks, conversely, excel at modeling implicit and continuous systems but struggle with the long-term and precise tasks that FSMs handle efficiently. This paper explores the integration of FSMs with spiking neural networks (SNNs) to harness the strengths of both paradigms.

In this work, we propose a novel approach using discrete-time spiking recurrent neural networks (DTSRNNs) for stable and general FSM emulation. DTSRNNs, inspired by biological neurons, use spikes to encode information, closely aligned with FSMs' discrete state transitions. We build a random-FSM dataset to evaluate models' performances and find that DTSRNNs, compared to traditional Discrete-Time Recurrent Neural Networks (DTRNNs), offer superior temporal stability and robustness. Our methodology includes the use of one-hot encoding to enhance network sparsity, crucial for learning complex FSM behaviors. Extensive experiments reveal that DTSRNNs, with one-hot encoded inputs, achieve longer decline periods, indicating better generalization and temporal stability. Furthermore, we introduce finite-state neural networks (FSNNs), a novel architecture that closely mirrors FSM structures, facilitating direct encoding of FSMs into neural networks. Our work presents a significant advancement in the emulation of FSMs using SNNs, offering a promising direction for applications requiring high temporal stability and robustness. The integration of discrete and continuous representations in DTSRNNs provides a

balanced approach to modeling complex systems, with potential implications for neuroscience-inspired computing architectures.

Finite state machines (FSMs) as a pervasive computation model lack mature emulation methods using neural networks.

Existing jobs neglect the generalization ability of models and focus on theoretical foundations without enough practical experiments.

Here we redefine FSMs and propose discrete-time spiking recurrent neural networks (DTSRNNs). FSMs are defined in a linear way which makes state transformation elaborate and visible. We benchmark DTRNNs and DTSRNNs with binary and one-hot encoding on the random-fsm dataset built by ourselves to verify generalization ability of models and compare models' temporal stability.

24-Epibrassinolide (EBL) promoted growth and organic compounds accumulation in *Dunaliella parva* by enhancing photosynthesis

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Abstract As a commonly used type of the sixth class of phytohormones brassinosteroids (BRs), 24-epibrassinolide (EBL) plays the important roles in plant growth and development. *Dunaliella parva* (*D. parva*) is an important lipid-producing microalga, and its growth and accumulation of organic compounds need to be further improved for higher application value. However, the effects of EBL on *D. parva* are still unclear now. In this study, *D. parva* was treated with different concentrations of 24-epibrassinolide (EBL) to evaluate its influence. Cell density of 0.5mg/L EBL treated group was 1.28-fold of control at 18 d. The contents of chlorophyll, carotenoid, carbohydrate, starch, protein of 0.5 mg/L EBL treated group were 1.31-, 1.18-, 1.49-, 1.35-, and 1.54-fold of control. The highest mRNA levels of *rbcS*, *rbcL*, *RuPE*, *PRK*, *TPI*, *FBPA*, *FBPase*, *SBPase*, *DpME*, *CA* in EBL treated group were 1.94-, 2.43-, 2.14-, 1.76-, 1.97-, 2.21-, 1.48-, 1.96-, 2.06-, and 1.89-fold of control. The highest enzymatic activities of ME, CA and RuBisCO in EBL-treated group were 1.27-, 1.23-, and 1.37-fold of control. Lipid content of 0.4 mg/L EBL treated group was 1.44-fold of control. This study demonstrated the great potential of EBL to obtain higher biomass and organic compounds accumulation. Our study indicates that EBL

treatment is valuable for the subsequent commercial production of biofuel and other high-value metabolites using microalgal biomass as raw material.

***Keywords*:** Brassinosteroids; *Dunaliella parva*; organic compounds; photosynthesis; gene expression; enzymatic activity

Dendritic Nonlinear Computation Inspired Spiking Neural Network Model

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Abstract:

Dendrite plays a crucial role in the biological brain networks by integrating information flow, regulating neural firing, and supporting synaptic plasticity through nonlinear processing. As the third generation of artificial neural networks, spiking neural networks (SNNs) perform more efficiency, robustness, and flexibility in brain-inspired architecture and biologically plausible computing. Despite these advantages, they still fall short in modeling dendritic nonlinear computation. Here, we propose the Kolmogorov–Arnold leaky integrate-and-fire neuron (KALIF) for SNNs, which expands the dendritic computation by incorporating the Kolmogorov–Arnold Network (KAN) into the leaky integrate-and-fire (LIF) model. Unlike traditional models where synaptic inputs are linearly summed, KALIF neurons allow synaptic inputs to be integrated nonlinearly in artificial dendrite branches before reaching the soma. This approach enables attention-based and preference-based information processing within a single KALIF neuron, guided by cell's internal state or external modulation signals. This is more aligned with biological circuits, where neuromodulators interact with complex dendritic structures and diverse receptor types. Introducing artificial dendrites to the KALIF model enhances the performance and

flexibility of SNNs, while also making them more biologically interpretable, bringing us closer to understanding the brain and the mechanisms of biological intelligence in nature.

Keywords: Dendritic Nonlinear Computation, Spiking Neural Network, Kolmogorov–Arnold Network

TianmouCap: Brain-Inspired Motion Capture System With Complementary Dual Pathways

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Abstract：

Optical motion capture (MoCap) to record the actions of targets, is crucial for medical fields such as gait analysis. In extreme scenarios, it is essential for MoCap systems to deliver high-precision and high-frame-rate data acquisition as the ground truth. However, high-performance MoCap systems based on conventional frame-based cameras lead to a substantial increase in bandwidth requirements and computational load. Here, we develop TianmouCap, a brain-inspired MoCap system that integrates the emerging brain-inspired vision sensor. The action-oriented pathway (AOP) of TianmouCap rapidly detects and tracks bright markers from sparse temporal-spatial difference information. Simultaneously, the cognition-oriented pathway (COP) of TianmouCap captures full scene semantic to generate adaptive masks and mitigates interference during marker detection. Additionally, COP can provide markerless MoCap information in cases where markers are occluded and AOP cannot work. We achieve stable MoCap at a frame rate of 1515 fps and conducted calibration within an indoor environment. Furthermore, we validate the reliability of TianmouCap in outdoor. These results highlight the potential of brain-inspired vision sensors to replace conventional MoCap cameras and drive the significant performance improvements in MoCap.

Spinal Dorsal Horn S100A8/A9 Heterodimers Regulate Chronic Neuropathic Pain

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Abstract: Objective Neuropathic pain (NP) has seriously troubled human health, but its pathogenesis is still unclear. The S100A8 and S100A9 proteins, which form S100A8/A9 heterodimers, play an important role in the pathological process of chronic inflammatory diseases. This study was undertaken to clarify the functions of S100A8/A9 heterodimers in chronic NP caused by nerve injury. **Methods** Using the chronic NP model of mice with nerve injury (CCI operation), the mechanism of S100A8/A9 heterodimers in NP was studied by western blot, immunofluorescence, and pain behaviour. **Results** The results showed that the S100A8 and S100A9 proteins were upregulated in the spinal dorsal horn of mice after CCI and were mainly expressed in astrocytes. It was further found that intrathecal administration of an S100A8/A9 heterodimer inhibitor in CCI model mice could relieve the NP caused by CCI. Intrathecal injection of the S100A8/A9 heterodimer can induce mechanical and thermal hyperalgesia in normal wild mice. **Conclusion** These results indicate that the S100A8/A9 heterodimers expressed by astrocytes in the spinal dorsal horn are involved in NP after nerve injury.

Construction of a Prognostic Model for Liver Cancer Using GSVA and Machine Learning, and Elucidation of the Biological Significance of Key Gene Sets

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Abstract:

Introduction: Hepatocellular carcinoma (HCC) is one of the most common and fatal malignancies worldwide. Despite significant advancements in diagnosis and treatment, the prognosis for HCC remains poor. With the growing availability of high-throughput genomic data, machine learning methods have been widely applied in liver cancer research. However, current studies mainly focus on single genes or simple gene expression features, often overlooking the complex interactions between genes and the overall effects of biological pathways. To predict liver cancer prognosis more accurately, there is an urgent need for integrative approaches that combine biological context with machine learning techniques.

Methods: This study employed Gene Set Variation Analysis (GSVA) to derive pathway scores from gene expression data sourced from multiple databases, including TCGA, GEO, and GTEx. We focused on gene sets related to metabolic pathways, programmed cell death (PCD) pathways, and immune infiltration. These scores were used as features in combination with clinical prognostic data from TCGA for survival analysis. Advanced algorithms, such as the Nonlinear Cox Proportional Hazards model and Extra Survival Trees, were utilized to construct prognostic models. To explain model significance, SHAP (SHapley Additive exPlanations) values were used to interpret the importance of gene set scores and reveal their roles in disease progression. Additionally, we incorporated single-cell RNA sequencing data to further analyze the expression and functions of these gene sets across different cell types.

Results: The results demonstrated that gene sets associated with metabolic pathways

exhibited outstanding performance in predicting liver cancer prognosis (C-index: 0.87). Metabolic pathway scores obtained through GSVA were significantly correlated with patient survival and effectively distinguished high-risk from low-risk patient groups. SHAP analysis further indicated the high importance of metabolic pathway scores in the model, confirming their critical role in liver cancer progression. Additionally, gene sets related to immune infiltration showed high significance, suggesting the crucial impact of the immune microenvironment on liver cancer prognosis. Through single-cell RNA sequencing analysis, we found significant differences in the expression of these key gene sets across different immune cell types, further supporting their functional relevance in liver cancer progression.

Conclusion: This study established an effective prognostic model for liver cancer by combining GSVA with advanced survival analysis algorithms. The model not only improves the accuracy of prediction but also provides deeper insights into how gene sets influence liver cancer progression. Our findings offer new perspectives for understanding the molecular mechanisms of liver cancer and propose novel viewpoints for the development of personalized therapeutic strategies, with potential clinical applications.

Keywords:

Bioinformatics; machine learning; prognostic prediction model; Gene Set Variation Analysis; hepatocellular carcinoma.

The Role of *pparg* in Zebrafish Heart Regeneration

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Abstract

This project focuses on the repair mechanisms following heart injury, with particular attention to the innovative role of adipocytes in the process of zebrafish heart regeneration. The zebrafish, known for its exceptional cardiac regenerative capacity, serves as an ideal model organism for the study of cardiovascular diseases. Research has revealed that when zebrafish sustain cardiac injury, a significant aggregation of adipocytes rapidly occurs around the ventricle, accompanied by a notable upregulation of genes associated with adiposity, such as peroxisome proliferator-activated receptor gamma (PPARG). This suggests that adipocytes and PPARG play a pivotal role in the repair and regeneration of cardiac tissue.Utilizing a zebrafish cryoinjury model in conjunction with molecular biological techniques, we systematically investigated the specific functions of PPARG in heart regeneration and its regulatory mechanisms. Experimental results confirm that PPARG not only promotes adipocyte differentiation and lipid deposition but also directly participates in the regulation of cardiomyocyte regeneration, vascular reconstruction, and inflammatory responses following heart injury. Furthermore, through an in-depth dissection of the PPARG signaling pathway, multiple potential targets have been identified, paving the way for the development of adipocyte-based therapies for cardiac diseases.

Rehmannia Polysaccharide Induces IFN-γ to Promote Zebrafish Heart Regeneration

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Abstract:

Objective: This study aims to investigate the molecular mechanisms by which Rehmannia polysaccharide (RPS) induces the expression of interferon-γ (IFN-γ) to promote cardiac regeneration in zebrafish. Methods: A myocardial infarction model was established by freezing injury, and the effects of the drug on cardiac regeneration were evaluated using immunohistochemistry, Picro Sirius Red staining, etc. Meanwhile, the expression of IFN-γ was detected by Western blot and quantitative PCR, and the relevant molecular mechanisms were explored. The results showed that Rehmannia polysaccharide treatment significantly increased the level of IFN-γ in zebrafish hearts after injury, promoted the proliferation of cardiomyocytes, and improved cardiac function. In particular, the number of proliferating cardiomyocytes was significantly increased on day 7 after injury, indicating that cardiac regeneration was active. Conclusion: Rehmannia polysaccharide may induce the production of IFN-γ through the NOD signaling pathway to promote cardiac regeneration in zebrafish, which also provides a new idea for the treatment of heart disease.

The role of Wnt1 protein/Wnt pathway in anti - aging by ASC transplantation

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Abstract

ASC (adipose-derived stem cells, ASC), as a type of mesenchymal stem cell that has been widely studied and applied in various diseases, has a good application prospect. However, under different receptor states and ASC states, the transplantation effects are not the same, which restricts the clinical application of ASC to a certain extent.

In this study, when the same ASC derived from young (2-4 months) mice was transplanted into different receptors, a good weight-loss effect was observed in old mice (≥18 months). The adipose tissue, especially the abdominal fat, was significantly reduced, and the relevant oxidative stress factors in the serum changed significantly. however, the above effects could not be shown in young mice and *leptin* gene - knockout mice (ob^{-}/ob^{-}). This results indicate that ASC from young donors can exhibit good weight-loss and anti-aging effects in old mice. However, during the *in vivo* transplantation process, ASC from old donors has no weight-loss and anti-aging effects either in young mice or in old mice.

In further research, it was found that after transplanting ASC from young donors, the expression levels of β-catenin and Wnt1 protein in the abdominal fat of old mice increased, while the expression of PPAR-γ decreased. Moreover, after activating the Wnt pathway, the phosphorylation of β-catenin in ASC from young donors was inhibited. When the Wnt pathway is inhibited, the opposite results occur. This study focuses on exploring the reasons for the differences in the transplantation effects of the same and different donor-derived ASC on different receptors, is committed to exploring the action mechanism of ASC transplantation effects, and hopes to remove the application limitations of ASC in different types of receptors by finding out the

key influencing factors in response to different transplantation effects.

Keywords： Adipose stem cells; stem cell therapy; anti-aging effect; Wnt pathway

HL-CPG: HIERARCHICAL LEARNING-BASED CONTROL FRAMEWORK INTEGRATING CENTRAL PATTERN GENERATORS FOR NATURAL QUADRUPED ROBOTS

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Most existing work on quadruped robot locomotion controllers has been based on conventional model-based control methods. While conventional control approaches have demonstrated impressive real-world performance, they often require significant domain knowledge for kinematic modelling and may struggle to generalize to unforeseen environments. This limitation has led to the emergence of learning-based control (e.g., Imitation Learning (IL)) as an attractive solution for training controllers that are robust to external disturbances. However, despite notable successes, learning-based control methods have struggled to achieve both agility and adaptability simultaneously within a single control architecture. For example, controllers trained using the IL paradigm can exhibit agility comparable to that of real animals but may suffer from catastrophic distribution shifts, leading to poor performance in environments beyond the training data. On the other hand, agents trained through the Deep Reinforcement Learning (DRL) paradigm are prone to adopting unnatural behaviours, and designing reward functions requires task-specific tuning.

To address this challenge, we propose a hierarchical learning-based control framework that integrates brain-inspired central pattern generators (CPG), a neural circuit located in the spinal cords of vertebrate animals that are capable of producing coordinated patterns of high-dimensional rhythmic output signals, trained using both DRL and IL paradigms. This framework is divided into two phases. In the first phase, we pretrain multiple CPG control policies using reference motion data sampled from real dogs. By leveraging the IL paradigm during this phase, our quadruped robot can

achieve various gaits (e.g., pace, trot, canter) with agility comparable to that of a real dog in varied speed. In the second phase, we use the DRL paradigm to modulate the selection among the CPG policies, adjust the swing and stance times, and optimize the maximum step length of each foot, enabling the robot to traverse complex terrains. This framework effectively leverages the exploration capabilities of DRL and the imitation strengths of IL, while mitigating each other's limitations. This approach significantly enhances the potential of learning-based controllers to achieve more natural, coordinated, yet diverse locomotion control in quadruped robots.

Study on the mechanism of action of Baduanjin on improving insulin resistance in type 2 diabetes patients

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Summary: Type 2 diabetes (T2DM) is a chronic metabolic disease characterized primarily by insulin resistance and insulin secretion defects. Insulin resistance is a key factor in the pathogenesis of T2DM, closely related to abnormalities in inflammatory factors and signaling proteins. Baduanjin, as one of the traditional Chinese fitness qigong practices, has attracted modern research attention due to its potential health benefits. This study aims to explore the improvement effect of Baduanjin on insulin resistance in T2DM patients and its mechanism.

Through systematic reviews and Meta-analyses of existing literature, combined with randomized controlled trials (RCTs), this study evaluated the impact of Baduanjin on insulin sensitivity in patients with type 2 diabetes mellitus (T2DM). The research findings indicate that regular Baduanjin exercise can significantly enhance insulin sensitivity in T2DM patients and reduce insulin resistance, thereby facilitating improved glycemic control.

The study also revealed that Baduanjin improves insulin resistance in skeletal muscle by enhancing mitochondrial function, promoting glucose uptake, and inhibiting the synthesis of inflammatory factors. Additionally, as a gentle aerobic exercise, the positive impact of Baduanjin on cardiovascular function and muscle metabolism in patients with type 2 diabetes mellitus (T2DM) may be attributed to its ability to improve insulin resistance.

Although Baduanjin demonstrates positive effects in improving insulin resistance in patients with type 2 diabetes mellitus (T2DM), there is still room for improvement in

terms of sample size and research quality in current studies. Future research needs to conduct larger-scale, multi-center, high-quality randomized controlled trials (RCTs) to further verify the effectiveness of Baduanjin and deeply explore its mechanism of action, providing a more solid scientific foundation for exercise intervention in T2DM patients.

Keywords: Baduanjin; type 2 diabetes; insulin resistance; exercise therapy; mechanism of action

Exosomal miRNA-155-5p from M1-polarized macrophages interrupt diabetic wound healing

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Key words: polarized macrophages; exosomes; microRNA; diabetic wound healing; angiogenesis; GDF 6

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Nootkatone immunomodulates alveolar macrophage via Sting/TBK1/IRF3 signaling pathway inhibition to protect against LPS-induced acute lung injury

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Background and Purpose: Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are characterized by diffuse pulmonary interstitial edema, lung infiltration by immune cells, and acute hypoxic respiratory insufficiency. Nootkatone (NKT) is an organic compound and a bioactive sesquiterpene ketone originally found in Alaskan yellow cedar, Cupressus nootkatensis, which has anti-inflammatory properties. Given the high morbidity and mortality rates and limited treatment options for ALI, this study aims to investigate the potential protective effects of NKT in lipopolysaccharide (LPS)-induced ALI models.

Experimental Approach: An ALI model was established through intratracheal administration of LPS in mice, following oral treatment with NKT. The anti-inflammatory effects and potential mechanisms of NKT were evaluated using ELISA, RNA sequencing, glycolytic and mitochondrial functional assays, mitochondrial ROS assays and immunoblotting.

Key Results: NKT inhibits the increase in total cell, macrophage and neutrophil counts in bronchoalveolar lavage fluid of the ALI mice, as well as pro-inflammatory cytokines (IL-6, TNF-α, and IL-1β). NKT also reduces the gene expressions of inflammatory mediator in AMs, including Cxcl10 (IP-10), Ccl4 (MIP-1β), Ccl3 (MIP-1α), Csf3 (G-CSF), Il22 (IL-22), Il12a (IL-12α), Il1b (IL-1β), Ccl5 (RANTES). NKT diminishes mitochondrial respiration and glycolysis in lung single cells and alveolar macrophages (AMs) of ALI mice almost to baseline. NKT significantly reduces the protein expression of phospho-Sting, phospho-TANK-binding kinase 1 (TBK1) and phospho-IFN regulatory factor 3 (IRF3) in the lungs and AMs, thereby inhibiting the Sting/TBK1/IRF3 pathway.

Conclusion and Implications: NKT may exert its anti-inflammatory effects in

LPS-induced ALI by suppressing the Sting/TBK1/IRF3 signaling pathway at the levels of AMs and lungs, providing strong evidence for further development of NKT for the treatment of ALI.

Keywords: Nootkatone; acute lung injury; metabolic reprogramming; alveolar macrophage; inflammation

The m.3290T>C variant might be a protective factor against m.3243A>G variant-related MELAS

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The m.3243A>G variant is the most prevalent mitochondrial DNA variant, which is likely to impact the structural stability, methylation, acylation, and codon recognition of tRNALeu (UUR), leading to biochemical deficiencies. Previous studies have revealed that the detrimental impacts of m.3243A>G could be counteracted by another variant. The m.3290T>C variant was found in pedigrees of diabetes and essential hypertension and is identified as a benign variant in humans. In 1995, Hammans et al. reported a three-generation m.3243A>G pedigree harboring a homoplasmic m.3290T>C variant, where some family members harbored high heteroplasmy of the m.3243A>G variant but lacked clinical symptoms. However, no similar clinical pedigree has been reported globally since then. Here, we report a six-generation pedigree harboring both the m.3243A>G variant and the homoplasmic m.3290T>C variant, providing additional clinical evidence for the protective function of m.3290T>C. The proband VI-1 was a 2-year-old boy who died of MELAS at 2.5 years of age, with a 98.43% level of m.3243A>G variant. Unexpectedly, we assessed the blood variant levels of more maternal relatives and observed that some carriers (V-1, V-2, IV-2, and III-3) with high variant levels did not exhibit clinical symptoms. V-1, aged 30 years, had an 86.9% variant level of m.3243A>G, and was reportedly normal. V-2, aged 27 years, was also reportedly normal, with a 66.00% variant level of m.3243A>G. IV-2 reported no symptoms. III-3 carried an 86.9% variant level of m.3243A>G and presented only with an increased heart rate occasionally. In addition, the m.3243A>G variant was not detected in blood samples of III- 4, IV-4, or V-3. Besides, affected individuals are primarily characterized by mitochondrial cardiomyopathy. For example, patient IV-11 died at 30 years of age with heart failure. IV-3, aged 44 years with an 80.20% variant level of m.3243A>G, was diagnosed with a fast heart rate and liver cirrhosis and returned to normal after treatment. Currently,

he has high blood pressure and is taking antihypertensive drugs. In conclusion, we report a large pedigree that carries both the m.3243A>G variant and the homoplasmic m.3290T>C variant. Our pedigree study suggested that the m.3290T>C variant might suppress the deleterious effect of the m.3243A>G variant, offering novel insights into the pathogenesis of m.3243A>G and expediting the development of effective treatments for mitochondrial diseases.

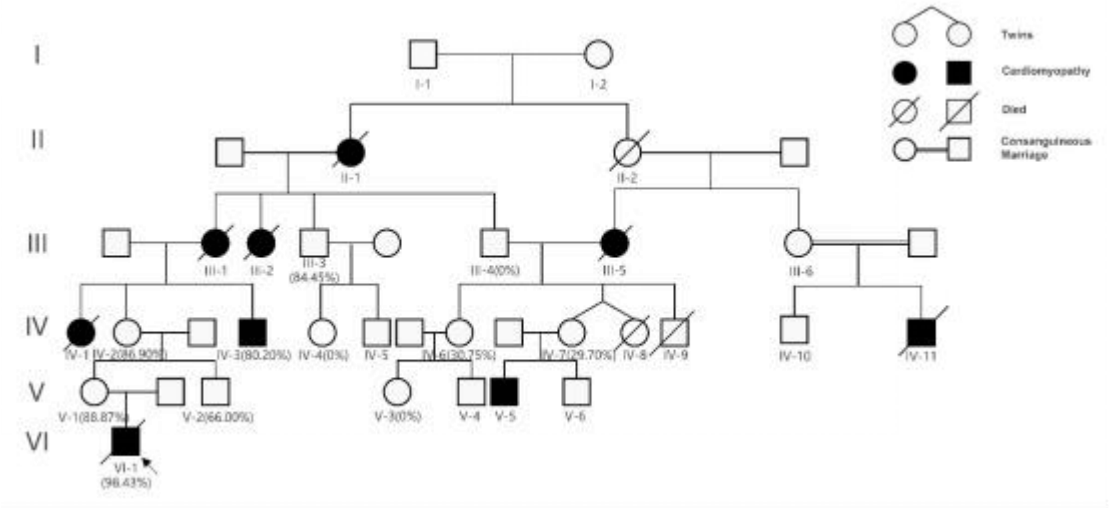

Figure 1. Pedigrees carrying both the m.3243A>G variant and the homoplasmic m.3290T>C variant. The numbers in parentheses are the heteroplasmy levels of m.3243A>G in blood. The black filling symbols indicate patients with cardiomyopathy. The arrow represents the proband.

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Fucoxanthin alleviates renal fibrosis in experimental diabetic nephropathy by regulating p62/Keap1/Nrf2 signaling and improving mitochondrial damage

Fucoxanthin (Fx) has a unique chemical structure that confers its biological effects and shows potential health benefits. The main purpose of this study was to explore whether Fx could alleviate renal fibrosis in diabetic nephropathy (DN) by regulating p62/Keap1/Nrf2 signaling and improving mitochondrial damage. We found that Fx improved renal function, lipid metabolism and renal fibrosis in STZ-induced diabetic rats and alleviated fibrosis in HG-induced GMCs. And Fx regulated protein levels of p62, Keap1 and Nrf2 in kidneys of diabetic rats and HG-induced GMCs. Fx also upregulated protein levels of LC3 II/LC3 I, SOD1 and HO-1, reversed the overproduction of mitochondrial superoxide, promoted the interaction between p62 and Keap1, improved mitochondrial morphology and mitochondrial membrane potential reduction and increased co-localization of p62 or Keap1 with mitochondria in HG-induced GMCs. Molecular docking study indicated the strong binding affinity between compound Fx and p62. Overall, Fx may be developed as a promising functional ingredient to alleviate DN.

The induction of paraptosis in melanoma by a novel iron chelator involves NCOA4 mediated mitophagy

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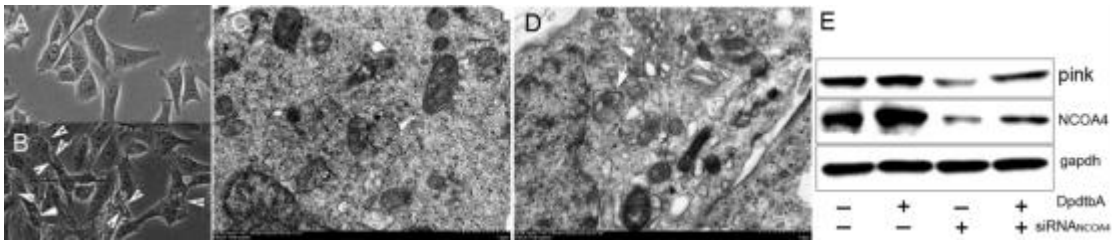
Apoptosis is an important event in the process of cell growth, regulating the cell lifespan. The induction of apoptosis involves the mechanisms of action of many drugs, but cancer cells can develop apoptosis resistance under drug stimulation. Obviously, developing other forms of cell death is an important strategy to solve the above dilemma. 2,2 '- Dipyridylketohydrazone dithiocarbamate s-butyric acid (DpdtbA) is an iron chelator with excellent inhibitory effects on various cancer cells, but the mechanism is unknown. When used to treat melanoma (A375) cells, it leads to the formation of a large number of cytoplasmic vacuoles (indicated by the arrow in Fig. A-B). Endoplasmic reticulum staining and transmission electron microscopy (TEM) observation confirmed that the cytoplasmic vacuoles were located in the endoplasmic reticulum (white vacuoles in Fig. D). It is interesting to note that large vesicles with damaged mitochondria inside (indicated by arrows) were also found in the TEM (Fig. D), suggesting occurrence of mitophagy possibly. The detection of the marker protein pink for mitophagy (Fig. E) indicated that DpdtbA treatment leads to upregulation of pink, further supporting the occurrence of mitophagy. On the other hand, preliminary mechanism studies have shown that DpdtbA can also upregulate NCOA4, indicating the occurrence of ferritinophagy. To explore the relationship between the two cellular events, the NCOA4 is knocked down by interfering RNA, the regulation of pink by the chelator can be significantly attenuated, indicating that mitophagy originates from NCOA4-mediated ferritinophagy. This clearly supports that the induction of paraptosis in melanoma cells by the novel iron chelator is achieved partly through NCOA4 mediated mitophagy.



Reference

Wang R, Li J, Fu Y, et al. Ferritinophagy-mediated apoptosis and paraptosis induction involved MAPK and PI3K/AKT pathway in mechanism of an iron chelator. Biochem Pharmacol. 2023;218:115874.

The growth inhibition induced by a dithiocarbamate derivative in melanoma cells involves NCOA4-mediated ferritinophagy

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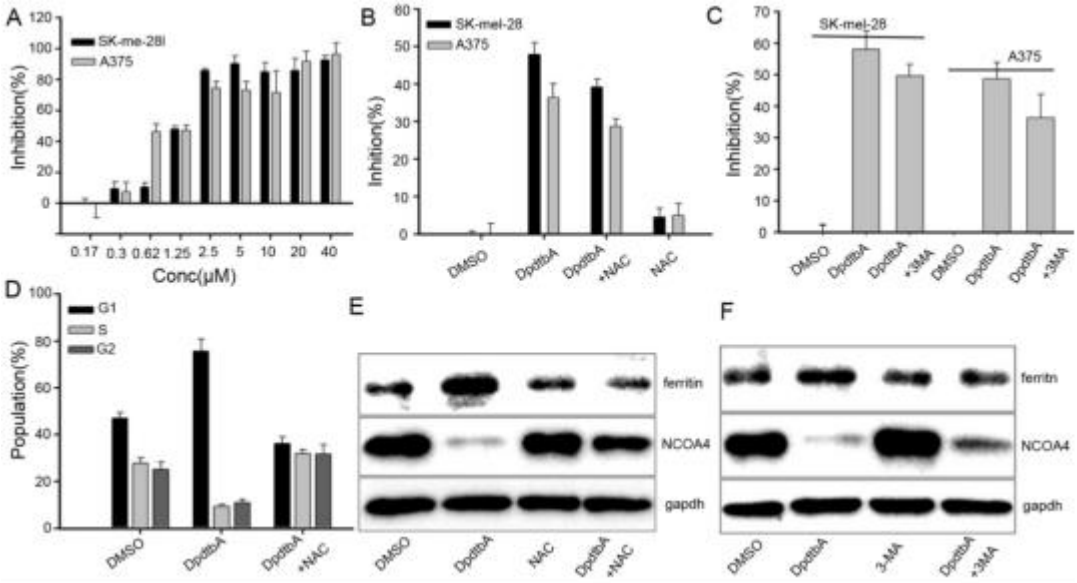
Melanoma is a common malignant tumor with poor treatment outcomes in clinical practice. In addition, melanoma cells have inherent resistance to ferroptosis, which limits the clinical application of ferroptosis inducers. 2,2 '- Dipyridylketon hydrazone dithiocarbamate s-butyric acid (DpdtbA), a dithiocarbamate derivative exhibited excellent inhibitory effects on melanoma cells (Fig. A: IC50 = 1.2 ± 0.2 μM for SK-Mel-28 cells); IC50 = 2.50 ± 0.1 μM for A375 cells). The ROS role in the growth inhibition was further assayed. The result shows that the ROS scavenger NAC can significantly reduce the inhibitory effect of the agent (Fig. B). In addition, autophagy inhibitor, 3-MA can also weaken the inhibitory effect of the agent (Fig. C). The cell cycle analysis showed that DpdtbA treatment can cause G1 arrest (Fig. D). Preliminary studies on the mechanism showed significant changes in NCOA4 and ferritin before and after the treatment (Fig. E), indicating that the inhibitory effect of the agent involved ferritinophagy. Pretreatment with ROS scavenger NAC can significantly counteract the agent's regulation of the aforementioned genes (Fig. E). Similarly, treatment with 3-MA can counteract the induction effect of the agent (Fig. F), which clearly indicates that the inhibitory effect of the drug is related to ferritinophagy and it may lead to ferroptosis. In summary, all the data indicate that the excellent biological activity of DpdtbA is related to its ability in ferritinophagy induction, and the detailed mechanism needs further investigation.



References

Wang R, Li J, Fu Y, et al. Ferritinophagy-mediated apoptosis and paraptosis induction involved MAPK and PI3K/AKT pathway in mechanism of an iron chelator. Biochem Pharmacol. 2023;218:115874.

Screening and evaluation of new drugs targeting ABCB8 for anti-renal fibrosis

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Abstract

Renal fibrosis is the common outcome of many chronic kidney diseases (CKD). The characteristics of renal fibrosis are the increase of matrix production, inhibition of matrix degradation, modulation of matrix receptors to facilitate cell–matrix interactions, mesangial cell and fibroblast activation, tubular epithelial-to-mesenchymal transition (EMT) and myofibroblast activation. Although it has been proven that the plasticity of tubular epithelial cells and the proliferation of interstitial fibroblasts are the two main factors in renal fibrosis, there is still no effective therapeutic approaches to renal fibrosis. In our previous study, we found that ABCB8 plays an important role in renal fibrosis and may be a potential target for treating renal fibrosis. Here, we used virtual screening of small molecule compounds targeting human ABCB8 to identify three natural products with high docking scores, and evaluated their anti-renal fibrosis effects. Preliminary findings suggest that these natural products have a certain improvement effect on EMT and mitochondrial dysfunction. Therefore, targeting ABCB8 for the treatment of renal fibrosis may be a potential direction.

The Mechanisms of Polygoni Multiflori Radix Processed With Black Bean Juice in Improving Alzheimer's Disease Based on Multi-Omics

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Objective: To investigate the mechanisms of Polygoni multiflori radix processed with black bean juice in improving Alzheimer's disease base on multi-omics. Methods: Network pharmacology was used to predict the potential mechanisms, and serum pharmacochemistry, behavioral experiment, and multi-omics approaches were used to validate the effects of Polygoni multiflori radix processed with black bean juice in improving Alzheimer's disease. Results: After processed, 12 special ingredients were more in the serum of processed Polygoni multiflori radix than raw Polygoni multiflori radix. It improved short-term memory, novel object recognition, and spatial memory in APP/PS1 mice. 10 differential metabolites, which were mainly enriched in glycolysis pathway and pentose phosphate pathway, were up-regulated or back regulated, alleviated energy supply deficiencies in brain tissue. By altering the gut microbiota structure and species richness, Lactobacillus johnsonii and Faecalibaculum rodentium became dominant, increased expression of ZO-1 and Occludin proteins in the colon, maintained intestinal barrier integrity. Additionally, it elevated levels of BDNF and NGF in brain tissues, provided neuroprotective effects through the "gut-brain" axis. Moreover, it adjusted the β-CTF/(β-CTF+α-CTF) ratio in the brain, reduced Aβ deposition in the hippocampus and cortex while increased the density of pyramidal cell arrangements in the CA1 region and the thickness of the dentate gyrus. Conclusion: Polygoni multiflori radix processed with black bean juice improves cognitive ability by enhancing cerebral energy metabolism, modifying gut microbiota structure, maintaining intestinal barrier integrity, increasing APP metabolism via the non-amyloidogenic pathway, and reducing Aβ deposition in the brain.

Construction and Computational Model of Spatiotemporal Memory Based on Spike Generation

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英文摘要：Understanding and modeling how the biological brain processes spatiotemporal information and constructs memory is crucial for advancing cognitive science and artificial intelligence. We propose a spike-generative model system based on latent variable models to simulate and compute spatiotemporal memory. This system comprises two components: an inference model, which calculates latent variables from observational data and simulates the short-term memory (STM) process; and a generative model, which associates these variables with memory activities or patterns to simulate long-term memory (LTM). Given the complexity of detailed parameters involved in memory processes, our approach effectively infers latent variables from limited data points, demonstrating strong reasoning and generative capabilities in complex scenarios. This not only offers a novel perspective for understanding brain function but also provides a critical computational framework for advancing cognitive neuroscience.

Deficiency of secreted phosphoprotein 1 impairs microglia function via compromising oxidative phosphorylation

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Abstract

Microglia were the primary immune cells of the central nervous system, responsible for phagocytosis and regulating immune responses, thereby maintaining brain homeostasis. However, the molecular mechanisms that regulated microglia function remained unclear. Secreted phosphoprotein 1 (Spp1) was a multifunctional protein that had been increasingly recognized in recent years for its association with altered microglia function in various central nervous system diseases. Although the role of microglia -derived Spp1 in disease contexts had been studied, how it regulated microglia function under normal physiological conditions was still not fully understood. In the present study, we found that Spp1 was highly expressed in the brain, particularly in microglia, during both early postnatal and aging stages—two critical periods when microglial behavior influenced brain development and supported brain function during aging. We further demonstrated that microglia-specific knockdown of Spp1 impaired phagocytosis, triggered pro-inflammatory cytokine secretion, and induced microglial senescence. In addition, Spp1 knockdown in microglia exacerbated neuroinflammation and memory impairments. Mechanistically, we revealed that Spp1 deficiency compromised microglial oxidative phosphorylation by inhibiting the AKT/PGC-1α/mitochondrial complex I pathway. Notably, administration of the phospho-AKT agonist SC79 rescued the microglial dysfunction induced by Spp1 deficiency. In conclusion, this study was the first to demonstrate that Spp1 deficiency impaired microglial function by disrupting oxidative phosphorylation, while treatment with a phospho-AKT agonist restored microglial function. Our study provided novel theoretical insights into the role of microglia-derived Spp1 in maintaining brain homeostasis.

CBMC-V2: A CNS-inspired Framework For Real-time Robotic Arm Control

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Abstract

In recent years, bio-inspired control algorithms for robotic arms have gained significant attention due to their adaptability. This paper introduces a real-time framework based on CBMC to control a 7-DOF robotic arm using a neuromorphic chip. The proposed framework consists of five modules: cerebral sensory cortex, cerebral motor cortex, cerebellum, brainstem, and spinal cord. These modules operate within a hierarchical structure with three control loops running at different frequencies. The effectiveness of our approach is validated through trajectory tracking control tasks in simulation. The algorithm is then deployed on a neuromorphic chip and tested on a robotic arm platform. Experimental results demonstrate the superior control effectiveness and robustness of our methodology in complex tasks compared to the previous version.

Melatonin improves postharvest passion fruit quality by regulating antioxidant and ethylene synthesis

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Abstract

Passion fruit tends to undergo rapid aging during the postharvest stage, necessitating the discovery of effective treatments to delay senescence. Melatonin was the focus of this study, which aimed to investigate its effects on postharvest passion fruit ripening and peel aging. The results showed that compared to the control group, exogenous melatonin treatment effectively delayed the degradation of antioxidants in postharvest passion fruit. It also inhibited ethylene biosynthesis and the respiration rate, while inducing the expression of genes related to antioxidant enzymes and ethylene biosynthesis. On the other hand, treatment with the melatonin synthesis

inhibitor p-CPA suppressed the biosynthesis of endogenous melatonin in passion fruit. In summary, this study emphasizes the positive impact of melatonin on antioxidant capacity and its inhibitory effect on ethylene biosynthesis, as well as the factors influencing the quality of postharvest passion fruit.

Keywords: Passion fruit; Melatonin; Postharvest; Quality; Antioxidant metabolism

Polychaete diversity in the Hainan intertidal zone

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Abstract

Polychaete is one of the dominant groups of marine benthic macrofauna. It contains about 80 families or groups with over 2,1000 valid species worldwide. Hainan is the only tropical island in China and has a high diversity of marine creatures, but limited records of polychaetes. Recently, we did a survey of polychaetes in the intertidal zone in Hainan. Specimens covering 18 families were collected. There are different taxon from different types of sediment. For example, Maldanidae and Capitellidae are dominant in the intertidal zone with mangrove, and Eunicidae and Terebellidae are dominant in rocky beach. Our work will help us better understand the biodiversity of polychaete in Hainan.

Keywords: Polychaeta; Biodiversity; Macrobenthos

Immunomodulation effects of isochlorogenic acid A from apple on RAW264.7 cells *via* modulation of TLR2 and TLR4 target proteins

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Abstract:

Background The sub-health caused by immune disorders due to shifts in contemporary dietary patterns and food consumption habits has become a major threat to human health. The immune level of the body should be adjusted bidirectionally so that the molecules in the body can coordinate with each other to maintain immune homeostasis in the body. Therefore, The incorporation of nutrients with immunomodulatory properties into the daily diet has emerged as a pressing health requirement.

Methods The aim of this study was to screen apple polyphenols with activity in modulating immune homeostasis in the body. Molecular docking technique was used to screen apple polyphenols that bind tightly to TLR2 and TLR4. The apple polyphenols with high docking scores were subjected to ADMET, water solubility, and toxicity prediction for screening polyphenols with potential immunomodulatory activity. Then the cellular assays were used to assess the immunomodulatory activity of apple polyphenols with potential immunomodulatory activity. And the binding mechanism between apple polyphenols and TLR2 and TLR4 was investigated.

Results The results showed that isochlorogenic acid A of apple polyphenols had high docking scores with TLR2 and TLR4. The isochlorogenic acid A exhibited favorable ADMET properties and water solubility. Cellular assays results showed that isochlorogenic acid A enhanced the viability of RAW264.7 cells and promoted the expression of NO, TNF-α, IL-1β, TLR2, and TLR4 in cells, and inhibited the expression of NO, TNF-α, IL-6, TLR2, and TLR4 in inflammatory cells. The isochlorogenic acid A bound to residues Phe325, Phe349, Leu350 and Pro352 of TLR2 by hydrogen bonding and hydrophobic interactions, and to residues Val82, Arg90, Ser127, Cys133 and Ser441 of TLR4-MD-2 *via* π-alkyl and hydrogen bonds. In summary, the immunoreceptors TLR2 and TLR4 play a crucial role as recognition receptors for isochlorogenic acid A of apple polyphenols in the regulation of cellular immune response and inflammation.

Keywords ： apple polyphenols, isochlorogenic acid A, TLR2, TLR4, immunomodulatory

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The abnormal changes of hippocampal synaptic plasticity in TLE rats associated with inhibition of the RhoA/Rock2 pathway

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Abstract Temporal lobe epilepsy (TLE) is the most prevalent form of refractory epilepsy, accompanied by cognitive dysfunction in patients. Its main pathological mechanism involves abnormal alterations in hippocampal synaptic plasticity (HSP), the changes in dendritic spines (DS) is a key component. The activation of the RhoA/ROCK2 pathway has been implicated in regulating DS plasticity, but in the progress of epilepsy, there is inconsistent literature reporting on the activation of this pathway. So further elucidation of the characteristics of aberrant changes of HSP and the activation of the RhoA/ROCK2 pathway will be of great value for TLE treatment research. We utilized the IntelliCage behavioral system finding that the spatial, punitive learning and memory, recognition memory, as well as novelty-seeking behavior reduced. Moreover, we observed that in the early stages of TLE, there was an increase in the number of newly generated granule cells in the subgranular zone of the hippocampus, however these newly generated granule cells underwent changes in polarity, the formation and maturation of DS decreased, which formed synapses in shorter synaptic surfaces, narrower synaptic clefts, and a decrease in postsynaptic density. Further research indicated that during the progress of epilepsy, there was abnormal inhibition of the RhoA/Rock2 pathway and a significant decrease in F-actin/G-actin ratio. Therefore, we speculated that the abnormal alterations in HSP and cognitive impairment during TLE progress may be associated with aberrant inhibition of the RhoA/Rock2 pathway and the imbalance in F-actin/G-actin ratio. The results could provide new insights for the pathological mechanism and treatment research in TLE.

海南大学-任非-墙报摘要及作者信息（墙报编号：H-20）

Polysaccharides from *Alpinia oxyphylla* fruit prevent hyperuricemia by inhibiting uric acid synthesis, modulating intestinal flora and reducing renal inflammation

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Discovery of Novel Fedratinib-Based HDAC/JAK/BRD4 Triple Inhibitors with Remarkable Antitumor Activity against Triple Negative Breast Cancer

封面：见附件

墙报：见附件

领域：药理学

关键词：Anti-tumor|Triple target inhibitors|Triple-negative breast cancer|apoptosis

摘 要 ： Multitarget HDAC inhibitors capable of simultaneously blocking the BRD4-LIFR-JAK1-STAT3 signaling pathway hold great potential for the treatment of TNBC and other solid tumors. Herein, novel Fedratinib-based multitarget HDAC inhibitors were rationally designed, synthesized, and biologically evaluated, among which compound 25ap stood out as a potent HDAC/JAK/BRD4 triple inhibitor. Satisfyingly, compound 25ap led to concurrent inhibition of HDACs and the BRD4-LIFR-JAK1- STAT3 signaling pathway, which was validated by hyperacetylation of histone and α-tubulin, hypo-phosphorylation of STAT3, downregulation of LIFR, MCL-1, and c-Myc in MDA-MB-231 cells. The multitarget effects of 25ap contributed to its robust antitumor response, including potent antiproliferative activity, remarkable apoptosis-inducing activity, and inhibition of colony formation. Notably, 25ap possessed an acceptable therapeutic window between normal and cancerous cells, desirable in vitro metabolic stability in mouse microsome, and sufficient in vivo exposure via intraperitoneal administration. Additionally, the in vivo antitumor potency of 25ap was demonstrated in an MDA-MB-231 xenograft model.

正文：

总结：In summary, a novel series of Fedratinib-based HDAC/JAK/ BRD4 triple inhibitors were rationally designed, synthesized, and biologically evaluated. As expected, these HDAC/JAK/ BRD4 triple inhibitors showed more potent antitumor activity against TNBC than the approved HDAC inhibitor SAHA. The anti-TNBC potency of one target compound 25ap was further well-established by apoptosis assay and colony formation assay. Mechanism study confirmed that 25ap could effectively block the BRD4-LIFR-JAK1-STAT3 signaling pathway involved in resistance to HDAC inhibitors.

More importantly, the acceptable toxicity and promising in vivo antitumor potency made 25ap a valuable antitumor lead compound, which warrants further research and development.

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General-purpose Dataflow Model with Neuromorphic Primitives

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Neuromorphic computing exhibits great potential to provide high-performance benefits in various applications beyond neural networks. However, a general-purpose program execution model that aligns with the features of neuromorphic computing is required to bridge the gap between program versatility and neuromorphic hardware efficiency. The dataflow model offers a potential solution, but it faces high graph complexity and incompatibility with neuromorphic hardware when dealing with control flow programs, which decreases the programmability and performance. Here, we present a dataflow model tailored for neuromorphic hardware, called neuromorphic dataflow, which provides a compact, concise, and neuromorphic-compatible program representation for control logic. The neuromorphic dataflow introduces "when" and "where" primitives, which restructure the view of control. The neuromorphic dataflow embeds these primitives in the dataflow schema with the plasticity inherited from the spiking algorithms. Our method enables the deployment of general-purpose programs on neuromorphic hardware with both programmability and plasticity, while fully utilizing the hardware's potential. The main contributions of this paper are: 1) We analyze the control logic of von Neumann programs from a neuromorphic perspective and devise the "where" and "when" primitives. 2) We propose a concise, neuromorphic compatible, programmable, and learnable neuromorphic dataflow model for general programs with control flows.

Exploration of Interstitial Cystitis-derived Bladder Stem Cells in Stemness Maintenance and Function

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Abstract: Interstitial cystitis (IC) is a chronic inflammatory disease, characterized by the main clinical symptoms such as frequent urination, urgency, and pain in the pelvic and perineal areas, accompanied by fibrosis of the bladder wall and deterioration of the barrier function, which already affected the patients' quality of life. The pathogenesis of IC has not been elucidated, and diagnostic criteria are vague, and treatment is challenging, which may lead to misdiagnosis or delayed treatment. Stem cell therapy has been attempted in the treatment of IC, but the therapeutic effects are not significant. Previous investigations on uroepithelial injury and epithelial regeneration have shown that uroepithelial cells initiate a rapid repair and regeneration process when the bladder is damaged. However, there is still a lack of comprehensive understanding of the types of basal cells in the bladder mucosal layer and their interactions in the repair process after bladder injury. From the perspective of bladder mucosal regeneration, we tested the self-replication ability by colony formation rate and growth curve, which found no significant difference between the disease group and the normal control group. Also, we use immunofluorescence staining and single-cell sequencing to analyze the cell sub-populations, and the results predict the presence of cellular heterogeneity in the mucosal layer. Furthermore, we will construct an in vivo differentiation model to explore the differentiation potential of bladder stem cells. This study aims to preliminarily observe the activity and function of bladder stem cells in patients, providing a theoretical basis for in-depth analysis of the pathogenic mechanism and the development of radical intervention strategies.

Opioid Peptide System Regulates Behavior and POMC Expression in Fructose-Preferring Rats

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This study investigates the impact of the opioid peptide system on the feeding and exercise behaviors of fructose-preferring rats. A fructose preference model was established using a metabolic analysis system (Columbus, USA) and an active running wheel system to monitor the rats' feeding, drinking, spontaneous activity, and exercise behaviors. The results indicated that, compared to the control group, the fructose intake of the model group rats increased significantly and decreased after naloxone treatment. Fructose consumption enhanced the spontaneous activity of the rats, while naloxone reduced their activity levels. Additionally, fructose feeding decreased the overall exercise volume of the rats, which was restored following naloxone treatment. These findings highlight the central role of the opioid peptide system in regulating the feeding and exercise behaviors of fructose-preferring rats.

Further research on the regulatory effects of glucose on the expression levels of pro-opiomelanocortin (POMC) derived neuropeptides in the lateral hypothalamus (LH) and nucleus accumbens (NAc) of fructose-preferring rats revealed that the expression levels of these neuropeptides in the LH and NAc regions changed following glucose intake, but not after saccharin intake. The data suggest that the opioid peptide system plays a role in the reward mechanisms of fructose-preferring rats, as well as in the regulation of their spontaneous activity and exercise behavior. Furthermore, glucose intake may influence these behaviors by modulating the expression of POMC-derived neuropeptides. This study offers a new perspective on the neuroendocrine mechanisms underlying abnormal feeding and exercise behaviors and identifies potential targets for treatment strategies.

Keywords:Opioid peptide system, Feeding behavior, POMC-derived neuropeptides, Reward mechanisms,

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High-Throughput Screening for Inhibitors of HIV-1 Vpu and Host Factors Interact

Abstract

Acquired immunodeficiency syndrome (AIDS) is a malignant infectious disease caused by human immunodeficiency virus (HIV), which causes severe destruction of immune function and eventually leads to opportunistic infections and tumors. Viral protein U (Vpu), an HIV-1 accessory protein, antagonizes or hijack a variety of host factors to allow the virus to evade host immune surveillance and facilitate viral release. Thus, blocking the interaction between Vpu and host factors will provide a promising strategy for anti-HIV therapy. Here, we report a NanoLuc Binary Technology (NanoBiT) based high-throughput screening assay to detect inhibitors that disrupt the Vpu-host target interaction. Out of more than 1000 compounds screened, eight inhibitors were identified with strong activity at nontoxic concentrations. In subsequent cell-based BST-2 and RXXX degradation assays, inhibitor YXXXXX and AXXXXX restored the cell-surface and total cellular level of BST-2 and RXXX in the presence of Vpu. Furthermore, the Vpu-mediated enhancement of pesudotyped viral particle production was inhibited by YXXXXX and AXXXXX. Our findings indicate that our newly developed assay can be used for the discovery of potential antiviral molecules with novel mechanisms of action.

Background

Acquired immunodeficiency syndrome (AIDS) is a malignant infectious disease caused by human immunodeficiency virus (HIV), which causes severe destruction of immune function and eventually leads to opportunistic infections and tumors.

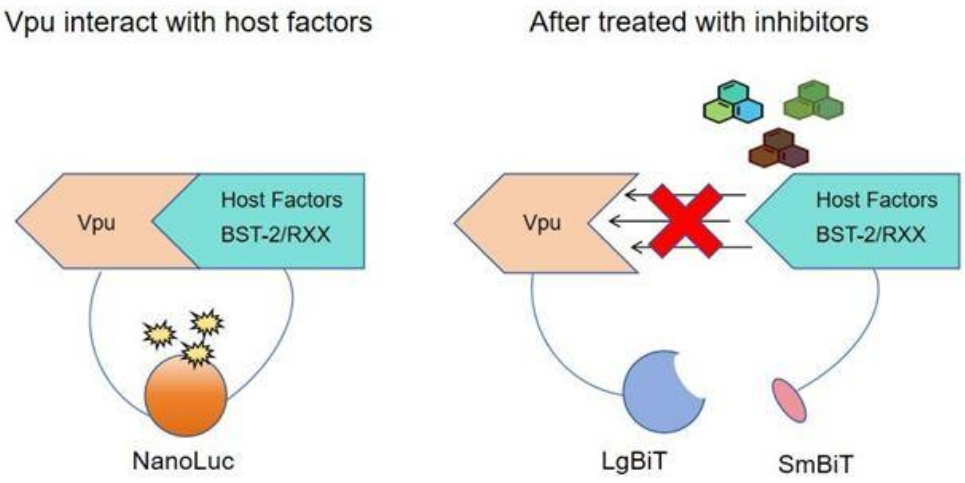
Viral protein U (Vpu), an HIV-1 accessory protein, antagonizes or hijack a variety of host factors to allow the virus to evade host immune surveillance and facilitate viral release.

NanoLuc Binary Technology (Nano-BiT) is a luciferase-based complementation reporter system that is widely used for the quantitative analysis of protein–protein interactions.

Here, we report a NanoBiT based high-throughput screening assay to detect inhibitors that disrupt the Vpu-host target interaction.

Conclusions

Using NanoBiT technology, we developed two high-throughput screening assay to monitor Vpu-host factors interactions in live cells. We identified eight compounds with inhibitory activity against the Vpu-host factor interaction. We further revealed that compounds, YXXXXX and AXXXXX inhibited viral particle production. Therefore, our study suggests a new application of NanoBiT technology in the development of novel antiviral drugs.



Spiking Structured State Space Model for Monaural Speech Enhancement

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Abstract

Speech enhancement seeks to extract clean speech from noisy signals. Traditional deep learning methods face two challenges: efficiently using information in long speech sequences and high computational costs. To address these, we introduce the Spiking Structured State Space Model (Spiking-S4). This approach merges the energy efficiency of Spiking Neural Networks (SNN) with the long-range sequence modeling capabilities of Structured State Space Models (S4), offering a compelling solution. Evaluation on the DNS Challenge and VoiceBank+Demand Datasets confirms that Spiking-S4 rivals existing Artificial Neural Network (ANN) methods but with fewer computational resources, as evidenced by reduced parameters and Floating Point Operations (FLOPs).

Enhancing Chip Design Efficiency: Accurate Routing Congestion Prediction Using Spiking Neural Network

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Routing congestion is a critical concern that detrimentally impacts chip performance, necessitating substantial time investment in detection and alleviation during the chip design process. Predicting congestion on the netlist significantly reduces time consumption by obtaining routing feedback immediately after design completion without going through subsequent steps. However, the constraints on chip production imposed by design specifications significantly influence routing, and it is ignored by previous studies, resulting in imprecise predictions and sub-optimal optimization. In this study, we design a heterogeneous graph introducing the influence of design specifications to aid netlist congestion prediction. Subsequently, we develop a spiking neural network that uses a two-level attention mechanism to capture the effects of netlist structure and design specifications. Experimental results demonstrate our method achieves fast and accurate congestion prediction with up to 19$\%$ accuracy improvement and 5.22$\times$ prediction speedup. To the best of our knowledge, it is the first work that integrates design specifications, enabling a comprehensive prediction of congestion arising from both the netlist structure and the design specifications.

Fermented Beverages (FH03) Inhibit Hypertrophy in High-fat Diet Rats: Reduce Appetite and Increase the Expression of Brown Fat Thermogenic Genes and Proteins

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Abstract: The increasing consumption habits and intake of sugary beverages have promoted the high incidence of obesity. Our previous studies showed that fermented drinks (FH03) have good flavor and anti-obesity efficacy in vitro, but the efficacy and mechanism in vivo are unclear. This study investigated the possible mechanism of FH03 in a high-fat diet (HFD) -induced obesity rat model of energy intake and energy consumption. The results showed that after 4 weeks, FH03 intervention significantly suppressed the weight gain and reduced the liver fat accumulation in obese rats (P<0.05), significantly promoted adiponectin secretion, reduced serum leptin levels, and increased insulin sensitivity (P<0.05). The FH03 intervention also significantly increased intestinal butyrate levels and serum appetite-promoting glucagon-like peptide-1 (GLP-1) levels, and conversely significantly reduced appetite-promoting neuropeptide Y (NPY) levels and average daily feed intake (P<0.05). RT-PCR and immunohistochemical analysis showed that the FH03 intervention significantly increased the gene and protein expression of the key thermogenic factor uncoupling protein (UCP-1) (P<0.05). Taken together, these results suggest that FH03 intervention may suppress HFD-induced obesity in rats through the effects of multiple targets such as reducing energy intake and increasing caloric expenditure.

Applications of BCI and VR in Cognitive Diagnosis and Treatment

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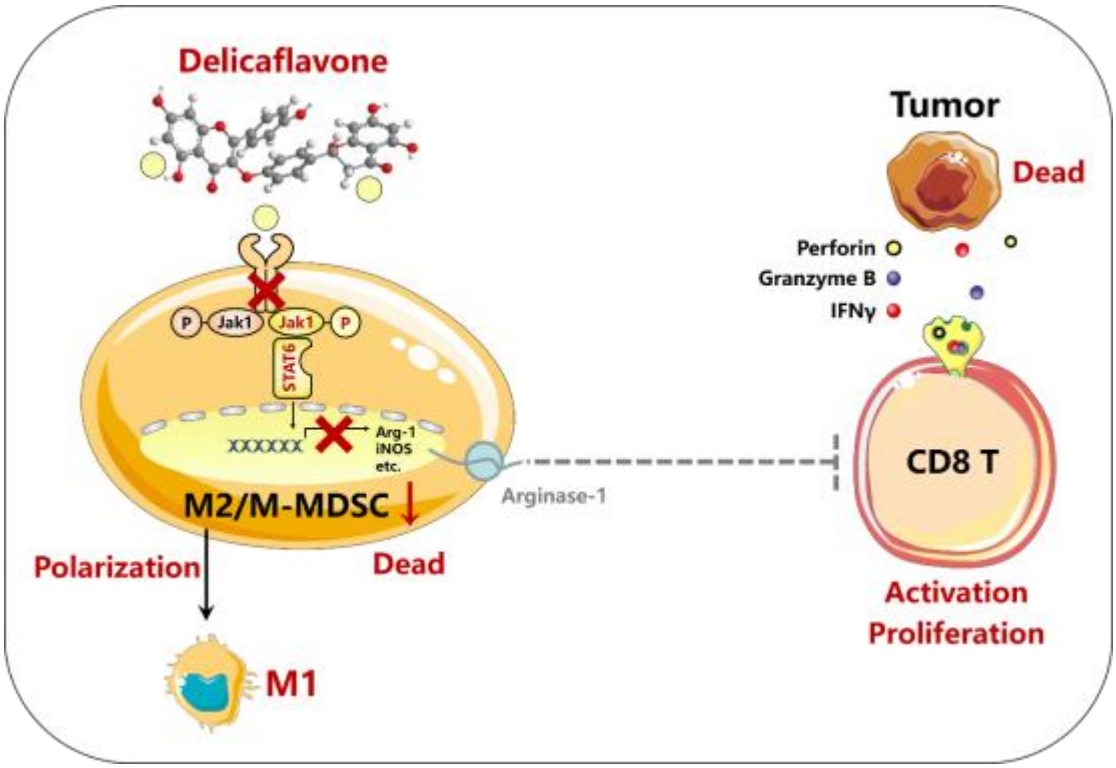
ABSTRACT Cognition encompasses essential processes such as attention, memory, and emotion, which are fundamental to the way humans acquire and apply knowledge. With the rapid aging of the global population, cognitive impairments, including Mild Cognitive Impairment (MCI), Alzheimer's Disease (AD), and dementia, have emerged as significant public health concerns. Early diagnosis and effective treatment of these cognitive impairments are crucial for improving patients' quality of life and reducing the societal burden associated with these conditions. However, traditional diagnostic and therapeutic methods, such as pharmacotherapy, Functional Magnetic Resonance Imaging (fMRI), and Functional NearInfrared Spectroscopy (fNIRS), face challenges including low diagnostic accuracy, limited efficacy, and a lack of comprehensive assessment tools. The integration of Brain-Computer Interface (BCI) and Virtual Reality (VR) technologies offers innovative solutions for cognitive diagnosis and treatment. BCI facilitates the exchange of information between the brain and external devices by analyzing brain signals, allowing for applications such as the rehabilitation of motor function disorders. VR, by creating immersive and interactive environments, provides realistic experiences that can be used for cognitive training and rehabilitation. The combination of BCI and VR technologies enhances the effectiveness of cognitive interventions by providing multi-sensory stimulation and real-time feedback, making these interventions more engaging and potentially more effective. This paper reviews

the current applications of BCI and VR technologies in cognitive diagnosis and treatment. It introduces various BCI diagnostic methods based on EEG, fMRI, and fNIRS, as well as VR-based diagnostic methods, and discusses the advantages and limitations of these technologies. Additionally, the paper explores the contributions of cross-individual, cross-scenario, and cross-task EEG signal analysis to the precision and effectiveness of cognitive impairment assessment. The review highlights the significant potential of BCI-VR technology in various cognitive therapy domains, including cognitive behavioral therapy, memory and attention training, neurorehabilitation, and emotion regulation. The discussion also acknowledges the challenges faced by BCI-VR technology, such as device complexity, the need for personalized design, and the limitations of experimental samples. Despite the promising outlook for BCI-VR technology, several challenges remain. The complexity of the devices, the lack of customization in virtual environments, and the adaptability of these systems across different individuals and scenarios are key issues that need to be addressed. The paper suggests that future research should focus on the miniaturization and cost reduction of BCI-VR devices, the development of multimodal BCI systems, and the application of large language models to enhance the functionality and accessibility of these technologies. Furthermore, the importance of strengthening collaboration among government, industry, academia, research institutions, and the medical field is emphasized as a critical factor in advancing the clinical translation of BCI-VR technology for cognitive diagnosis and treatment. The review concludes that while traditional methods have paved the way for understanding cognitive impairments, BCI-VR technologies hold the potential to revolutionize both the diagnosis and treatment of these conditions. By overcoming current technical challenges and fostering interdisciplinary cooperation, BCI-VR systems could become integral tools in the global effort to improve cognitive health and enhance the lives of individuals affected by cognitive disorders.

Delicaflavone reactivates anti-tumor immune responses by abrogating monocytic myeloid cell-mediated immunosuppression

Graphical abstract

A flavone monomer isolated from *Selaginella doederleinii*, named Delicaflavone，blocks Jak1/STAT6 signaling pathway in immunosuppressive monocytic myeloid cells, including M2-TAMs and M-MDSCs. Delicaflavone restrains the viability and immunosuppressive proporties of M-MDSCs and M2-TAMs, as well as re-educates the remaining M2-TAMs into M1 like phenotype, thus abrogating these monocytic myeloid cell-mediated T cell suppression. The restored T cells contribute to the anti-tumor effect of Delicaflavone.



rTMS promoted brain-derived nerve regeneration and regulates the functional reconstruction in rats after neural network tissue transplantation

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Spinal cord injury (SCI) causes the interruption of the brain-spinal cord nerve conduction and retrograde neurodegeneration, which greatly restricts functional reconstruction. In this study, we constructed neural network (NN) tissue based on engineering strategy using gene-modified neural stem cells (NSCs). Noninvasive repetitive transcranial magnetic stimulation (rTMS) combined with NN tissue transplantation was used to treat for transsectional SCI rats. The results showed that rTMS could inhibit inflammation and the apoptosis of somatosensory motor cortex (SMC) neurons, activate SMC neurons and improve their regeneration ability. In fact, the results showed that rTMS treatment could not only promote the axonal regeneration of corticospinal tract (CST), but also promote the axon regeneration of 5-HT positive nerve fibers forming synaptic connection with the transplanted neurons, ultimately enhancing motor evoked potential and improving the motor function of the paralyzed limb. These results indicated that rTMS further enhanced the potential of transplanted neurons to relay brain-derived neural information by regulating the axonal regeneration of CST and 5-HT positive nerve fibers, thus promoting the recovery of motor function of the hind limbs. Therefore, rTMS combined with engineering NN tissue transplantation is expected to provide a new strategy of SCI treatment. This study also provides a reference for formulating a combined treatment strategy of tissue engineering and neural stimulation to address central nervous system injuries.

Brain-inspired Simultaneous Localization and Mapping via Integrating Event Camera and IMU

Jiarui Dou[1], Fangwen Yu[2], Xianlei Long[1], Fuqiang Gu[1,*]

Abstract: Visual Simultaneous Localization and Mapping (SLAM) is a popular positioning method for robots, which has been successfully applied to a variety of tasks such as grasping and unmanned inspection. However, most existing visual SLAM methods suffer from low accuracy, poor robustness, and positioning failure in challenging environments such as texture-less or dim scenes. To address these challenges, we present EvBrainSLAM in this study, a novel brain-inspired visual SLAM that integrates event camera and Inertial Measurement Unit (IMU). Different from existing visual SLAM approaches, which use either graph optimization or filtering methods for pose estimation, EvBrainSLAM estimates the position of the robot using a Continuous Attractor Neural Network (CANN). This makes it have better positioning accuracy and robustness especially in the challenging environemnts.

Index Terms—Biologically inspired navigation, event camera, intelligent robotics, SLAM

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Insulin-like Growth Factor 1 Receptor Inhibits the Proliferation of Acute Myeloid Leukaemia Cells via NK Cell Activation

摘要：

Acute myeloid leukaemia (AML) denotes a heterogeneous category of cancers occurring within the bone marrow that are initiated by the unrestricted proliferation of hematopoietic stem cells. Various factors effectuate the dysregulation of AML cell proliferation; for instance, the upregulation of insulin-like growth factor 1 receptor (IGF1R) within AML cells influences their proliferation. However, there is a current dearth of research assessing the association between IGF1R and prognostic risk as well as its potential as an AML immunotherapeutic. This study aims at elucidating the role of IGF1R in AML progression and evaluating its prognostic value. To this end, RNA-sequencing (RNA-seq) data from The Cancer Genome Atlas (TCGA) database was analysed to compare IGF1R expression between AML and normal tissues. Moreover, a Kaplan—Meier survival analysis was performed to determine whether IGF1R is correlated with patient overall survival (OS). TCGA data revealed an upregulation of IGF1R expression in the peripheral blood of AML patients compared to that in healthy individuals. IGF1R expression was positively correlated with patient OS. Additionally, elevated IGF1R expression promotes NK cell expansion and enhances its functional activation, thereby inhibiting AML cell proliferation. Collectively, these findings highlight the clinical potential of IGF1R in the effective treatment of AML through the activation of NK cell proliferation and function and present it as a potential predictive marker of AML prognosis.

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20(*R*)-ginsenoside Rg3 alleviates the progression of Alzheimer's disease by inhibiting apoptosis *via* regulation of the Ras signaling pathway

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ABSTRACT: 20(*R*)-ginsenoside Rg3 [20(*R*)-Rg3], a bioactive component of *Panax notoginseng*, exhibits diverse biological activities, but its neuroprotective mechanisms remain unclear. This study investigated the anti-Alzheimer's disease (AD) effects of 20(*R*)-Rg3 *in vivo and in vitro* and elucidated its underlying molecular mechanism. An integrated approach combining network pharmacology, molecular docking, surface plasmon resonance, and experimental validation was employed. 20(*R*)-Rg3 significantly enhanced the viability of $A\beta_{25\text{-}35}$-treated PC12 cells, reduced the LDH leakage and attenuated Aβ aggregation, ROS and Ca^{2+} production. In APP/PS1 transgenic mice, 20(*R*)-Rg3 ameliorated cognitive deficits, mitigated Aβ deposition, and alleviated hippocampal neuronal damage. It significantly inhibited apoptosis both *in vitro* and *in vivo* by modulating the RAS signaling pathway. These findings support the potential of 20(*R*)-Rg3 as a novel medicine food homology candidate for the treatment of anti-AD.

KEYWORDS: 20(*R*)-ginsenoside Rg3, Alzheimer's disease, Network pharmacology, Apoptosis, Ras signaling pathway

Development of a double-encapsulated essential oil of wampee nanoparticle-sodium alginate coating solution based on passion fruit preservation

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Abstract

In this study, zein-pectin nanoparticles loaded with Wampee [*Clausena lansium (Lour.) Skeels*] (WEO) were developed. It mainly focuses on exploring the effects of encapsulation time, concentration of essential oil and encapsulation temperature through one-way experiments, with particle size, PDI (polydispersity index), potential and encapsulation effciency (EE) as the optimisation parameters. Response surface modelling analysis was established to derive the optimal preparation conditions of nanoparticles. The optimised nanoparticles were characterised with particle size, potential, PDI and EE of 515.9±36.4 nm, -39.3±0.3 mV, 0.4±0.1 and 89.7±3.7%, respectively. The nanoparticle-stabilised Pickering emulsion was analysed by laser confocal microscopy. Subsequently, the coating solutions were prepared by doping the nanoparticle-stabilised Pickering emulsion into sodium alginate solution. The rheological properties of the coating solutions were determined. In addition, the coating solution was applied as a novel, safe as well as biodegradable coating agent for the preservation of passion fruit, and the physiological qualities of passion fruit were evaluated during the storage period and the relevant antioxidant enzyme activities were determined.

Revalidation of Aging-Stimulation on Protein Diffusion in U2OS Cells

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AIMS: This study aims to investigate and revalidate the asymmetric effects of accumulated damaged proteins in cells due to aging. Understanding these dynamics is crucial for elucidating the underlying mechanisms of aging and its associated pathologies.

BACKGROUND: Aging is a complex biological process characterized by various molecular and cellular changes, particularly involving proteins. Recent research has highlighted the significance of protein-based biological age clocks and core regulatory proteins in mediating aging-related cellular mechanisms, including mitochondrial function, immune responses, and gene regulation. This study employs fluorescence correlation spectroscopy (FCS) to assess the diffusion rates of fluorescently tagged GFP proteins within U2OS cells, providing insights into pathological changes associated with aging.

METHODS: U2OS-GFP cells were cultured in DMEM supplemented with 10% FBS and 1% penicillin-streptomycin. The cells were divided into two equal groups for observation. Cultures were maintained at 37°C in a humidified atmosphere with 5% CO2. For the experimental group, Blebbistatin was added to mimic aging conditions. After 24 hours, we utilized an FV3000 confocal microscope with a 60x oil immersion objective and a 488 nm laser for excitation. Initial targeting focused on vinculin-active zones, such as cellular membranes and adhesion sites, with laser intensity reduced to 0.02% for data collection. The autocorrelation function (ACF) was calculated from fluorescence fluctuations over a 20-second period, with each condition measured in triplicate to ensure reproducibility.

RESULTS: Our findings revalidate previous research regarding the asymmetric

effects of accumulated misfolded or damaged proteins due to cellular aging. We employed a novel signal processing method(ACF) to enhance the accuracy of our measurements. The results indicate significant alterations in protein diffusion dynamics in aging cells, providing a clearer characterization of aging-related protein behavior. This study not only reaffirms the critical role of protein dynamics in aging but also offers new perspectives for developing targeted interventions and diagnostics for aging-related diseases.

In conclusion, this research contributes to a deeper understanding of the molecular underpinnings of aging and highlights the potential for targeted therapeutic strategies aimed at mitigating the effects of protein misfolding and accumulation in aging cells.

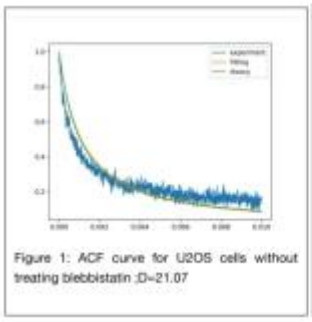


Figure 1: ACF curve for U2OS cells without treating blebbistatin ;D=21.07

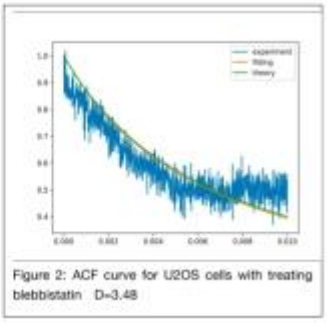
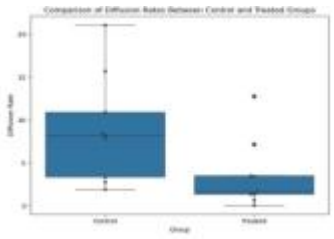


Figure 2: ACF curve for U2OS cells with treating blebbistatin D=3.48



A study on the regulatory mechanism of airway basal cells in Tracheobronchopathia Osteochondroplastica

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Airway epithelium cells are the cornerstone of lung structure and function, and airway Basal cells (BCs) maintain the balance and functional regeneration of the epithelial barrier during injury. In many lung diseases, such as chronic obstructive pulmonary disease (COPD), asthma and cystic fibrosis, BCs undergo pathological changes. Tracheobronchopathia Osteochondroplastica (TO) is a chronic respiratory disease that should not be overlooked, mainly characterizes by the presence of osseous and/or cartilaginous nodules in the submucosa of the tracheobronchial wall. Because of its non-specific respiratory symptoms and unclear etiology, it is easy to be misdiagnosed or missed diagnosis, and there is still a lack of effective treatment strategy. Based on the team's early experiments, we found that the genomic expression status, cell activity and cell differentiation ability of BCs in the TO lesion region were significantly different from those in healthy controls, suggesting that the functional abnormality of BCs in the TO lesion region originated from epigenetic changes. Therefore, in order TO further analyze the regulatory mechanism of BCs in TO, this study used CUT&Tag technology to carry out epigenetic analysis of histone modifications (H3K4me1, H3K27ac) and transcription factors (JUNB), then CRISPR/Cas9 technology was used to selectively and specifically activate or knock out cell models of upstream targets. And to verify its effect on cell function, so as to realize the correction of stem cell function.

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