Biomedical Seasonal Update
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SMART MAGAZINE

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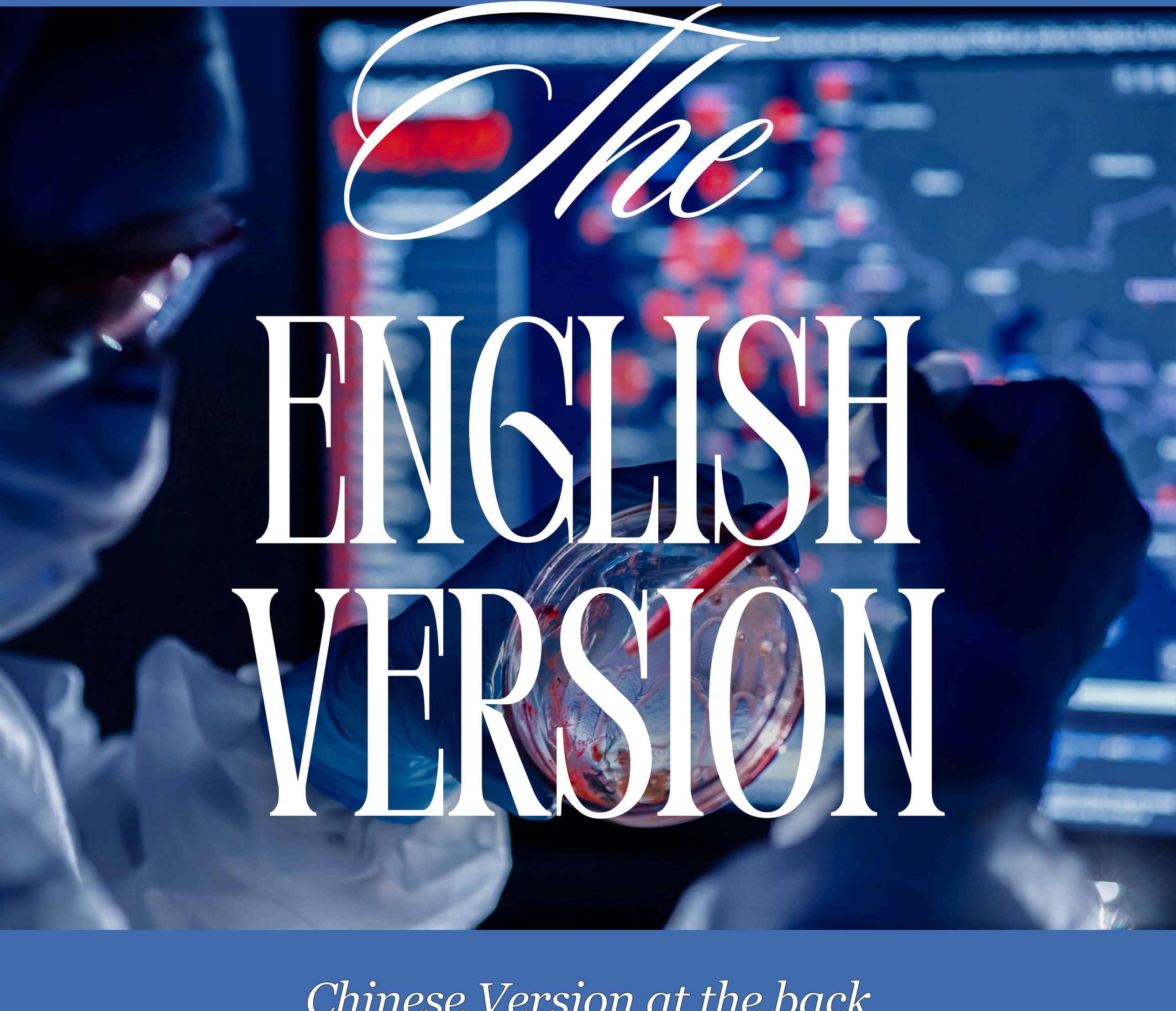

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SCIENCE MAGAZINE

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Pancreatic Caner

Introduction:

Pancreatic cancer is a formidable and often aggressive disease that arises from the cells of the pancreas, an essential organ located behind the stomach. This type of cancer is notorious for its late detection, rapid progression, and low survival rates. Pancreatic cancer can manifest in various forms, with the most common being pancreatic ductal adenocarcinoma (PDAC), which originates in the cells lining the pancreatic ducts. Symptoms of pancreatic cancer can be subtle initially, making early diagnosis challenging. As a result, understanding the risk factors, symptoms, and available treatment options for pancreatic cancer is vital in improving outcomes for those affected by this challenging condition.

1.Risk Factors

There are several non-modifiable risk factors: age, sex, blood group, and diabetes. As a person grows older his or her risk of getting pancreatic cancer increases, and the majority of the patients are over 55 years old. For sex, women are usually less susceptible to pancreatic cancer than men, and for the blood group, type O has less risk of developing pancreatic cancer than other types. This may be due to different regulations of inflammation, which affects the promotion of metastasis, in different ABO blood groups. Also, people with diabetes have a higher risk of developing pancreatic cancer.

There are also modifiable risk factors, including smoking, alcohol, and obesity. A study has shown that smokers have a 74% increased risk of pancreatic cancer. Cigarette smoke and its ingredients could increase stem cell characteristics, which allow pancreatic cells to self-renew and differentiate into different cell types. For alcohol, studies have shown that people who drink more than 30g per day have a significantly higher risk of getting pancreatic cancer than people who don’t. Also, the risk of getting cancer increases when people get obese. This is because for rapidly proliferating cancer cells, lipid oxidation, and biosynthesis are essential for cell survival. The KRAS mutation in obesity also contributes to the formation of pancreatic cancer.

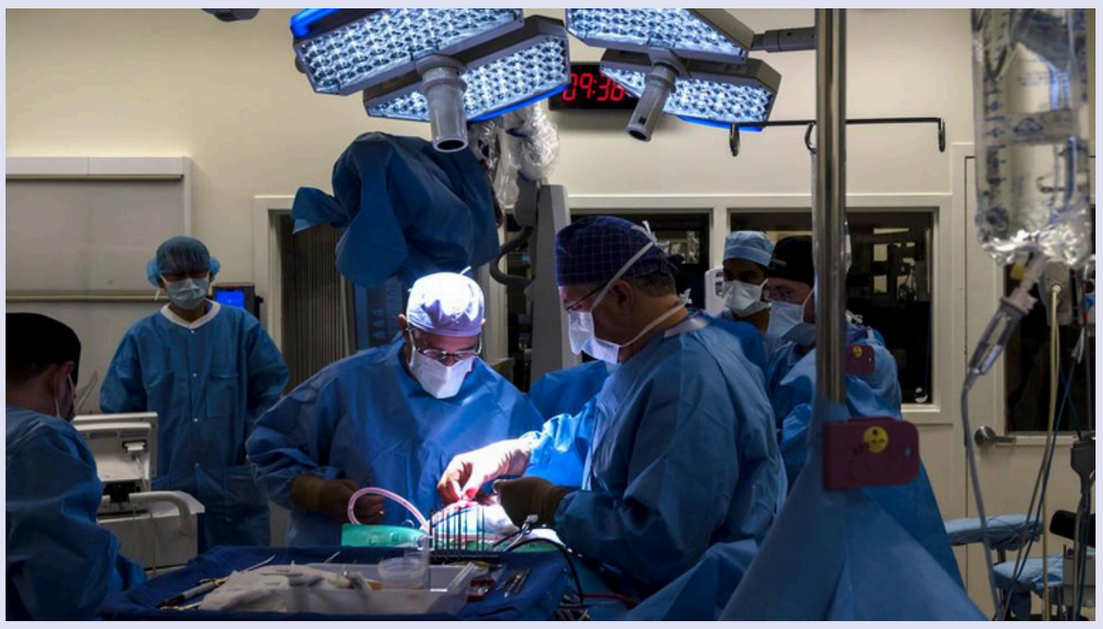
2.Symptoms

Pancreatic cancer often presents with vague and nonspecific symptoms, and that is why it is often called the "silent killer." Early-stage symptoms may include abdominal or back pain, unexplained weight loss, jaundice (yellowing of the skin and eyes), and digestive issues like nausea and changes in bowel habits. These symptoms can be subtle and easily attributed to other less severe conditions, which may lead to delayed diagnosis and treatment initiation.

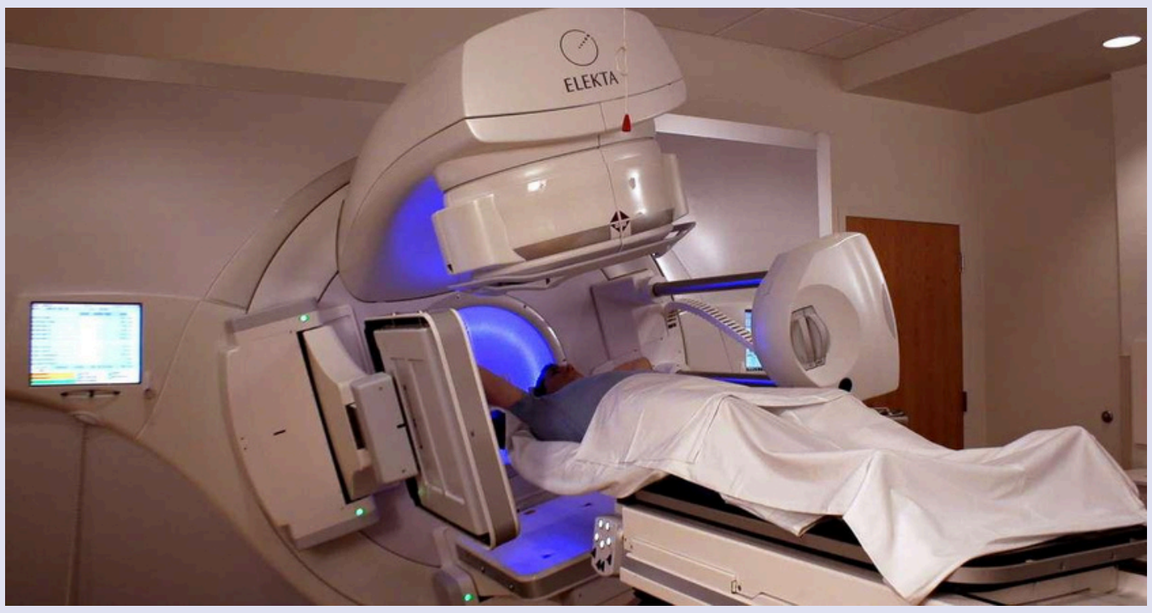
As pancreatic cancer progresses, symptoms may intensify, with individuals experiencing fatigue, loss of appetite, new-onset diabetes, and even blood clots. Advanced stages of the disease can cause more severe complications such as bowel obstruction, ascites (fluid buildup in the abdomen), and severe pain. Recognizing these symptoms and seeking medical attention promptly is crucial for early detection and improved outcomes in individuals at risk of or suspected of having pancreatic cancer.

3.Treatment Options

One treatment for pancreatic cancer is surgery. Whether surgery is the appropriate treatment depends on the position of the tumor. Tumors located distal to the pancreatic head can be removed by distal pancreatectomy. However, the majority of the tumors arelocated in the head, and they can be removed by pancreaticoduodenectomy(PD). PD first appeared in 1889, and its mortality rate remained high for decades. Still, todayits mortality rate has decreased from about 30-45% to a more acceptable 1-3%, and the median 5-year survival after surgery in modern reports is around 20%.



Though the surgeries are becoming increasingly successful, there is still a problem of a high overall recurrence rate of 70-80%, which may be due to micro-metastasis at the time of surgery. Thus, treating patients with neoadjuvant chemotherapy is necessary. They can target tissues more effectively and address the issue of micro-metastasis. This treatment can achieve more negative margin resection rates and turn unresectable patients into resectable ones.



Another possible treatment is radiation therapy. It can be employed before surgery (neoadjuvant), or after surgery (adjuvant), and it uses high-energy X-rays or other forms of radiation aimed to destroy cancer cells and shrink tumors by damaging their DNA, inhibiting their ability to grow and divide. Its application in pancreatic cancer is carefully restricted to prevent damage to surrounding healthy tissues the pancreas. Precise delivery of radiation therapy helps maximize treatment efficacy while minimizing side effects.

4.Future Outlook

The future outlook for pancreatic cancer holds promise with ongoing advancements in research and treatment strategies. Efforts can be focused on improving early detection methods to diagnose the disease at more treatable stages, and personalized medicine approaches are being explored to tailor treatment plans based on individual genetic profiles. Immunotherapy and targeted therapies are emerging as potential treatment options, aiming to boost the immune system's response against cancer cells and target specific molecular pathways involved in tumor growth. These advancements underscore a growing momentum in the fight against pancreatic cancer, offering optimism for better treatment outcomes and quality of life for patients in the future.

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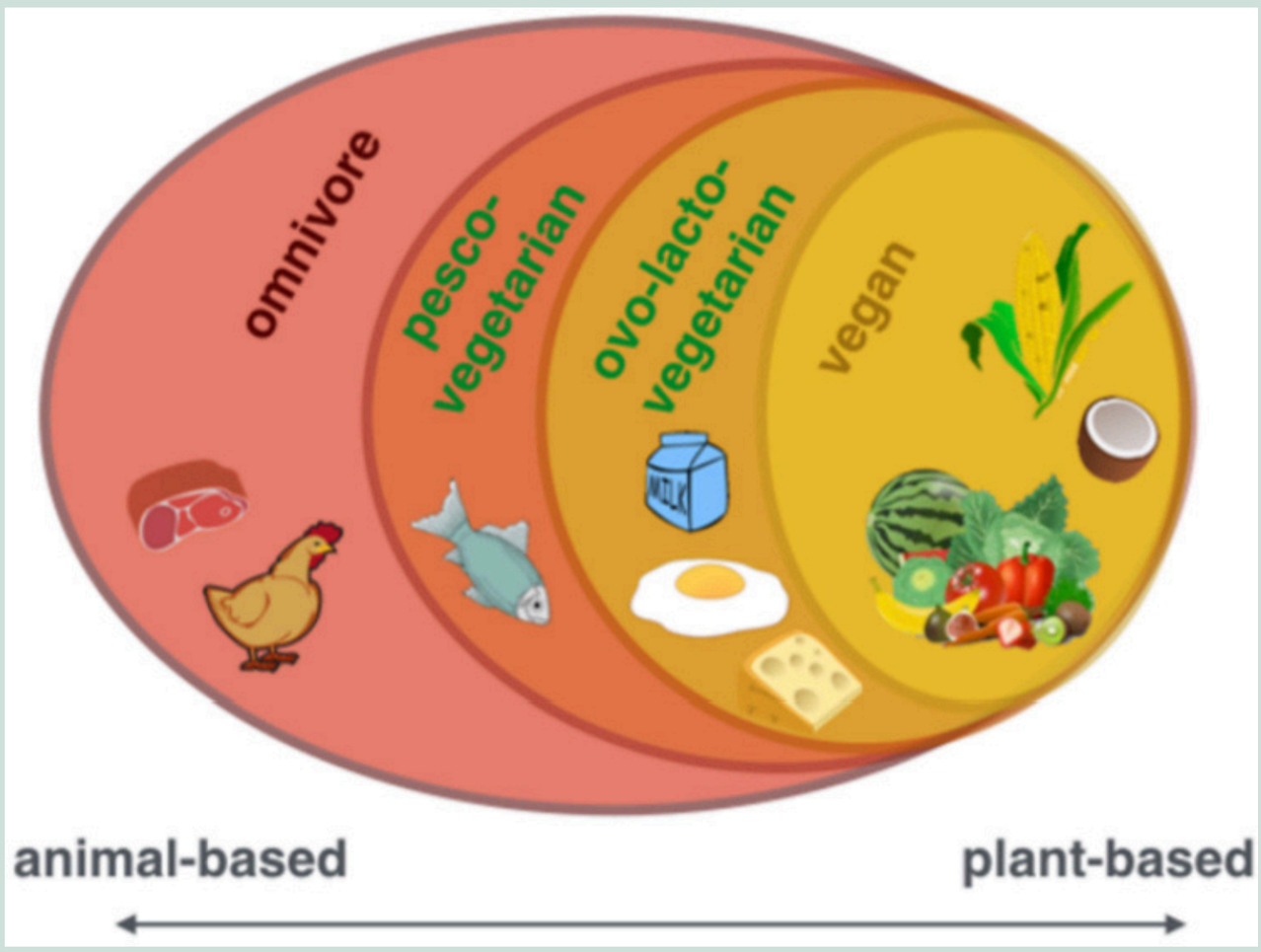
Is the Vegetarian Diet Healthy

Introduction:

Keywords:vegetarian diet, nutritional deficiency, cardiovascular diseases, type 2 diabetes, cancer.

In recent years, the rise of extreme vegan activism has incurred severe public backlash and incited doubts on whether a vegetarian diet is truly healthy and desirable. For this reason, many people hold to the belief that dwelling on a long-term plant-based diet can lead to nutritional deficiencies, causing the body to lack essential nutrients like vitamin B12, vitamin D, and iron, which are obtained primarily from animal sources. Curiously, an opposite narrative, in the meanwhile, has also gained traction in popular media– that “all vegetarian diets are healthy”.

Both of these beliefs, however, fail to capture the full picture– a plant-based diet encompasses a wide variety of diet styles, and each nuance might cast different influences on an individual’s physical health. For instance, vegetarianism does not automatically equate to a healthier diet because French fries, cakes, and many other types of “junk foods” are by definition vegetarian, but they contain a high volume of fat, sugar, and refined carbohydrates and are therefore lacking in nutritional value.



Variety of Plant-based Diet

Vegetarian is an umbrella term comprising a wide array of dietary patterns. It generally refers to people who avoid eating meat, poultry, and seafood, but variances may exist between each type in the consumption of dairy products and eggs.

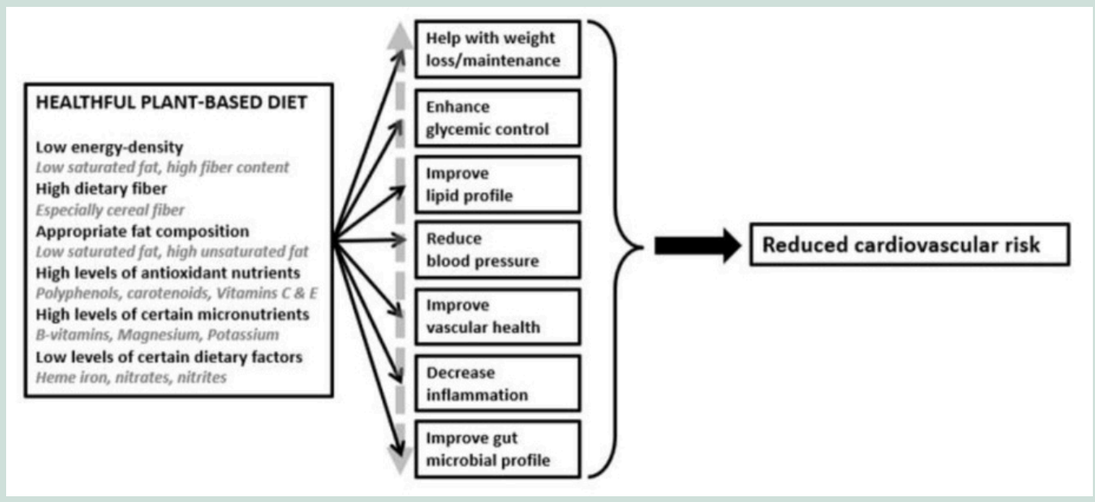
- Vegans: a strict form of vegetarianism that avoids all animal products, including meat, poultry, fish, dairy, eggs, and often honey, as well as any products derived from animals (eg. gelatin and rennet).
- Lacto-ovo vegetarians: allow the consumption of dairy products(lacto) and eggs(ovo) but avoid meat, poultry, fish, and seafood.
- Lacto vegetarians: consume dairy products but avoid meat, poultry, fish, seafood, and eggs.
- Ovo vegetarians: consume eggs but avoid meal, poultry, fish, seafood, and dairy.
- Partial vegetarians: avoid red meat but may occasionally include poultry and fish.

Health Benefits

Despite the myth that plant-based diets are prone to nutritional deficiencies and potentially detrimental to health, a vegetarian diet, regardless of the type variations, is one of the most effective ways of maintaining health and tends to produce more health benefits than a meat-prevalent diet. A vegetarian diet (that relies on unprocessed food) typically contains lower calories, lower levels of saturated fat and low-density lipoprotein (LDL) cholesterol, and more dietary fiber, vitamins, minerals, antioxidants, and phytochemicals. Numerous studies provide proof of its positive health outcomes by measuring the risks of heart disease, cancer, diabetes, and blood pressure.

Heart Disease

A vast literature of research studies has documented the substantial health benefits of plant-based diets in its consistent inverse association with cardiovascular diseases. In one of the largest studies- 48 188 participants with no history of cardiovascular disease– researchers tested associations of vegetarianism with risks of ischaemic heart disease. Over 18 years of follow-up, they found that vegetarians had 22% lower rates of ischaemic heart disease than meat eaters.



“Potential mechanisms underlying the cardiovascular effects of healthful plant-based diets” (Satija and Hu).

A healthy plant-based diet, with an emphasis on grains, fruits, vegetables, and nuts, is typically low in energy density, largely due to low saturated fat and high fiber content. High fiber content can promote satiety by triggering gastric distention, thus reducing overall energy intake and assisting in weight control. Additionally, high fiber also reduces LDL cholesterol levels by restricting cholesterol absorption and bile acid synthesis.

Plant-based diets (such as nuts) contain rich polyphenols and antioxidants which can protect against oxidative stress, support vascular health, and reduce inflammation. Other nutrients prevalent in plants such as potassium and magnesium improve cardio-metabolic health by regulating blood pressure and reducing the risk of stroke.

On the other hand, certain components found in animal products are shown to increase cardiovascular risk. Heme iron, for instance, found in meat-based products, elevates oxidative stress, which is linked to inflammation and damage to blood vessels. Moreover, compounds like choline and L-carnitine, found mainly in red meat, are converted to TMAO. Affecting cholesterol metabolism, inflammation, and atherosclerosis, elevated TMAO levels hence heighten the risk of cardiovascular events.

Type 2 Diabetes

Diets can play a crucial role in the prevention of diabetes as well. Multiple studies have substantiated the vegetarian diet’s potential to curb the risk of developing type 2 diabetes. The Adventist Health Study 2 (AHS-2), with a cohort of approximately 96,000 participants, investigated the health implications of vegetarian diets. The study found that vegetarian diets “are associated with lower BMI values, lower prevalence of hypertension, lower prevalence of the metabolic syndrome, lower prevalence and incidence of diabetes mellitus, and lower all-cause mortality”(Orlich and Fraser). In regards to diabetes, it was found that vegetarians have a significantly lower risk of developing diabetes, with vegans having a prevalence of 2.9% and an incidence rate of 0.54%, compared to 7.6% and 2.12% for nonvegetarians.

This effect could be possibly attributed to the high fiber intake that consists of most vegetarian diets. Dietary fiber can exert a slowing effect on the absorption of sugar into the bloodstream, helping to regulate blood sugar levels and enhance insulin sensitivity. Enhanced insulin sensitivity means that the body's cells respond more effectively to insulin, allowing glucose to be used more efficiently for energy and reducing the risk of insulin resistance, a precursor to type 2 diabetes. Plant-based foods, furthermore, tend to have a lower glycemic index. The glycemic index is a measure of how quickly a food causes blood sugar levels to rise after consumption. Foods with a low GI release glucose more gradually and steadily, contributing to more stable blood sugar levels. This slow, sustained release of glucose can help prevent the rapid fluctuations in blood sugar that can lead to cravings, overeating, and, over time, metabolic disorders like diabetes

Cancer

In the AHS-2 study, preliminary findings from studies suggest that vegetarian diets potentially have a reduced risk of developing various types of cancer, although the difference is not significant. The overall hazard ratio (HR) of 0.92 indicates an 8% lower risk of cancer among vegetarians compared to non-vegetarians. Specifically, vegetarian diets are observed to be particularly effective in preventing gastrointestinal cancers, including cancers of the stomach, colon, and rectum, which might be attributed to certain characteristics consistent in vegetarians. This may imply the high intake of fiber, vitamins, and antioxidants in a plant-based diet.

Health Concerns

Despite the many positive health outcomes associated with a primarily plant-based dietary choice, there still exists widespread concern about the insufficiency of vital nutrients that are not typically found in plants, namely protein, Vitamin B12, Zinc, and Omega-3 fatty acid.

Protein. Although some myths have it that vegetarians tend to lack proteins and that athletes should not adopt a plant-based diet, this is not true. A plant-based diet can obtain a sufficient amount of proteins from protein-rich sources such as legumes, nuts and seeds, soy products, and grains. Plant protein is equally effective in supporting muscle strength as animal-derived protein, as research studies fail to find any difference in muscle strength and mass between animal protein and plant protein supplementation.

Vitamin B12. Vitamin B12 is a nutrients that assist in the body’s production of red blood cells and DNA and is found in animal products only. However, for vegetarians open to dairy and egg food sources, B12 deficiency is not a concern. Yet for vegans who avoid all kinds of animal products, it is necessary to take vitamin B12 supplements to prevent B12 deficiency.

Iron. Although studies have confirmed that the amount of iron intake remains the same for meat-eaters and non-meat eaters, the iron produced in animals, heme iron, is more readily absorbed by the body, whereas non-heme iron contains naturally occurring absorption inhibitors. Therefore, vegetarians need to compensate for this by consuming 1.8 times more iron than non-vegetarians.

Omega-3 fatty acids. Diets that exclude fish and eggs tend to be low in EPA and DHA, the two main types of omega-3 fatty acids. However, vegans can nonetheless obtain a variety ofomega-3 fatty acids from walnuts, flaxseed, chia seeds, hemp seeds, edamame, seaweed, and algae, and from supplements.

Conclusion

Affirming the health benefits associated with a plant-based diet, however, does not mean that everyone should be a vegetarian hence force and entirely ditch any meat consumption. While a plant-based diet offers a reduced risk of heart disease, cancer, and type 2 diabetes, it's essential to approach this dietary choice with balance and awareness. adopting a plant-based diet doesn’t require a complete elimination of animal products for everyone, but rather a mindful shift towards more plant-rich meals. Focusing one’s diet towards more unprocessed, plant-based food sources would be enough to enjoy the plethora of health advantages of a vegetarian diet, contributing to significant health improvements and a more sustainable way of living.

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SMART MAGAZINE AUTHOR: Livana TRANSLATOR: Lily

Bird calls also have dialects

As the saying goes, “three miles of different tunes, ten miles of different sounds”, the human world's dialects are colorful, constituting the characteristic symbols belonging to each boundary, even when people leave their hometowns at a young age, they often retain their native accents. But dialects aren’t exclusive to the human world–they exist widely across the animal kingdom as well. Birds as the animal kingdom “singer”, rely on calls for communication in activities like foraging, self-defense, and mating. Therefore, the diversity of bird languages often exceeds that of most animals, and according to statistics, there are nearly 3,000 different styles of language in the world's more than 9,000 known species of birds. In addition to differences between languages and bird types, same species of birds in different geographic regions, their language will also alter, and this is bird’s “dialect”.

How do “dialects” form? To understand we have to start with the bird's vocalizations. Bird vocalizations can be divided into two categories based on length, complexity, and context: songs and calls. In ornithology and bird-watching, songs are considered to be relatively complex vocalizations, often associated with territory defense, courtship, or mating. Calls, on the other hand, are usually simpler and used to signal alarms or maintain contact with fellow birds. For complex songs, since bird populations tend to be stable within specific regions, different groups develop distinct singing styles over time. Within the same “dialect area” there is a high degree of consistency in the singing style of birds, while in different “dialect areas” there are differences in the length, syllables, and timbre of bird calls.

Do birds themselves realize that the tone of local birds is different from that of foreign birds? To prove it there is a very simple experiment that could be done: birdwatchers only need to record the calls of foreign birds in advance, and then play the calls of foreign birds in the “dialect zone” to the local birds to observe the behavior of the local birds. It has been found that males with a stronger sense of territory will first approach the source of the sound, look for potential competition, and then try to expel the other side. This indicates that due to geographical separation, birds have come to recognize birds with different dialects as outsiders, even though they share the same overall language system. The subtle differences in their calls are the clues they use to identify non-locals.

Bird dialects, like human dialects, can be passed on. Both bird and human languages are passed on to the next generation through vocal learning. Due to geographic separation, different groups of birds of the same species can develop small differences in their vocalizations over time, which eventually develop into a new dialect - similar to the process by which humans develop different accents, dialects, and languages.

However, the “dialects” of birds are also indicative of environmental pollution. Bird calls tend to be more frequent in cities because they are filled with loud and heavy noises, and to better communicate with their peers, urban birds have to respond to noise pollution with higher-frequency sounds.

As society's concern about noise pollution gradually increases, from January 1, 2025, a unified nationwide network for automatic monitoring of sound environment quality will be established. However, these automatic monitoring devices will not only record noise but also capture nearby bird songs, insect sounds, frog calls, and the sounds of wind, rain, and thunderstorms, potentially affecting the assessment of actual noise levels. This initiative not only helps with noise pollution control but also aids in recording the richness of the sounds of bird species in the wild. While filtering and identifying natural sounds, researchers also discovered "dialects" in bird calls. They observed that birds of the same species exhibit regional differences in their calls. By listening to these recordings, researchers can not only identify the bird species but also determine which region the bird comes from, and even distinguish their emotional states. This provides valuable information for further research into communication among birds.

An ancient saying goes: "The forest grows quieter as cicadas chirp, the mountain grows even more serene as birds sing." In the vastness of nature, birds’ crisp and melodious songs embellish the trees, flowers, and plants, enriching our lives. Bird dialects offer us a unique perspective for studying the behavior of bird communities. As noise pollution decreases, we can expect to see more birds living alongside us, truly allowing us to live in a world filled with the sounds of nature.

Reference

CCTV News 7-01, "Birds Also Have Their Own 'Dialects'! Come Listen to the Sounds of Nature"

SMART MAGAZINE AUTHOR:Rosy TRANSLATOR: Yaqi

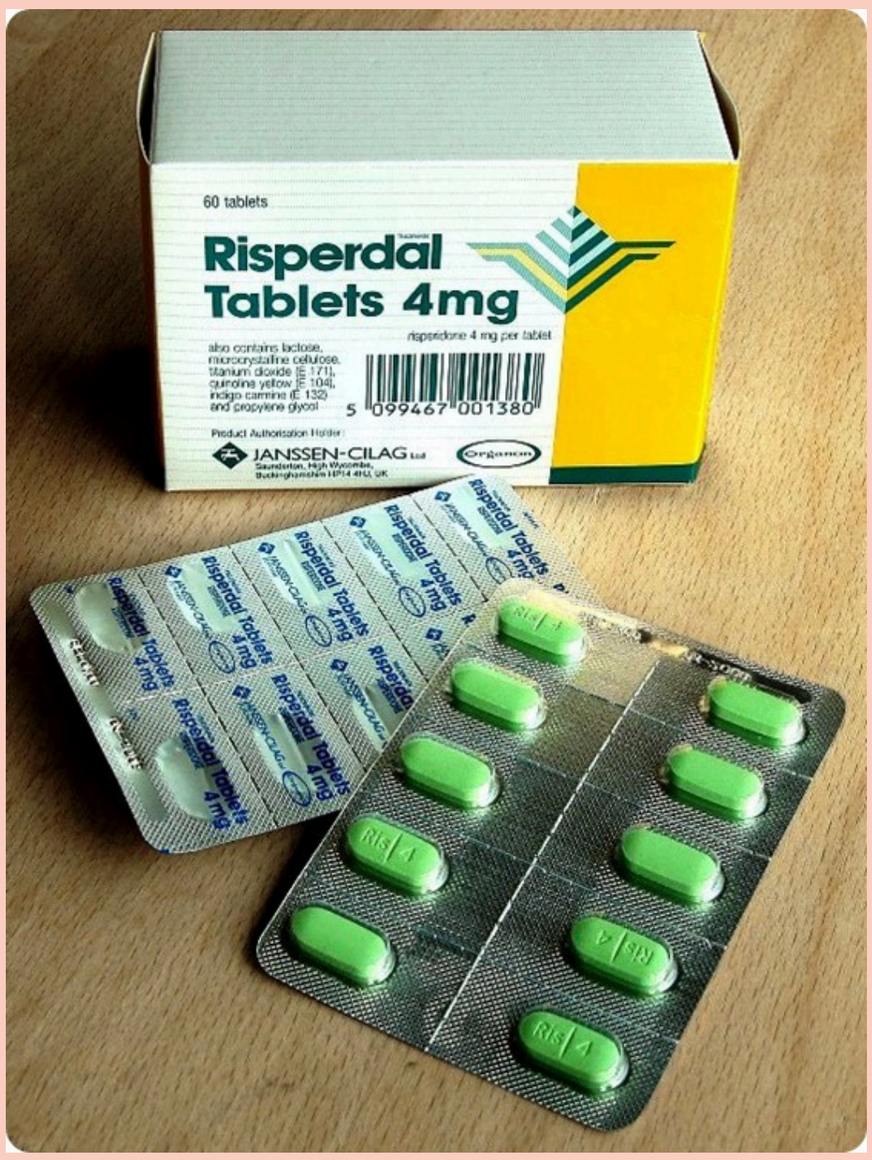
Research Progress on the Combined Use of the Main Drugs Chlorpormazine and Paroxetine in the Treatment of Schizophrenia

Keywords: Schizophrenia, Chlorpromazine, Paroxetine, Combined medication

1. Schizophrenia

Schizophrenia is a heterogeneous disorder that includes both positive and negative symptoms. Positive symptoms include delusions, hallucinations, and thought disorders, while negative symptoms manifest as anhedonia, avolition, social withdrawal, and cognitive dysfunction. Although there are many antipsychotic drugs available for treating schizophrenia, their efficacy often falls short of expectations, with slow onset of action and frequent severe side effects. While the exact cause of schizophrenia remains largely unknown, pathologists primarily focus on dopamine and glutamate systems. However, several other neurotransmitters and neuromodulators, including serotonin (5-HT), gamma-aminobutyric acid (GABA), glycine, D-serine, and neuroactive steroids, are also implicated in the condition [1].

At present, 108 genetic loci associated with schizophrenia have been identified, and many of these genes have been used to create animal models of schizophrenia [1]. For example, mutations in the gene for the cell adhesion molecule Neuregulin 1 (NRG1) and its receptor ErbB4 increase the risk of developing schizophrenia. NRG1 is expressed in synapses within the central nervous system and plays a significant role in the expression and activation of neurotransmitter receptors, including glutamate receptors. Mice with heterozygous mutations in NRG1 or its receptor ErbB4 exhibit behavioral phenotypes that overlap with those seen in schizophrenia mouse models, further proving the connection between NRG1, ErbB4 genes, and schizophrenia [2].

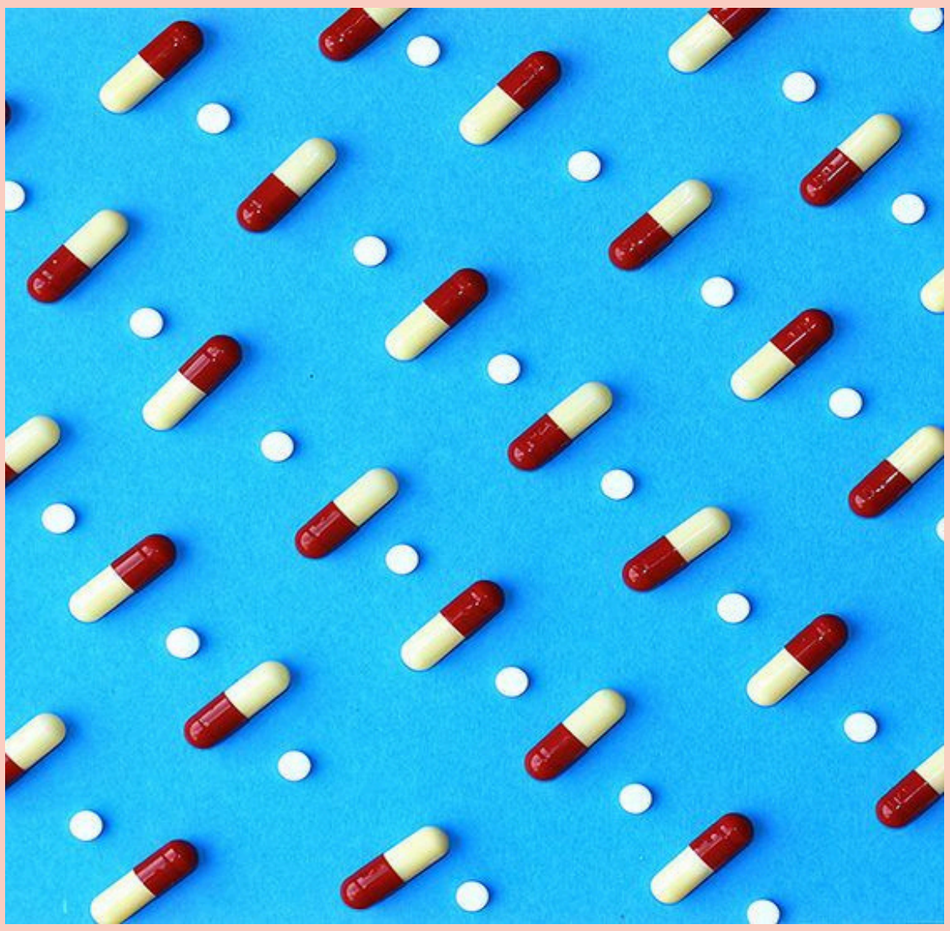


2. Mechanism of Action of Chlorpromazine

Chlorpromazine is one of the most widely used drugs for the treatment of schizophrenia . It primarily works by blocking dopamine (DA) receptors, particularly D2 receptors, and also has blocking effects on alpha (α) receptors and muscarinic (M) receptors. While the exact antipsychotic mechanism of chlorpromazine is not fully understood, it is believed that schizophrenia's clinical symptoms result from excessive dopamine activity in the brain, with an increased density of D2 receptors. Phenothiazines, such as chlorpromazine, are potent D2 receptor antagonists, and their antipsychotic effects are thought to occur through blocking D2 receptors in the mesolimbic and mesocortical pathways. Clinically, chlorpromazine is mainly used to treat various types of schizophr enia, showing better efficacy in acute patients. However, long-term use is required to maintain therapeutic effects and reduce relapse rates [3].

3. Combined Use of Chlorpromazine and Paroxetine

Chlorpromazine has a large safety margin, but long-term and high-dose use can lead to numerous adverse reactions. These adverse effects are categorized into general reactions, extrapyramidal reactions, and allergic reactions. General side effects include drowsiness, fatigue, blurred vision, nasal congestion, tachycardia, dry mouth, and constipation, affecting both the central and autonomic nervous systems. Extrapyramidal reactions include Parkinson's syndrome, acute dystonia, and tardive dyskinesia. Common allergic reactions are rashes, photosensitive dermatitis, and acute agranulocytosis.



Paroxetine is a commonly used medication for treating mental disorders. As a phenylpiperidine derivative, it interacts with serotonin (5-HT) transporters, reducing serotonin reuptake at the presynaptic membrane. This helps alleviate depressive symptoms and, to some extent, boosts vitality. In treating schizophrenia, paroxetine can be combined with antipsychotics for better therapeutic results. Liu Ping et al. [4] studied the clinical effects of using paroxetine in combination with chlorpromazine. The study showed that the group treated with both medications had significantly lower scores for depression and anxiety than the group treated with chlorpromazine alone. Additionally, the combination group experienced fewer side effects. Therefore, using chlorpromazine and paroxetine together is considered a relatively effective and gentle treatment option.

4. Outlook

While the combination of paroxetine and antipsychotic medications has been shown to improve the clinical treatment of schizophrenia, its use is still relatively new, and the mechanisms are not yet fully understood. Clinical experience with this treatment approach is still limited. Therefore, physicians must continue to gather experience during treatment to establish a foundation for future therapies. Hospitals should also create platforms for physicians to exchange insights and perform case analyses to better understand paroxetine's properties and optimize its dosage in clinical applications, ensuring the best possible therapeutic outcomes.

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SMART MAGAZINE AUTHOR: Zeke TRANSLATOR: Zeke

De novo design of protein homo-oligomers with modular hydrogen-bond network-mediated specificity

Keywords: Protein circuits design, HBNet

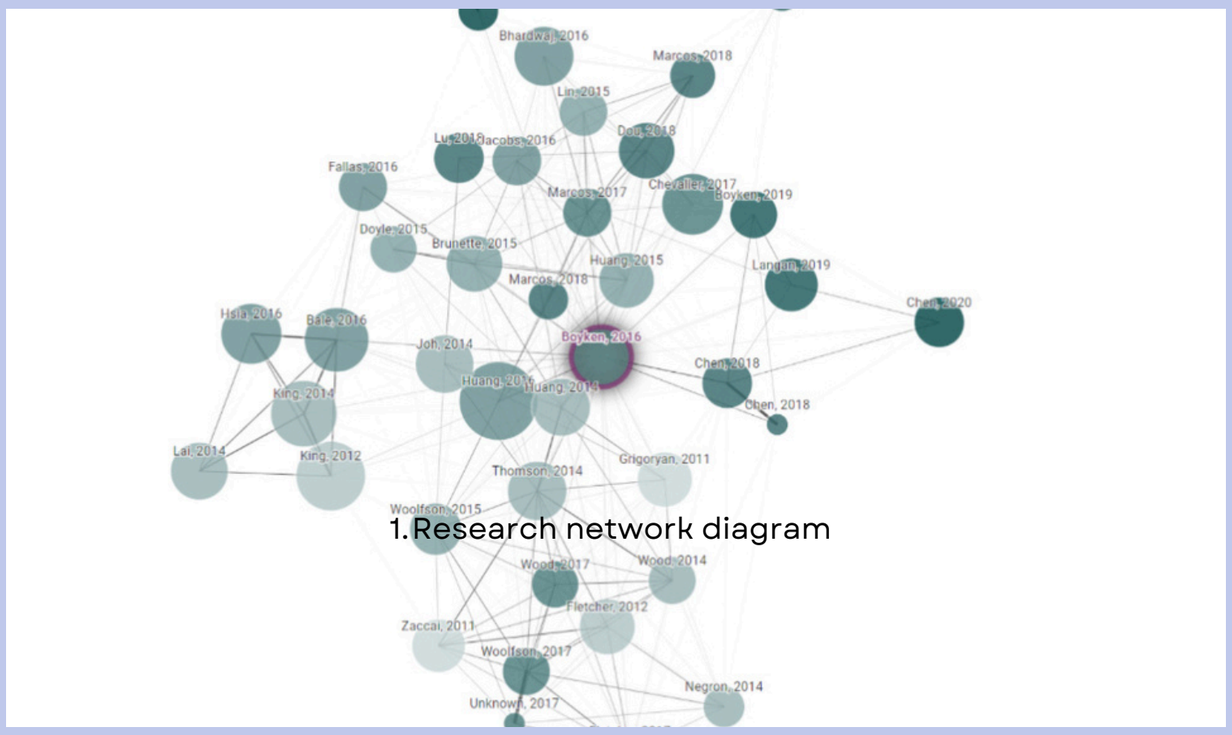
Background:

The development of protein circuits can be traced back to the 1990s. Early research primarily focused on constructing molecular circuits through gene regulation, using regulatory elements such as promoters, transcription factors, and reactors to control gene expression. However, traditional genetic circuits were limited by the timescales of transcription and translation and fixed regulatory factors, making it difficult to achieve rapid and precise signal processing.

With a deeper understanding of proteins and protein interactions, researchers began shifting their attention towards designing protein circuits. The main advantage of protein circuits lies in their ability to respond quickly and process more complex signals and dynamic regulation through various chemical modifications. This fast response mechanism gives protein circuits greater flexibility in complex environments.

Basic research primarily focuses on the design, construction, and functional characterization of protein circuits, aiming to uncover the mechanisms of protein interactions and signal transduction. Applied research, on the other hand, seeks to apply protein circuits in biomedical and pharmaceutical fields, such as tumor therapy, molecular diagnostics, and drug delivery.

This article was published in Science in 2016, and PI Zibo Chen has continued research in this direction. In 2018, a review titled "Programmable Protein Circuit Design" was published in Cell . In related protein studies, David Baker's lab and the RosettaDesign system have played a critical role.



1. Research network diagram

Protein circuit design is an emerging interdisciplinary field grounded in the concept of molecular computation. Proteins have diverse structures and functions, and through interactions, modifications, and regulations, they can couple with other proteins as well as intracellular and extracellular pathways. These properties make proteins ideal components for designing and constructing complex molecular circuits. However, the diversity of proteins also poses challenges in the design and control of protein circuits, such as selecting appropriate protein components, regulating protein interactions, and maintaining circuit stability.

In recent years, researchers have sought to address the challenges of protein circuit design by focusing on principles like orthogonality and composability. Orthogonality means that the components within the circuit do not interact with other molecules in the cell, thus maintaining the independence of the circuit. Composability refers to the ability to construct diverse circuit-level functionalities using a limited set of engineered protein components. By leveraging these principles, researchers have successfully designed and built protein circuits that can sense, transmit, and process information. These circuits can dynamically control cellular behavior, develop new therapeutic strategies, and provide powerful tools and paradigms for programmable biology.

Innovation:

Innovative Design Method: Researchers developed a computational method called HBNet, which can quickly enumerate all possible hydrogen bond networks in an input backbone structure. This method allows for the precise design of large-scale hydrogen bond networks at the atomic level, representing a significant breakthrough in protein design. Using this method, the specific programming of protein oligomers becomes achievable, offering new possibilities for synthetic biology applications.

Innovative Structural Topology: Leveraging the HBNet method, researchers designed homomeric protein oligomers with modular hydrogen bond networks, optimizing them using RosettaDesign. They created dimer, trimer, and tetramer structures with novel topologies, such as triangles, squares, and superhelices, that had not been seen before. These innovative structures showcase the diversity and flexibility in designing protein oligomers.

Innovative Experimental Validation: The designed homomeric protein oligomers underwent further structural characterization through circular dichroism spectroscopy, protein crystallography, and small-angle X-ray scattering analysis.

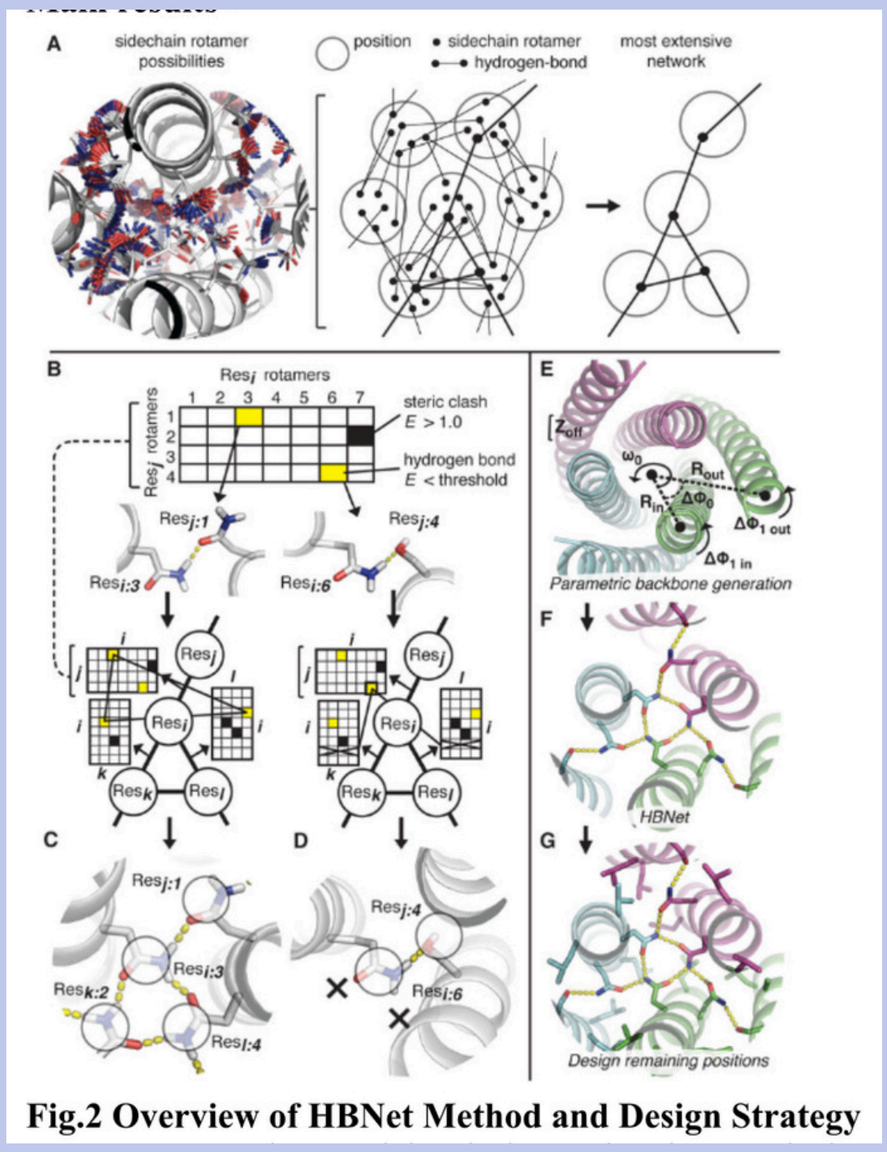
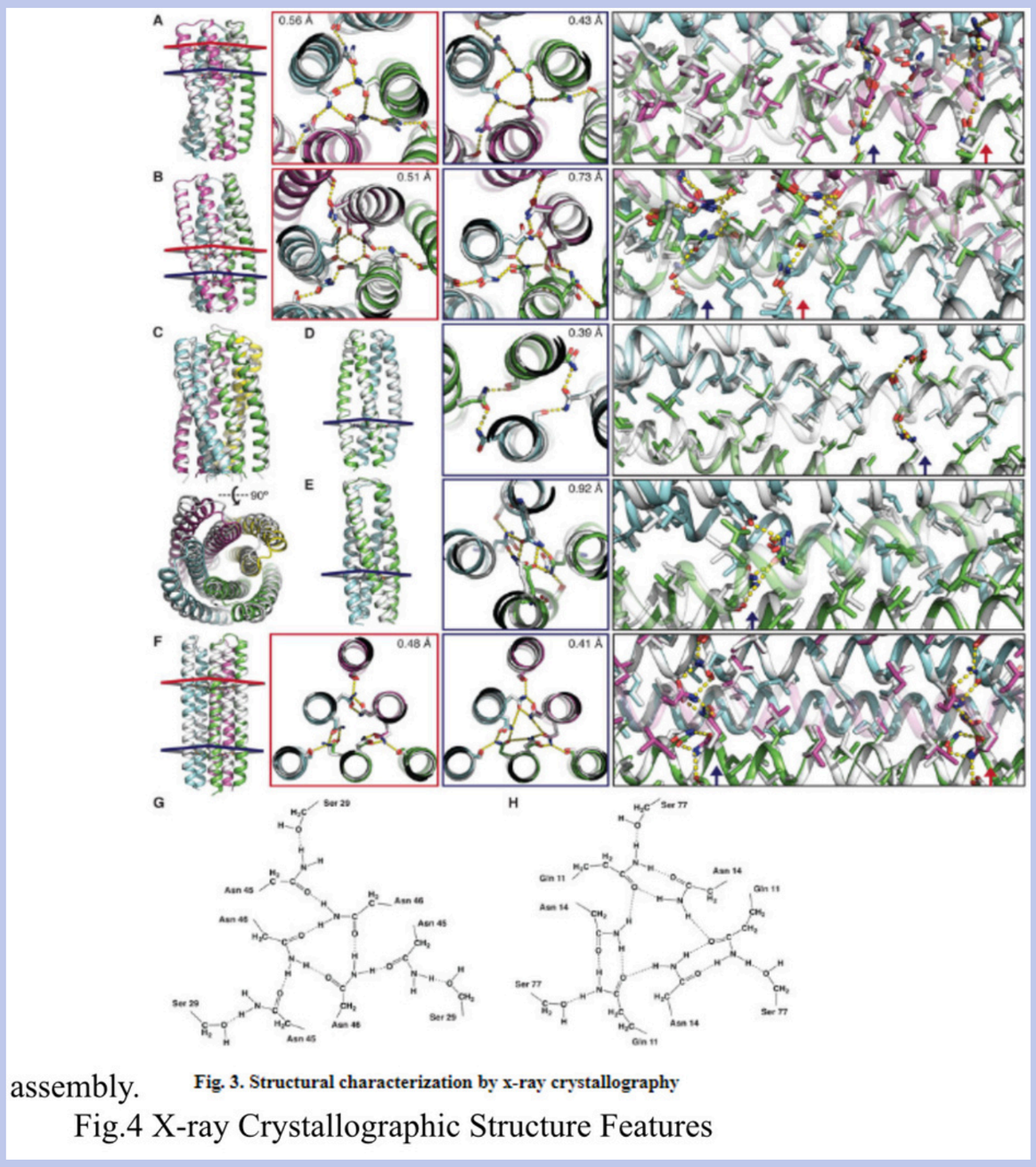


Fig.2 Overview of HBNet Method and Design Strategy

HBNet starts by examining the interactions between hydrogen bonds and steric clashes among all conformations (rotamers) of polar side chain pairs. This method efficiently identifies low-energy hydrogen bond networks, thus optimizing protein structure design. These energy states are stored in a graph data structure, where nodes represent residue positions, and spatially proximal positions are connected by edges. Each edge is represented by a matrix indicating the interaction energy between different rotamers at the two positions. HBNet traverses this graph to identify networks of three or more residues connected by low-energy hydrogen bonds with minimal steric clashes. In panel C, the method highlights the lowest-energy, most extensive hydrogen bond networks identified within the specified protein backbone, which are used in subsequent design optimizations to stabilize the overall protein structure. Panel D shows rejected hydrogen bond networks, which feature buried donors and acceptors that are unmet. During the design process, these unmet hydrogen bonds may result in unstable or unsuitable protein structures and are thus identified and excluded from further consideration.

The researchers used coiled-coils as the protein scaffold since coiled-coils possess a repetitive geometric cross-section and can be parametrically generated. They constructed a host structure with two concentric rings, each made of helical hairpin monomer subunits. The outer helix was connected to the inner helix by a short linker, ensuring tightness in the overall protein structure, enhancing thermal stability and functionality. By systematically sampling the radius, pitch, z-offset between the inner and outer helices, and overall superhelical twist, they generated a wide range of scaffolds. Subsequently, the team searched for networks across intermolecular interfaces within these scaffolds and used RosettaDesign to optimize rotamer positions of the remaining residues, enabling the design of complex hydrogen bond networks. The study provided a comprehensive analysis of the designed proteins' stability and structural characteristics, revealing their typical features in circular dichroism (CD) spectroscopy and thermal stability. A comparison between the two-ring design and the single inner-ring design highlighted the importance of the outer ring for protein stability.



assembly. **Fig. 3. Structural characterization by x-ray crystallography**

Fig.4 X-ray Crystallographic Structure Features

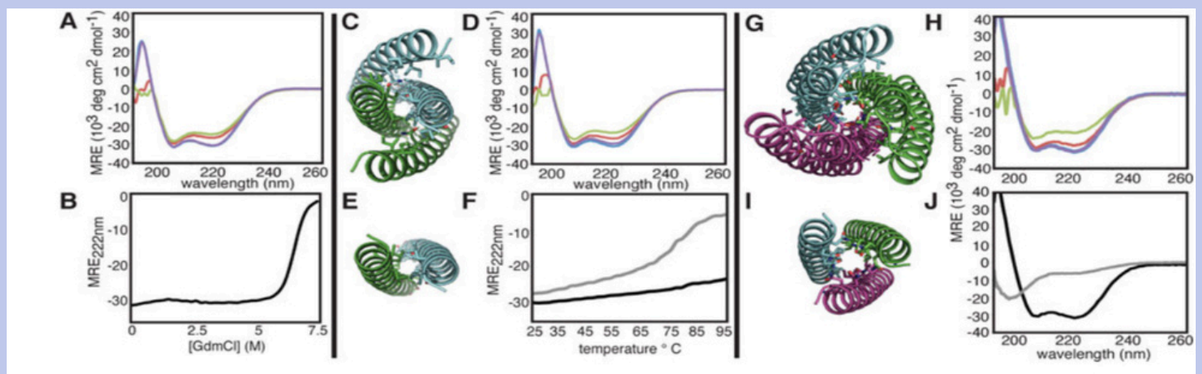


Fig. 2. The outer ring of helices increase thermostability and can overcome poor helical propensity of the inner helices

Fig.3 Helical Outer Ring Structure Enhances Thermal Stability

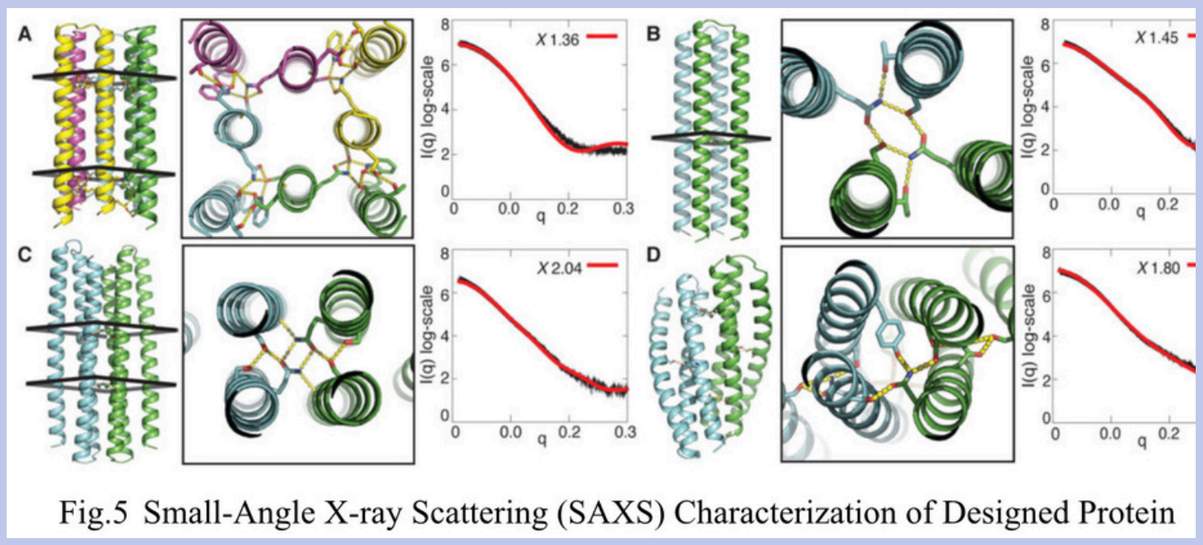


Fig.5 Small-Angle X-ray Scattering (SAXS) Characterization of Designed Protein

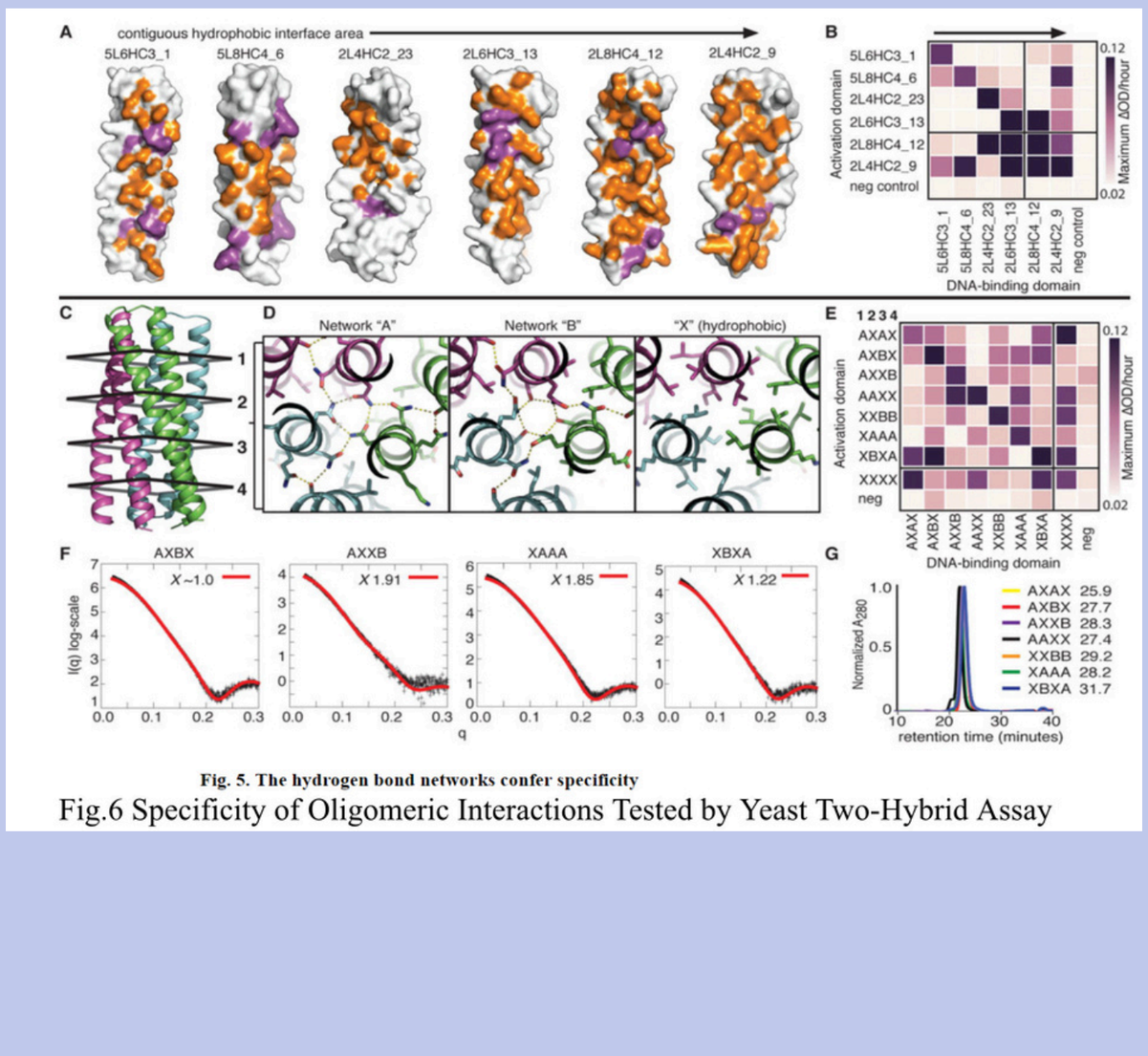


Fig. 5. The hydrogen bond networks confer specificity

Fig.6 Specificity of Oligomeric Interactions Tested by Yeast Two-Hybrid Assay

Structures in Solution:

SAXS analysis revealed the presence of square, untwisted tetrameric and dimeric forms (A & B), along with helical dimer forms exhibiting two superhelical geometries, right-handed (C) and left-handed (D). SAXS experimental data closely matched the designed models, confirming that the designed proteins formed the expected oligomeric states in solution. The results demonstrated that hydrogen bond network designs, which divided the hydrophobic interface into relatively small areas, exhibited higher specificity compared to designs with large continuous hydrophobic patches. The designs that partitioned hydrophobic areas across the entire oligomeric interface, with each helix contributing at least one side chain, showed a particularly high degree of specificity. Despite having the same backbone and highly similar sequences, the combination designs exhibited a notable specificity, while the fully hydrophobic control designs were more prone to nonspecific interactions. The central hydrogen bond network clearly mediated the interaction specificity.

Insights and Reflections:

The HBNet method proposed in this study represents an innovative approach in the field of protein structure design, as it allows for the rapid and efficient search for hydrogen bond networks within scaffold structures. The modular hydrogen bond network topologies designed in this research demonstrate novel and diverse geometries and interaction patterns. These oligomers can serve as modular components for different logic gates, which, when assembled, could construct biochemical logic circuits with various computational functions.

Compared to gene circuits, protein-based circuits react faster and can detect and respond to changes in intracellular and extracellular conditions in real-time. This capability enables the construction of closed-loop feedback circuits for precise control of cellular processes, such as regulating cell proliferation, differentiation, and apoptosis. Protein circuits can function within cells or across multiple cells, coordinating activities at the tissue and organ levels. This opens the door to constructing multicellular regulatory networks akin to electrical signaling.

The design principles of modularity and orthogonality in protein circuits provide a novel approach to the design of synthetic biological circuits, contributing to the standardization and systematization of biological system construction. Sensing and actuator modules based on protein circuits can enable the precise and dynamic detection of various signals, allowing for programmable control over biological behaviors.

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SMART MAGAZINE AUTHOR: Nox TRANSLATOR: Rick

Science Fiction Becomes Reality? The Magic of Constructing Organs In Vitro!

Keywords: Organoids, Organs-on-Chips

Introduction:

Organoids and organs-on-chips are two rapidly developing 3D cell culture technologies that bridge the gap between traditional in vitro 2D cell culture and animal models. In July of this year, researchers from the University of Toronto published a review article titled "Integrating organoids and organ-on-a-chip devices" in Nature Reviews Bioengineering. This article provides clear definitions for these two emerging technologies for the first time, explores the challenges in their development, and demonstrates their current applications in the medical field. The article concludes by discussing the integration of these two technologies to meet the requirements and limitations of creating integrated devices.

The Significance of 3D Cell Culture

In drug development, the commonly used traditional in vitro models include animal models and 2D cell culture models. However, animal models are not only expensive but also pose significant ethical controversies. On the other hand, traditional in vitro 2D cell models cannot accurately reflect the effects of drugs in vivo, and drugs screened through in vitro models still have a high possibility of failing in clinical trials. 3D cell culture technology, however, can better simulate the physiological environment in vivo, thereby increasing the success rate of in vitro drug screening. 2D Cell Culture: Cells are cultured on plastic or glass surfaces, which cannot accurately reproduce the complex physiological structures.

3D Cell Culture: Cells are surrounded by other cells and extracellular matrix (ECM) as they would be in vivo, better replicating the physiological structures of cells in the body. 3D cell culture technologies include spheroids, organoids, organs-on-chips (OoCs), and tissue engineering relying on hydrogels or polymer scaffolds.)

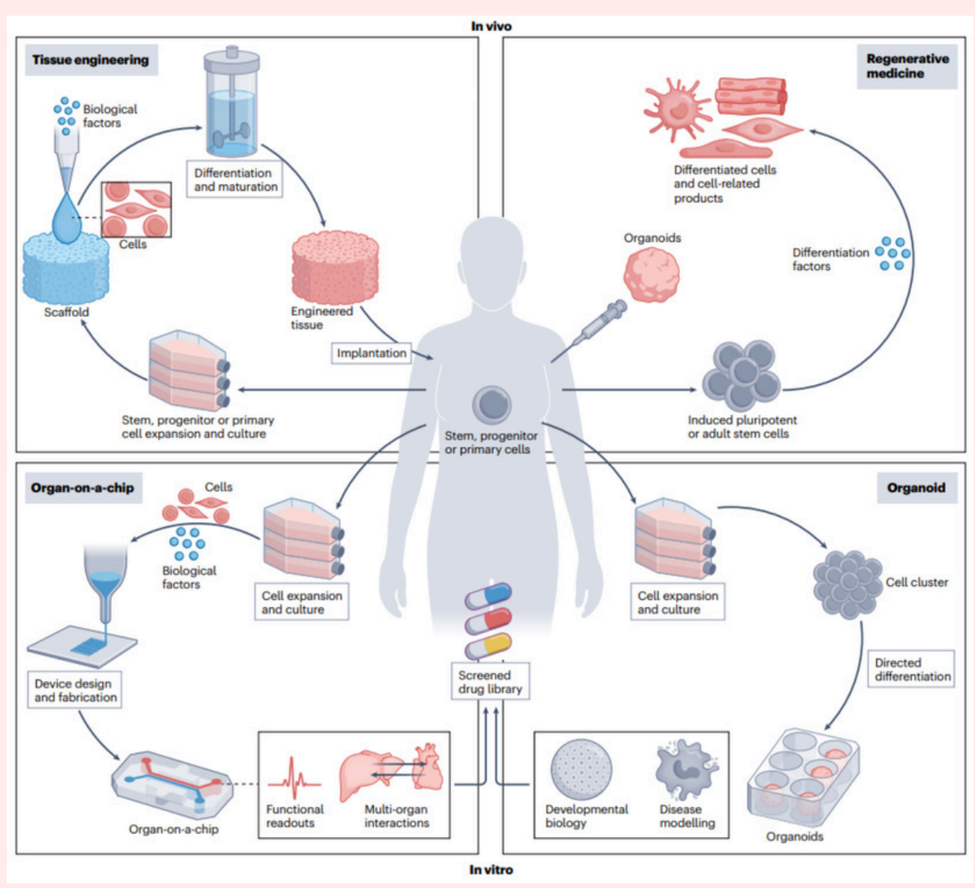
First Clear Definitions

Organoids: Organoids are self-organizing structures (i.e., they can spontaneously organize from cells). They are typically derived from human pluripotent or adult stem cells that proliferate and differentiate. Organoids contain multiple cell types and have cellular structures and functional characteristics similar to specific organ regions. Some organoids, such as intestinal or kidney organoids, are almost indistinguishable from natural organs histologically. However, organoids lack interactions with other organs and tissues and often do not have vasculature or an immune system. To overcome these limitations, researchers have developed assembloids, which are self-organizing cellular systems formed by merging different types of organoids.

Organs-on-Chips (OoCs): Organs-on-chips are engineered or microfabricated culture systems that support cell assembly into tissue-like structures to measure the functional characteristics of simulated organs. Although OoCs do not fully replicate entire organs, they can provide more accurate 3D cell culture to simulate the physiological responses of one or more tissues. OoCs can integrate multiple cell types in a single device, using membranes or pillar arrays to facilitate the transport of nutrients and oxygen, and controlling geometry and multi-axis stretching through tissue fixation–functions that are usually not achievable in traditional 2D cell cultures.

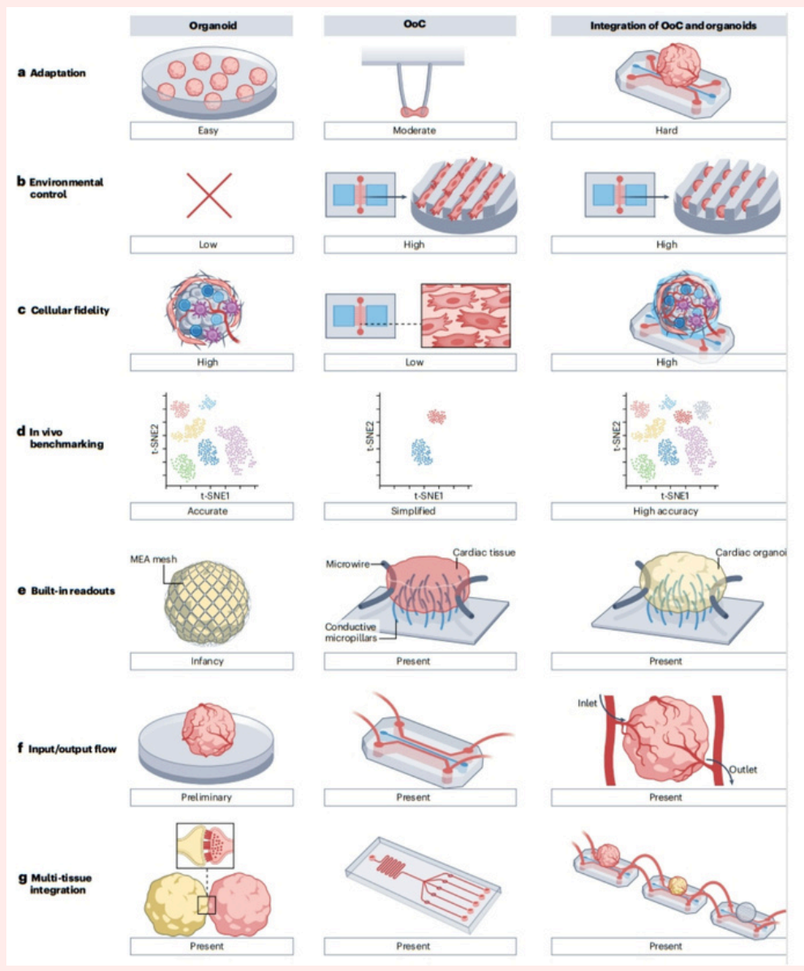
Applications of 3D Cell Culture

Organoids and organs-on-chips can be used in tissue engineering and regenerative medicine applications, with organs-on-chips typically being smaller in scale than organoids. Tissue engineering involves the integrated use of cells, biomaterial scaffolds, and bioreactors to create tissues that can detect disease etiology, drug efficacy, and developmental mechanisms, and that can replace or enhance the structure of native tissues. Regenerative medicine, on the other hand, uses pluripotent or adult human stem cells and related technologies (such as gene editing) to replace or repair damaged tissues and organs. By inducing stem cells to form organoids, these organoids can be transplanted in vivo to repair or replace damaged organs (such as the liver and intestines). Both regenerative medicine and organoid research use directed differentiation protocols, which rely on cytokines to activate pathways responsible for organogenesis during development, achieving highly specific cell differentiation.



Challenges in Development

While 3D cell culture technologies can simulate certain biological processes of target tissues, many challenges remain, including issues related to vascularization, routine evaluation of pharmacokinetics and pharmacodynamics, identification of drug resistance mechanisms, and off-target effects. Additionally, in terms of size and fidelity, their working scale is often between hundreds of micrometers to 1 centimeter, making it impossible to fully replicate human organs. For example, while heart organ chips can replicate myocardial contraction by providing bundles of cardiomyocytes, they cannot replicate the four chambers of the heart, nor can they replicate the ventricular walls.



Integration of Organoids and Organs-on-Chips

Integrating organoids and organs-on-chips aims to combine the strengths of both technologies: on one hand, organoids can provide complex cellular composition, enhancing the functionality of organs-on-chips. On the other hand, the precise geometry and microfeatures of organs-on-chips help guide organoid development, improving consistency and maturity, and enabling real-time functional readings through built-in sensors. However, integrating organoids into organs-on-chips may restrict organoid growth characteristics and cell lineage determination due to the constraints of defined boundaries. Moreover, integration may make imaging of organoids more challenging.

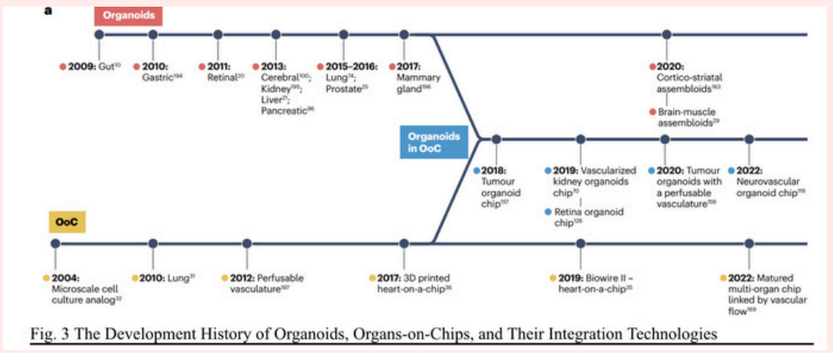


Fig. 3 The Development History of Organoids, Organs-on-Chips, and Their Integration Technologies

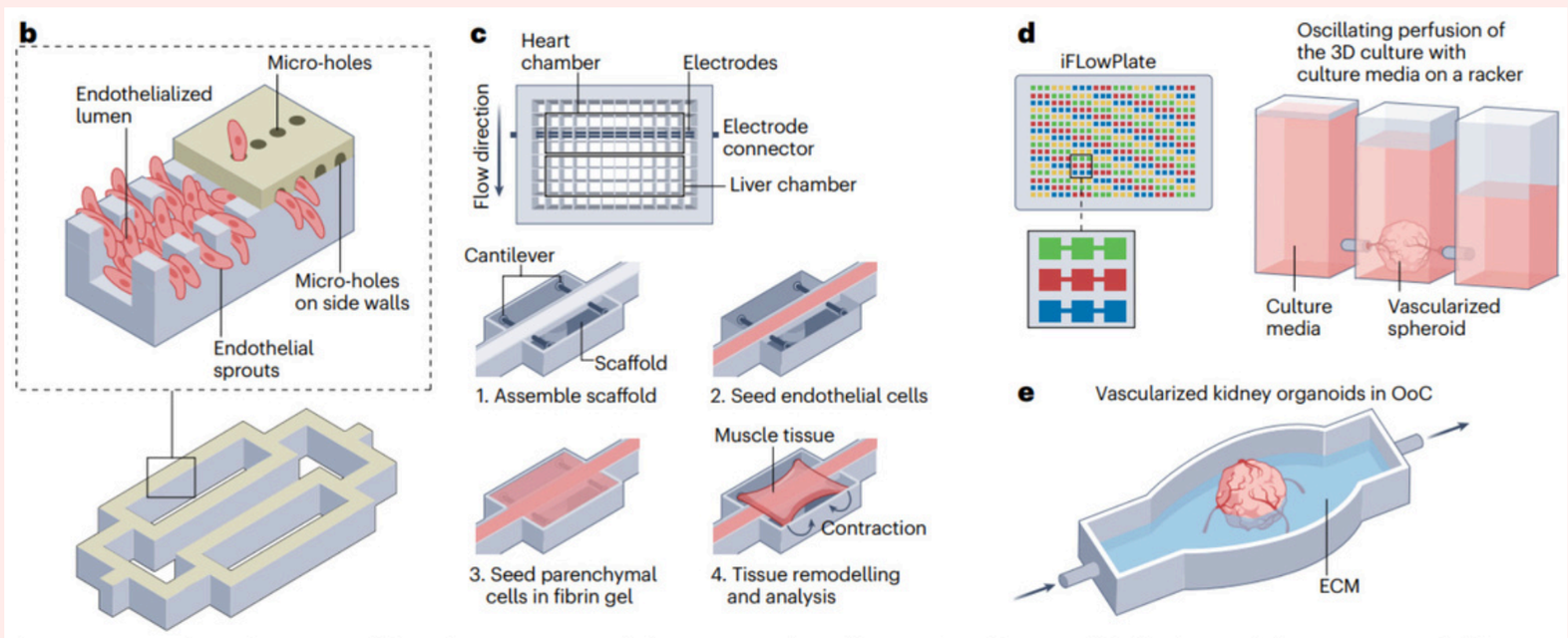


Fig. 4 Examples of Organoid and Organ-on-Chip Integration (b.c. Vascular Scaffold, d.e. Kidney Organoids)

Currently, by integrating organoids and cell chips, various physiological models have been preliminarily constructed, including those of the intestines, kidneys, lungs, liver, pancreas, nervous system, heart, and tumors. Taking the kidneys as an example, by inducing pluripotent stem cells to differentiate on 3D-printed perfusable chips, kidney organoids with certain epithelial transport functions have been successfully created.

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SMART MAGAZINE AUTHOR: Molly TRANSLATOR: Zona

How do people with diabetes eat protein?

Key words: diabetic nephropathy, protein, old age

Introduction

Kidney disease is one of the common complications of diabetes, and about 40% of diabetic patients are troubled by kidney disease. In addition to daily exercise and reducing smoking, controlling diet is also an important means of improving prognosis. National Kidney Foundation（NKF）Kidney Disease Outcomes Quality Initiative (KDOQI) recommends a low-protein diet, defined as a daily protein intake of 0.6-0.8 g/kg of body weight, for patients with diabetes and chronic kidney disease who do not rely on dialysis. Low-protein diets have been shown to slow the progression of kidney damage and proteinuria, but this can lead to malnutrition, protein metabolism disorders, increased carbohydrate ratio and other problems, which is not beneficial to control blood sugar levels and affect patient prognosis.

Research Method and Design

Using 1999-2018 data from the National Health and Nutrition Examination Survey (NHANES) database, the researchers stratified data from 2,901 subjects in accordance with the Kidney Disease: Improving Global Outcomes (KDIGO) Guidelines 2022, after excluding individuals with missing data.

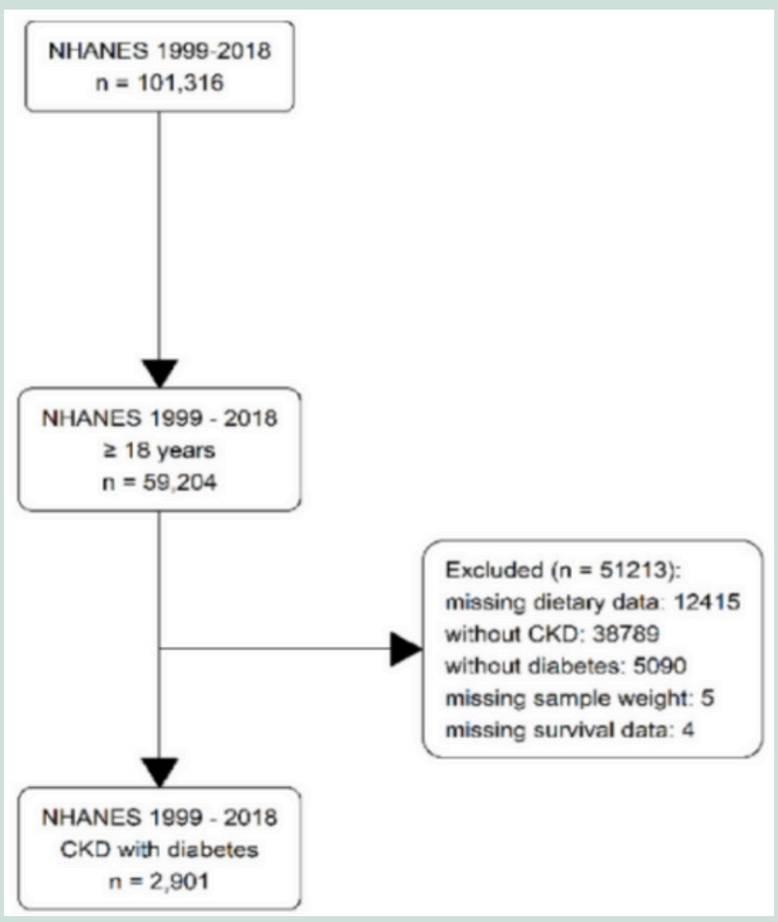

Figure 1
Screening flow chart based on 1999-2018 NHANES data

Result and Discussion

Combined with the analysis and follow-up results, moderate increases in dietary protein were associated with reduced mortality in diabetic nephropathy patients.

So how much protein should you eat? In contrast to the recommended intake in the KDOQI guidelines, stratified analysis showed that maintaining a daily protein intake of 0.6-1.2 g/kg of body weight was beneficial for patients over 60 years of age and could reduce mortality to some extent. Dietary protein intake of 1.0-1.2g/kg was significantly associated with a reduced risk of death in patients with all causes of diabetes. Of course, for the elderly with other chronic diseases or special conditions, this value will change, for example, for hemodialysis patients, considering the loss of protein during dialysis, patients need more nutritional intake; For older adults with high blood pressure, protein intake of 0.8-1.0 g/kg of body weight per day was associated with a lower risk of death; But for very high-risk patients with a poor prognosis for diabetic nephropathy, the value is 0.6-0.8 g/kg of body weight per day.

However, further analysis of the data found that increased animal protein intake was associated with increased mortality.

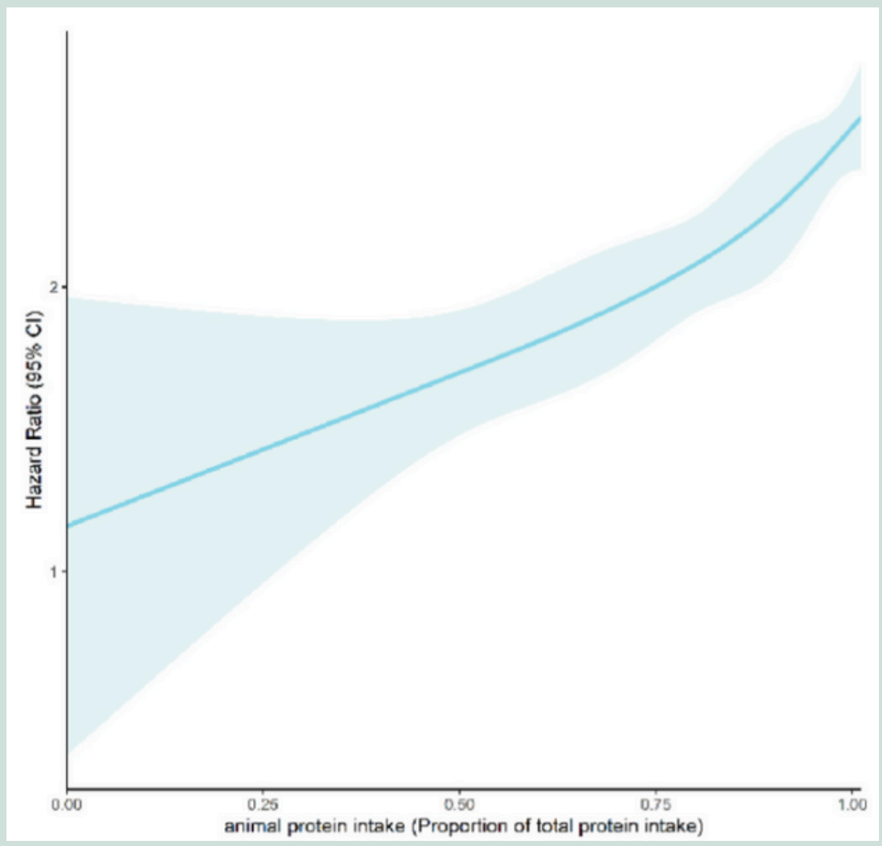

Figure 2
RCS analysis of proportion of animal protein intake and all-cause mortality

Relevant research data show that compared with plant protein, the kidney load is greater when eating animal protein. Animal protein contains more methionine and alanine, and after hydrolysis, more ammonia and sulfur compounds are generated, which will disturb the stability of intestinal flora, improve the incidence of cardiovascular diseases, and may lead to inflammation. Eating a lot of red meat, especially prepared meat, can increase the risk of high blood pressure and damage kidney function. In this regard, one theory is that methionine, as a precursor of cysteine, can increase asymmetric dimethylarginine levels and inhibit nitric oxide (NO) from playing a role in lowering blood pressure. Another theory is that protein and fat produce Advanced glycation end products (AGEs) during the Maillard reaction in a state of high heat, which stimulates the production of angiotensin II, induces vasoconstriction, and ultimately leads to an increase in blood pressure. In popular terms, fried high-fat meat and egg products may have the effect of raising blood pressure, and people with hypertension and renal dysfunction should eat less.

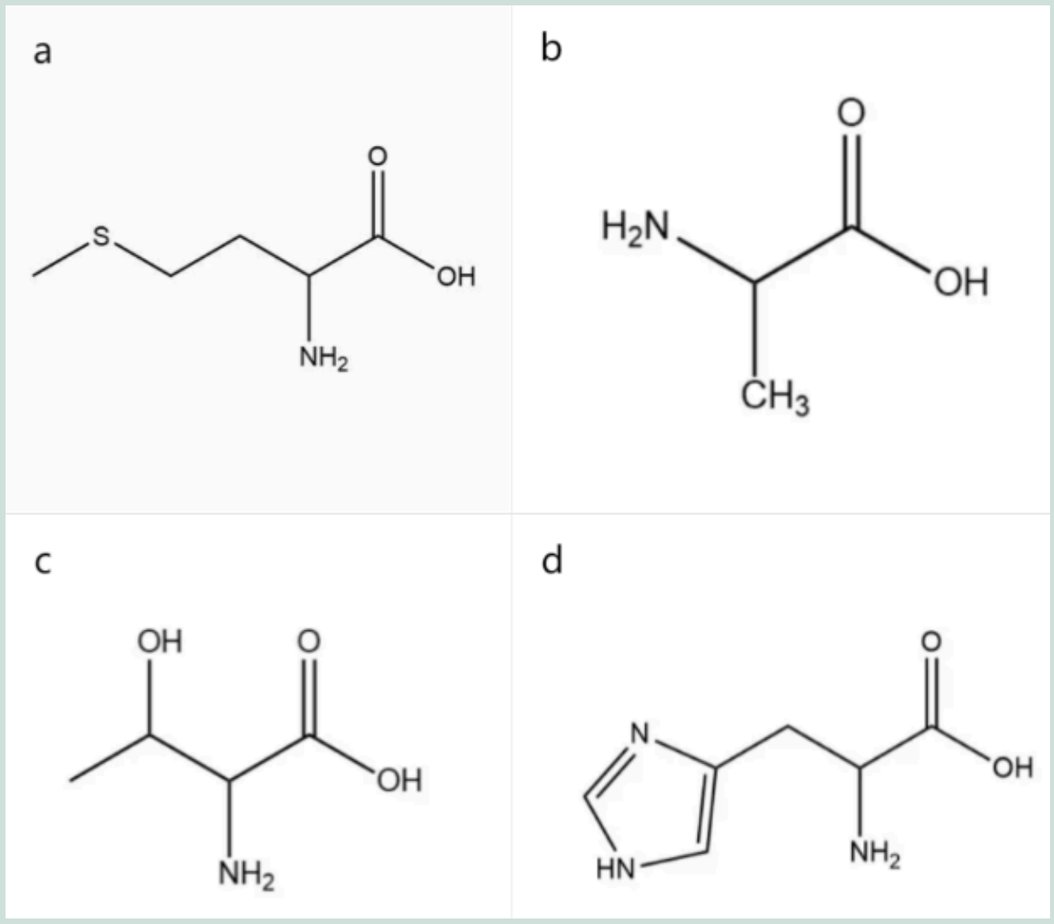

Figure 3
Partial amino acid structure simple formula (a: methionine; b: Alanine; c: Threonine; d: histidine)

Plant protein and animal protein are rich in amino acids, and plant protein is rich in threonine and histidine, which have been shown to lower blood pressure and protect the kidneys. In addition, plant protein can affect cholesterol metabolism, reduce oxidized LDL cholesterol and uric acid levels, and is very beneficial for patients with impaired kidney function. Therefore, for patients with impaired kidney function, a higher proportion of plant protein intake is beneficial for the kidneys.
All in all, it is recommended that diabetic patients take in more protein, of which eating more plant protein products is more beneficial to kidney health.

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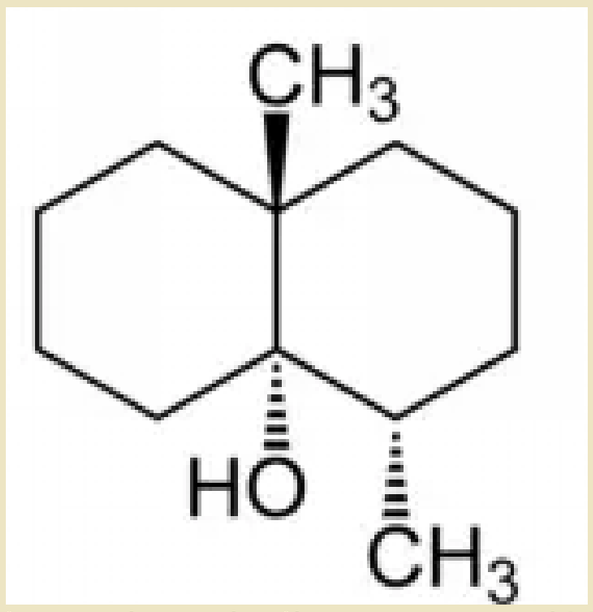
SMART MAGAZINE AUTHOR: Kita

The fresh aroma after rain actually is the scented trap of soil fungi

Keywords: botany, microorganism, soil fungi, collembolax

Introduction:



For hot summer days, several rains undoubtedly are the best gift from God. After the rains, rambling on the road, we find that leaves are greener, flowers are more vivid, and the air filling with fresh aroma from the earth. However, where does the fresh scent of soil come from? Actually, this is the scent trap made by soil fungi. Today, let’s unravel the secret behind this fresh aroma.

1. The volatile material released by soil fungi

The earth contains a large amount of actinomycetes, slime bacteria, cyanobacteria, and a volatile compound VOCs emitted by filamentous fungi; usually , this kind compound contains Geosmin and 2-MIB. [1] 2. Where does the fresh scent of soil come from?

The exploration of soil scent can be traced to 1881, and Berthelot and Andre found that fresh soil scent can be extracted by distilling. After that, some scientists found that slime bacteria living in the nutrient mediums also produced this kind of scent; therefore, they speculated that the scent was relative to the fungi living in the soil.

Until 1964, Australian scientists I.J.BEAR and R.G.THOMAS gave the explanation for this scent and named it “petrichor.” They pointed out that this scent came from one special substance living in the soil---Geosmin. When rains fell into the soil, it could roll this scent and form many small bubbles. When the rains stopped evaporating after rains, this scent was released into the air with vapor, and we could smell the fresh scent from the soil.

It is worth mentioning that microorganism biologist chairman Mark Buttner in Jhon Innes Centre claimed for BBC that the moist soil smell that people can smell is actually due to the molecules produced by certain bacteria. This molecule is named Geosmin, produced by streptomyces. Most healthy soils contain streptomyces; also, they are used to make antibiotics. Droplets pumping to the ground stimulate Geosmin to release into the air, and the concentration of Geosmin after rain is higher than before rain. Many creatures are sensitive to it, especially humans. 3. What’s the scent trap?

Actually, the scent of Geosmin not only appears in the soil but also common in our daily life. It's just that when these smells are present in drinking water or food, you will feel the "water smell" or "rancid taste". That is, the water or food has been infected by microorganisms. [2]According to this research, the scent emitted by soil fungi not only perceived by human, also attracts some small animals such as Collembola. This is a small arthropod preferring a moist environment, feeding in actinomycetes, slime bacteria, and other fungi. In this case, the scent of Geosmin is a signal for Collembola about Dinner time!

However, even though the soil fungi are the food source for Collembola, the hypothesis about trap where it is from?

To be more specific, scholars analyzed one kind of actinomycetes- streptomyces ceolicolor- in the soil in the experiment. Streptomyces is a type of gram-positive bacteria that produces spores when it is ready to multiply that can spread nascent bacteria. The metabolites of this streptomyces spores are geosmin and 2-methylisocamphanol, which attract the jumping insects and successfully allow the jumping insects to help spread the spores.

Therefore, we are not difficult to understand the description of the trap. The soil fungi use aroma to make the next trap to utilize Bollembola to help them to spread the spores.

Especially, researchers observed the reaction of Bollembola to volatile scent and found that Collembola is not only attracted by Geosmin but also stimulate Collembola‘s tentacles by the intermediates of synthesized Geosmin germacradienol and sub-product Geranie-D to have electrophysiological responses. [3]

1. The reciprocate relationship between Collembola and the soil

With the above introduction, I believe you have also realized that the relationship between jumping insects and soil fungi is not a one-way profit drive, but a special mutually beneficial relationship. Let's take a look at how this mutually beneficial relationship is manifested.

4.1

Streptomyces is the food for Collembola

Streptomyces produces some harmful metabolites that are not conducive to invertebrate consumption. However, Streptomyces is the only source of food for springworms, mainly due to the multiple gene clusters associated with detoxification mechanisms contained in the genome of springworms. Additionally, Streptomyces can produce a variety of antibiotics to help jumping worms kill pathogens in the body. Therefore, Streptomyces has fatally become food for jumping worms.

4,2

Collembola can help spread Streptomyces

Although Streptomyces is food for the jumping worms, the jumping worms are also very helpful for the spread of Streptomyces. Jumping worms can help the spread of fungal spores and help Streptomyces complete its life cycle.

There are two means for spreading Streptomyces

1. body surface adhesion

Studies have shown that the body surface of the jumping insects is covered with a hydrophobic waxy layer, which has a certain resistance to sticking, and most fungi cannot adsorb on the body surface of the jumping insects, but the spores can. Research data show that there are 10,000~100,000 streptomyces spores on the body surface of the jumping insects exposed to Streptomyces, which are mainly adsorbed on the bristles of the jumping insects.

2. spread by secretion

According to the research, in the secretion form Collembola, there are 70.8% Collembola’s secretion containing active streptomyces sprods. This finding confirms that sprods can live in Collembola’s intestine and spread via secrete. [3]

2. other reasons about the fresh scent

In fact, we smell many other mixing fresh scents except the soil scent after rains. For example, the smell of essential oils volatilized by plants after rain, or the ionization of oxygen molecules in the air into positive and negative oxygen ions, will also make us feel fresher.

In this case, after rains, let’s go outdoor and heavily breath the fresh air!

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SMART MAGAZINE AUTHOR: Dora

A brief analysis of ethical issues in animal experimentation

Keywords: laboratory animals

Laboratory animals are an indispensable part of medical experimentation; however, the ethics and welfare of these animals have long been a focus of social debate.

Supplementary: Laboratory animals refer to organisms that have been domesticated by humans over a long period, selectively bred according to scientific requirements, controlled for microorganisms they carry, and have a clear genetic background or known origin. Animals used in education, production, testing, and scientific research are often referred to as "living reagents."

For laboratory animals, sacrifice and contribution seem to have become their destined role. But does this mean we can disregard their inherent life value, using and disposing of them solely according to human will? If not, where should the boundaries lie for practitioners during actual use? With the increasing number and fields of animal experimentation, these questions have clearly become a matter of broad discussion and controversy beyond the scientific community, garnering attention from all sectors of society.

In Western countries, the early seeds of animal protectionism can be traced back to philosophical discussions on the rights of non-human entities in ancient Greece and Rome. With the rise of Christianity, anthropocentric thought came to dominate, positioning animals as subordinate beings created by God to serve humans. However, during the Renaissance and Enlightenment periods, the philosophy of benevolence began to take root, emphasizing kindness and compassion toward animals. In this period, concern for animal welfare increased, and calls to protect animal rights emerged.

In recent years, the proportion of animal experiments in all scientific research has continued to increase. It is estimated that in 2015 alone, the number of animals used for scientific research worldwide reached as high as 192.1 million; in 2021, the global market for laboratory animals was valued at around $20 billion, with the United States alone potentially using up to one billion laboratory animals between 2017 and 2018. In recent years, the demand for laboratory animals in China has also steadily risen. In 2015, the annual usage of laboratory animals in China reached 11.595 million.

Ethical issues arising from animal experimentation have also gained increasing attention. For example, in 2011, researchers from MIT, Harvard Medical School, and the Broad Institute published a paper in Nature titled “Selective killing of cancer cells by a small molecule targeting the stress response to ROS,” reporting that a small molecule, piperlongumine, could selectively kill cancer cells in mice. In September 2015, Nature issued a correction, retracting part of the data from the study due to some mice's tumor volumes exceeding the maximum allowable diameter of 1.5 cm. The resolution included a public apology from the authors, along with a mandate from Nature requiring future studies involving animal experiments to state the maximum tumor size permitted by the Institutional Animal Care and Use Committee and confirm this limit would not be exceeded during experimentation.

Although China began addressing animal welfare and ethics in research later than Western countries, significant legislative progress has been made. However, the following issues still exist:

Limited Awareness Among Professionals Regarding Animal Welfare and Ethics

Many medical researchers have a superficial understanding of animal welfare ethics, often viewing it merely as providing adequate care for laboratory animals. The specifics of implementation remain unclear to many, and some individuals perceive ethical reviews for animal welfare as a mere formality with little actual value.

Need for Strengthening and Enhancing Animal Welfare Ethics Committees

Many institutions still lack adequate awareness of animal welfare ethics and do not prioritize it sufficiently. Ethical committee members often lack specialized training, and some even show indifference toward ethical issues related to laboratory animals. This slows the progress of discussions on animal welfare, often failing to meet expected outcomes. Unexpected challenges frequently arise, and adherence to animal welfare principles largely depends on the professional integrity and ethics of practitioners. Therefore, a key focus should be on managing projects effectively throughout their duration and ensuring comprehensive oversight. This is essential to prevent welfare practices from becoming superficial and to realize genuine animal welfare.

Insufficient Infrastructure for Laboratory Animal Research Platforms

Laboratory animal breeding and care require specific environments, specialized feed, and bedding materials. The scale and quality of laboratory animal research platforms directly impact the progress and quality of research projects, as well as the level of welfare provided to the animals. However, the development of laboratory animal platforms lags behind the needs of current medical research, with noticeable regional disparities. These issues hinder the implementation of animal welfare ethics, the enhancement of research quality, and the translation of research outcomes.

In summary, to ensure the ethical welfare of laboratory animals, the following areas need improvement:
(1) Ensure Physiological Needs: Provide adequate nutrition to prevent hunger and thirst, supporting animals' growth and development.
(2) Protect Psychological Needs: Shield animals from fear and distress, preventing them from experiencing mental suffering.
(3) Provide Environmental Conditions: Ensure adequate shelter or comfortable living spaces where animals can avoid extreme weather and other natural hazards.
(4) Provide Sanitary and Health Conditions: Prevent and reduce injury, illness, and pain, ensuring sick animals receive timely medical treatment.
(5) Ensure Natural Behavioral Expression: Provide sufficient space and conditions that meet animals' needs for interaction and other normal behaviors.

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SMART MAGAZINE AUTHOR: Nox

Silent high-pressure society: Microglia-mediated social dysfunction

Keywords：microglial cell；Microglia type I interferon；
Synaptic loss；human communication disorders

Introduction:

In various dystopian and realistic films and television works, we can often feel the alienation between people, helplessness and the numbness of society as a whole through the camera -- expressionless employees in office buildings, children with lost eyes in slums, workers without thinking on assembly lines.....

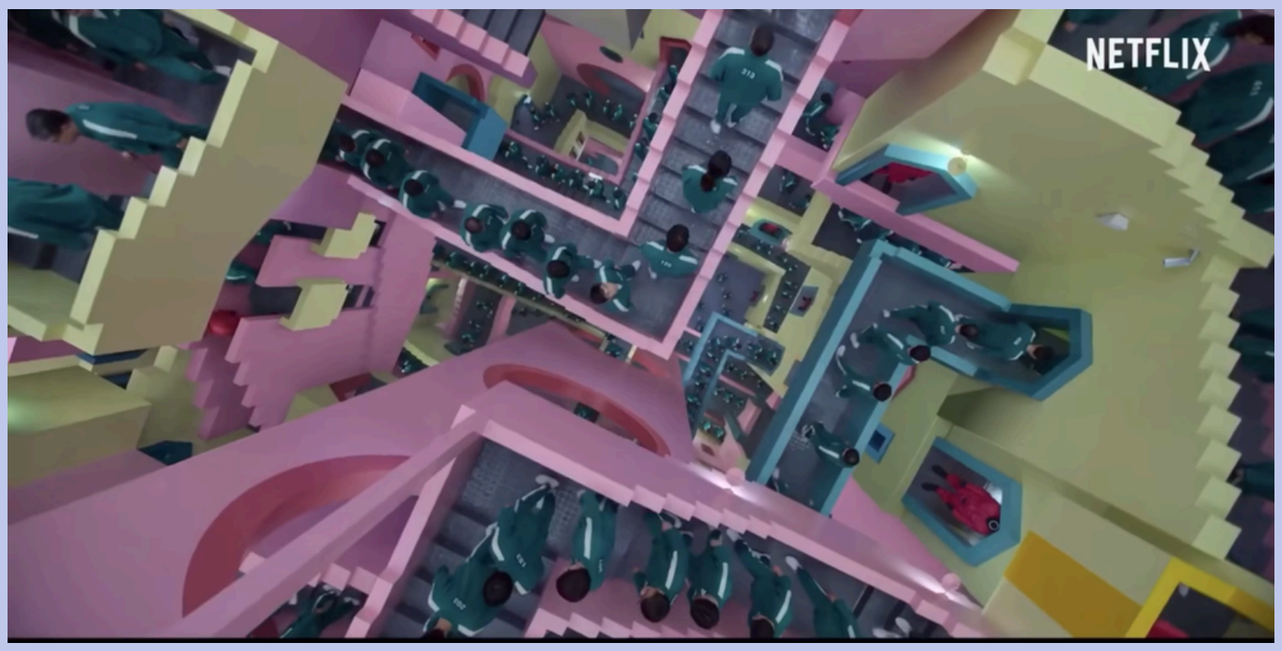


Figure 1. Still of Squid Game

Today, with the rapid rise of science and technology, the alienation of people is becoming more and more serious, and indifference seemsto have become a common disease of The Times.In this society that seems like a pressure cooker, mental diseases such as depression, schizophrenia and other mental diseases caused by chronic pressure go hand in hand with the social status of silence and alienation, among which social disorders are one of the core diseases of these diseases. This condition has previously been linked to synaptic dysfunction and loss of dendritic spines in the prefrontal cortex of the brain. [1] A study published in August in Molecular Psychiatry by Anil Kumar Pillai of the University of Texas Health Science Center at Houston, USA, suggests that type I interferon receptors (IFNAR) in microglial cellsplay a key role in regulating synaptic plasticity and social behavioral deficits associated with chronic stress conditions. [2]

Figure 2. The abridged general view of Three-chamber test

The Three-chamber test assesses the social preferences of mice with strangers. The experimental apparatus is divided into three connected compartments, two side chambers and an intermediate chamber.

At the start of the experiment, a mouse was placed in the middle chamber, and either a strange mouse or an empty compartment was placed in each of the two side chambers. By looking at the amount of time a laboratory mouse spends in various compartments, its preference for social interaction can be assessed. The Reciprocal social interaction test evaluates the physical interaction between a mouse and an unfamiliar mouse. Two mice are placed in the same environment, usually an open test box. Contact, chasing, sniffing and other interactions between the two mice were recorded, as well as their reaction time and frequency.

The Y-maze test assesses spatial working memory in mice. The mouse was placed in one of the arms, allowing the mouse to freely explore the maze, recording the order and frequency in which it entered the different arms to assess the mouse's spatial learning and memory ability.

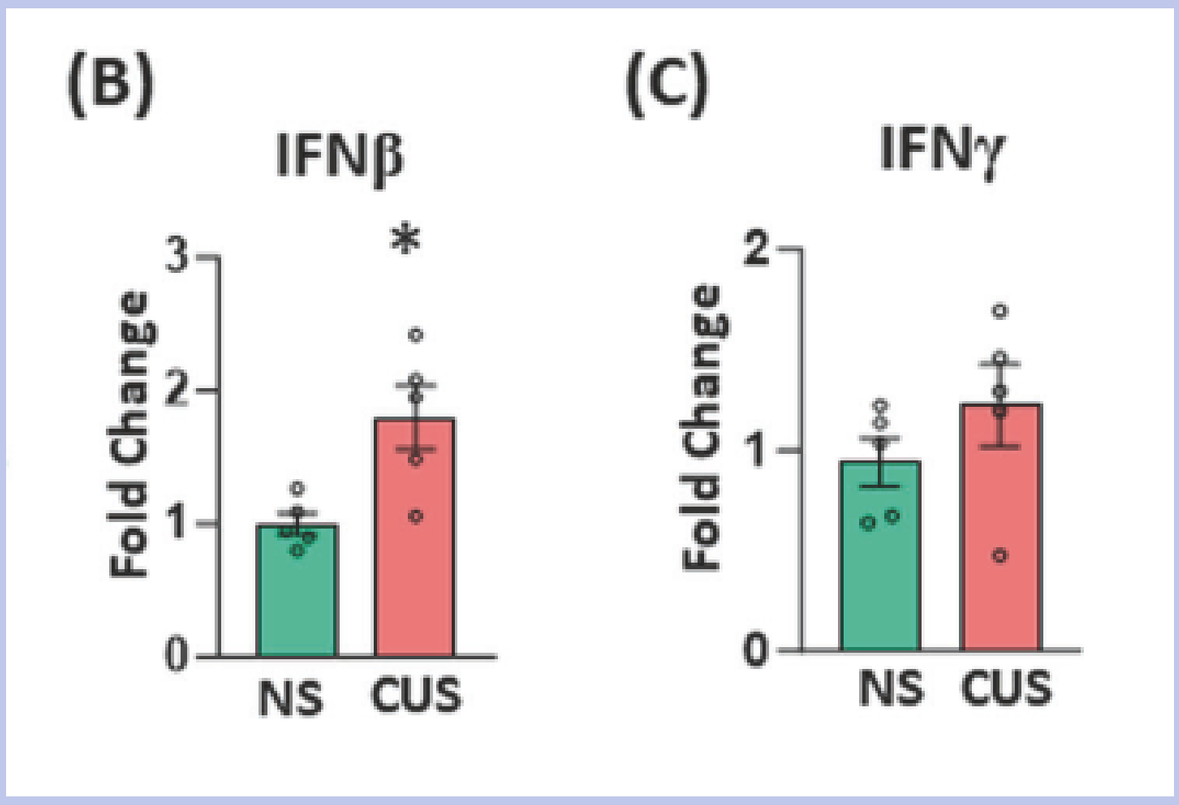


Figure 3. IFN levels were increased in CUS group

This study further elucidates the important role of microglia in mediating social impairments caused by chronic stress.

The researchers then examined mRNA levels of several pro-inflammatory and anti-inflammatory cytokines and found that they were significantly increased in the PFC of CUS mice, suggesting that CUS promotes neuroinflammation. After skeletonization analysis, it was found that the synaptic density in PFC of CUS mice was significantly reduced compared with that of normal mice. With significant increases in serum IFNβ levels and microglial activation found in PFCS, the researchers next investigated the role of microglia IFNAR in mediating cus induced social behavioral deficits. After knocking out IFNAR in microglia, chronic stress-induced social impairment and synaptic loss were reduced in mice.

The results showed that the expression of inflammatory factors in the PFC of mice exposed to Chronic unpredictable stress (CUS) increased substantially. The inflammatory factor IFN binds to IFNAR on microglia, thereby activating the expression of genes associated with synaptic loss in microglia. The loss of synapses in the PFC further leads to social dysfunction in the organism.

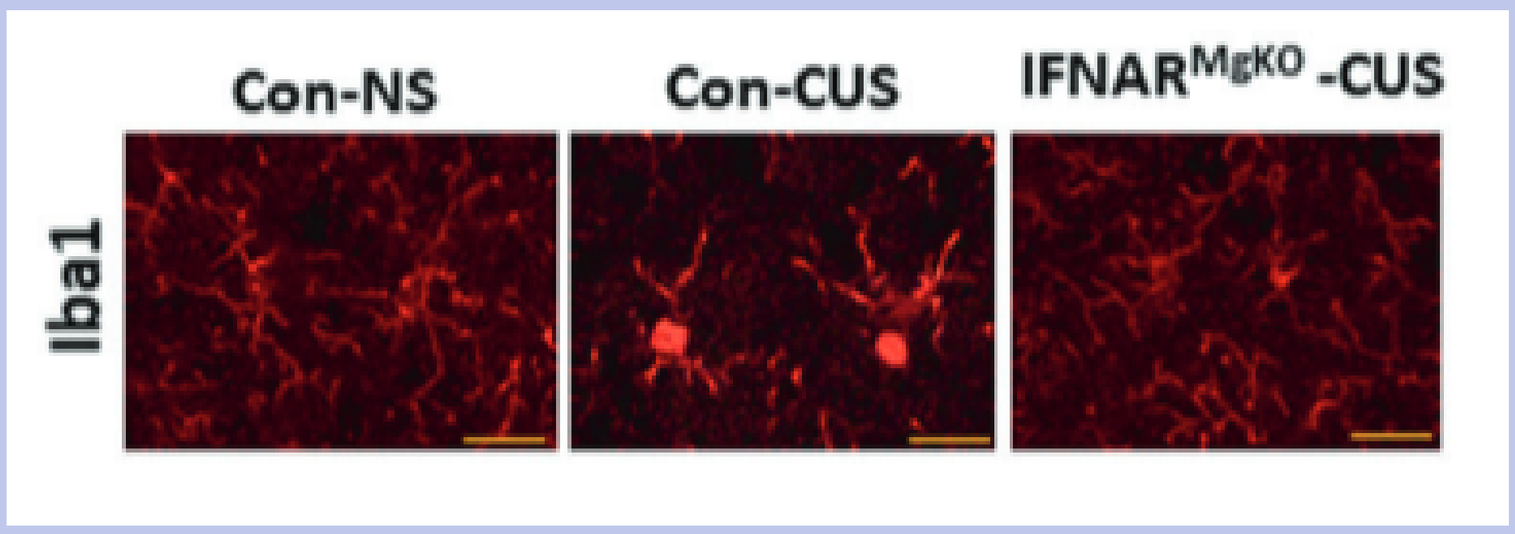
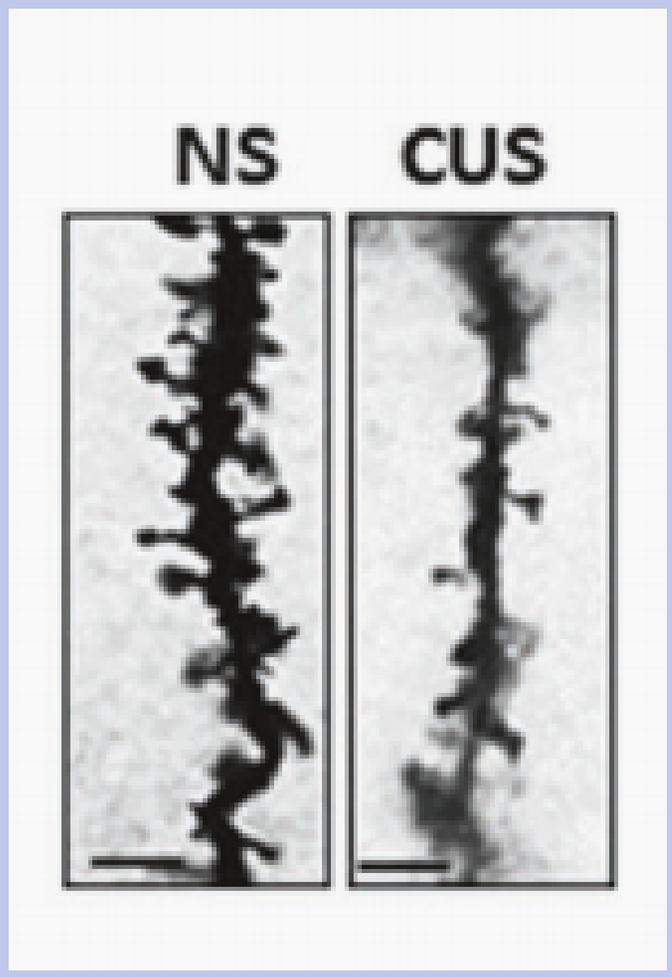


Figure 5. Microglial cell morphology of normal mice, CUS mice and IFNAR mutant mice under CUS

Figure 4. Decreased synapses in CUS group



Research significance:

The study found that chronic stress exposure induced an increase in IFNAR expression in microglia, and that mice with microglia-specific IFNAR deletion were protected from chronic stress-induced damage to synaptic density and social behavior. Treatment with IFN has previously been shown to worsen depressive symptoms in multiple sclerosis patients with a history of depression [3], and this study further demonstrates the neurotoxic effects of IFN. Furthermore, the study provides a potential therapeutic strategy targeting IFNAR for the treatment of chronic stress-related behavioral deficits.

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SMART MAGAZINE AUTHOR: Ariana

Subverting Cognition! Can Salt actually help fight cancer?!

Keywords: High-Salt Diet, Adoptive Immunotherapy, CD8+ T Cells, Glutamine Metabolism

Introduction:

Sodium chloride (NaCl), commonly known as table salt, is an indispensable seasoning in daily life, holding an almost unshakeable position on the dining table. Recent studies have shown that NaCl can promote tumor regression through T cells.

Research Introduction:

In recent years, studies have increasingly discovered that sodium chloride (table salt) can regulate the immune system in various contexts, highlighting its multifaceted immunomodulatory effects on cell activation, differentiation, and effector function. This raises an intriguing question: what impact does sodium chloride have on cancer?

Recently, a team led by Enrico Lugli in Italy found that sodium chloride can enhance the anti-cancer effects of T cell therapy in mice. This discovery suggests that the efficacy of T cell-based immunotherapies such as CAR-T and TCR-T could be further enhanced by simple treatments, facilitating rapid translation into clinical applications. Notably, they also confirmed in mice that a high-salt diet can enhance the anti-cancer capacity of T cells and inhibit tumor growth.

It is worth noting that this is the first-time scientists have found that sodium chloride can enhance the activation state and effector function of human CD8+ T cells, thereby boosting their tumor-killing ability. Thus, it can act as a positive regulator of anti-tumor immunity. This research reveals the potential mechanisms by which sodium chloride aids cancer treatment, helping to improve the efficiency of adoptive immunotherapy and allowing more cancer patients to benefit from this approach.

Experimental Process and Results:

The researchers first treated CD8-positive naive T cells with high salt (80 mM) and another group of T cells with urea and mannitol to simulate the osmotic pressure changes caused by high salt as a control group.

Compared to the control group, the experimental group showed a significant increase in the expression of granzyme B genes, indicating that high salt induces the activation of effector memory T cells. RNA sequencing results further revealed widespread changes at the transcriptome level induced by high salt, with transcripts related to effector or cytotoxic functions and stemness being upregulated. They also found that the main regulatory factors inducing T cell metabolic reprogramming, genes encoding plasma membrane glutamine transporters, and genes related to glycolysis were upregulated. This indicates that high salt also reshapes T cell metabolism.

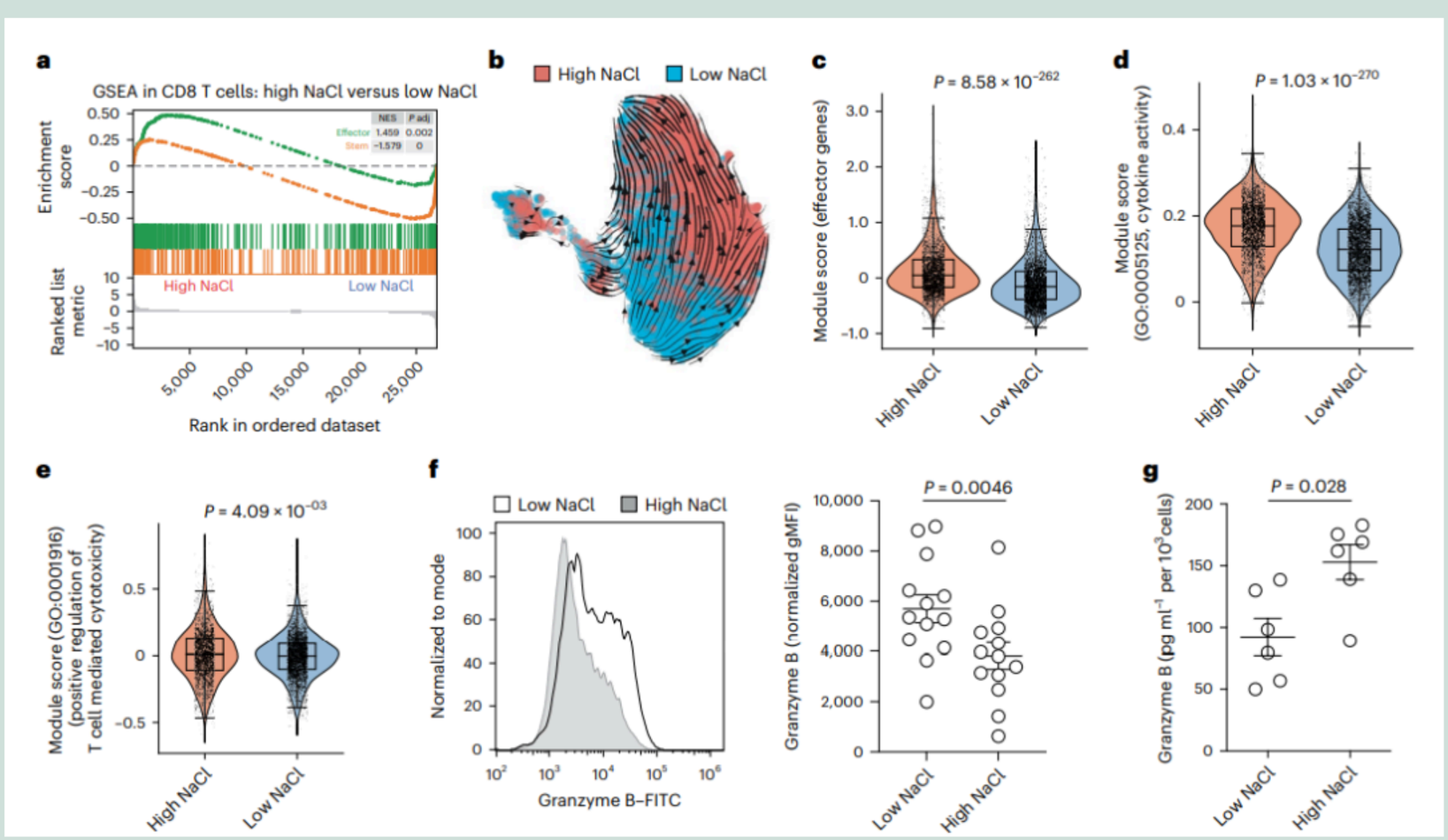

FIGURE 1: SODIUM CHLORIDE CAN ENHANCE T CELL ACTIVITY.

From the perspective of cellular functional changes, compared to the control group, high salt treatment increased interferon-γ and degranulation markers. In vitro cytotoxicity assays showed that T cells treated with high salt were more efficient at killing melanoma cells. Furthermore, they noted enhanced T cell receptor (TCR) signaling; for high salt to exert its effects, it must be combined with TCR activation stimuli.

Based on the above findings, the researchers propose that high salt promotes the effector differentiation of human CD8-positive T cells. They then boldly extended the research to the in vivo environment to investigate the effects of a high-salt diet on tumor immunity in mice.
They provided the mice with a high-salt diet (with 4% salt in food and 1% salt in water) and allowed them to eat freely. Two weeks after starting the high-salt diet (HSD), they transplanted MC38 colon adenocarcinoma cells into the mice and found that the high-salt diet caused sodium chloride to accumulate in the tumors, inhibiting tumor growth, while accumulation in other organs was minimal, without affecting the overall health of the mice.
In terms of anti-tumor effects, the high-salt diet significantly inhibited tumor growth compared to the normal salt diet (NSD). However, after using anti-CD8 monoclonal antibodies to deplete CD8-positive T cells in the mice, the anti-tumor effects of high salt completely disappeared, indicating that CD8-positive T cells are critical for the anti-tumor effects of a high-salt diet.
After analyzing the immune cell changes in the tumors of mice, scientists found that the frequency of CD8-positive T cells, natural killer cells, and CD4-positive T cells was more than twice that of the control group in the high-salt diet group.
Specifically, regarding CD8-positive T cells, compared to the control group, the high-salt diet group had a decrease in transcripts associated with terminal differentiation and exhaustion, while transcripts encoding cytotoxic molecules or related to activation and effector differentiation increased.

It is evident that a high-salt diet promotes immune activation while eliminating immune suppression.Notably, they also discovered that the transcriptional profiles of CD8+ T cells induced by the high-salt diet exhibited positive changes, characterized by downregulation of genes associated with terminal differentiation and exhaustion, and upregulation of genes related to cytotoxicity, activation, and effector differentiation, similar to those induced by PD-1 inhibitors. The high-salt diet enhanced the effector function of CD8+ T cells, inhibited their terminal differentiation, and accelerated the process of tumor clearance by CD8+ T cells.

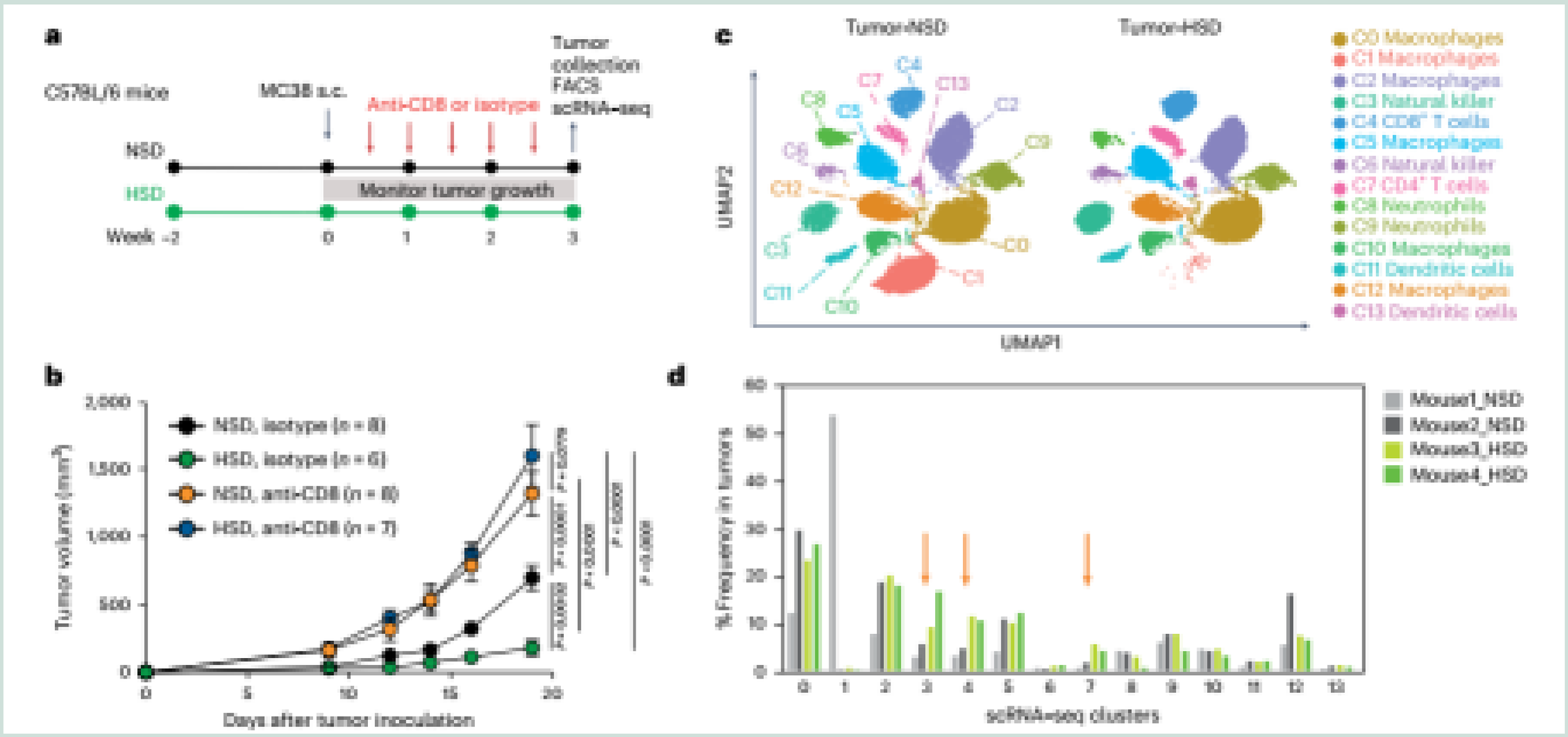

Figure 2: Schematic diagram of the design of in vivo experiments (a); average tumor volume of male B6 mice fed a normal salt diet (NSD) or a high-salt diet (HSD) after treatment with anti-CD8 antibodies or control antibodies (b); single-cell RNA sequencing (scRNA-seq) data collected from mice fed NSD or HSD on day 19 post-tumor inoculation (c); bar chart showing the frequency of each cluster of cells in mice, with arrows indicating clusters that changed in mice fed a high-salt diet (d).

Next, the researchers explored the mechanisms by which a high-salt diet reshapes CD8-positive T cells. They found that NaCl-mediated reprogramming largely depends on increased uptake of glutamine from the microenvironment. In simple terms, a high-salt diet promotes the intake of glutamine by CD8-positive T cells, achieving T cell reprogramming at the epigenetic level and enhancing their anti-tumor activity.

Biological Mechanism

During the culture of CD8+ T cells, NaCl supplementation induces effector cell differentiation, interferon-γ (IFN-γ) production, and cytotoxicity, while maintaining the gene networks responsible for stem-like plasticity. Thus, in humanized mouse models, this results in superior anti-tumor immune responses generated by the infusion of specific tumor T cells. In mice, a high-salt diet (HSD) suppresses terminal differentiation in a CD8+ T cell-dependent manner and enhances the effector capacity of CD8+ T cells, thereby inhibiting tumor growth.

Mechanistically, NaCl enhances glutamine consumption, which is crucial for transcription, epigenetic, and functional reprogramming. In simple terms, this is a glutamine-dependent process. After treating CD8-positive T cells with high salt, the expression of genes encoding glutamine transporters is upregulated, promoting the uptake of glutamine by CD8+ T cells; the metabolic products of glutamine can increase the activity of demethylases, enhancing chromatin accessibility at specific gene loci in CD8-positive T cells.

In humans, CD8+ T cells that recognize antigens in tumors and predict a good response to immune checkpoint blockade (ICB) therapies are similar to those induced by NaCl. Therefore, NaCl metabolism is a regulator of the effector functions of CD8+ T cells and has potential implications for cancer immunotherapy.

Future Prospects:

This finding reveals the potential immunoprotective role of NaCl and provides new insights into the metabolic reprogramming of immune responses, which has profound implications for immunotherapy. It is important to note that while the research demonstrates that sodium chloride can enhance anti-tumor immunity, this conclusion is still in the preclinical exploration stage, requiring rigorous human clinical trials to validate its efficacy and safety. Moreover, a high-salt diet is a major contributor to various serious health issues. Therefore, we cannot conclude that a high-salt diet can fight cancer or even prevent cancer based on these two studies, nor should we attempt the experimental methods mentioned.

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Personally, the excessive use of colors to emphasize keywords and key sentences, along with insufficient emphasis on subheadings, makes the entire article visually uncomfortable and somewhat chaotic. The formatting is not ideal; I suggest reducing some colors and emphasizing subheadings with underlining or bolding.

The consequences of a high-salt diet in enhancing immunity could be illustrated with appropriate examples, and this article could explain some technical terms.
In the “Experimental Process and Results” section, you could explain the original functions of T cells and the effects of high salt on them, as well as the benefits and changes associated with metabolic reprogramming.

SMART MAGAZINE AUTHOR: Molly TRANSLATOR: Anaya

Only using petty skill, works like magic

Keywords: Toxoplasma gondii; protein medicine; neuron; drug delivery

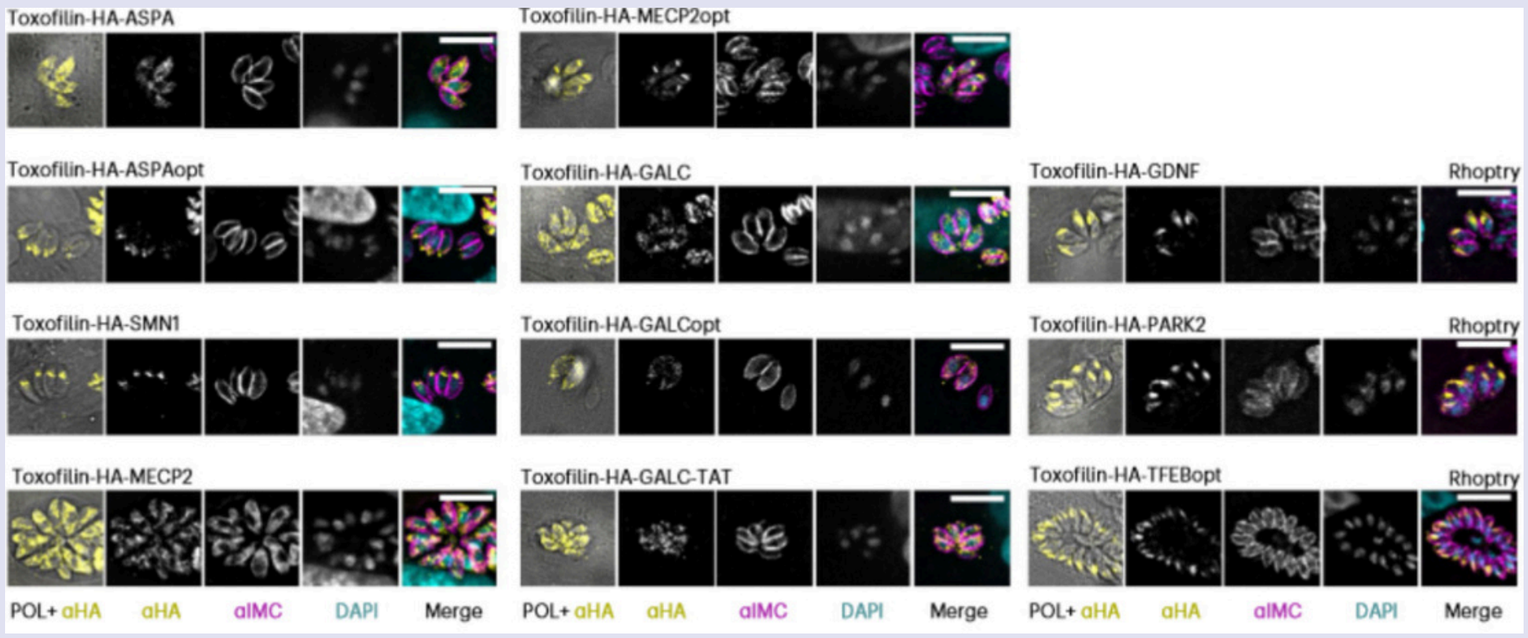
Introduction:

Delivery of macromolecules through biological barriers, such as the blood–brain barrier, is difficult, limiting its application in vivo. Toxoplasma gondii is a parasite that naturally transmits from the human gut to the central nervous system (CNS) and can deliver proteins to host cells. In the present study, we utilized the endogenous secretory system of Toxoplasma gondii–rod bodies and dense granules to deliver multiple large (> 100 kDa) therapeutic proteins into neurons by translational fusion with actin–binding protein and GRA16, and demonstrated the effectiveness of drug delivery.

Methods and design

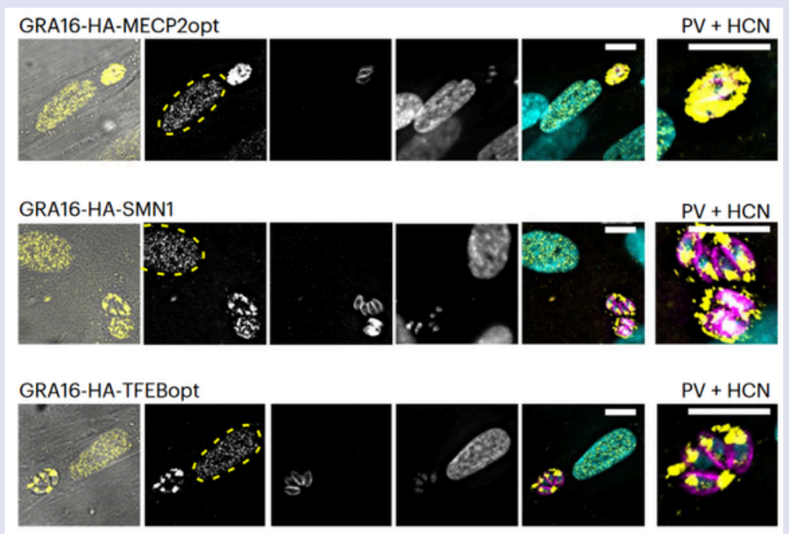
Researchers use toxoplasma gondii as a vehicle to deliver protein. Toxoplasma gondii is ubiquitous, and they can actively migrate into the central nervous system, cross the blood–brain barrier through complex forms of co-evolution and adaptation with the host, and then largely persist in the central nervous system.

Intracellular RH Toxoplasma gondii stably expressing different actin–fused therapeutic proteins

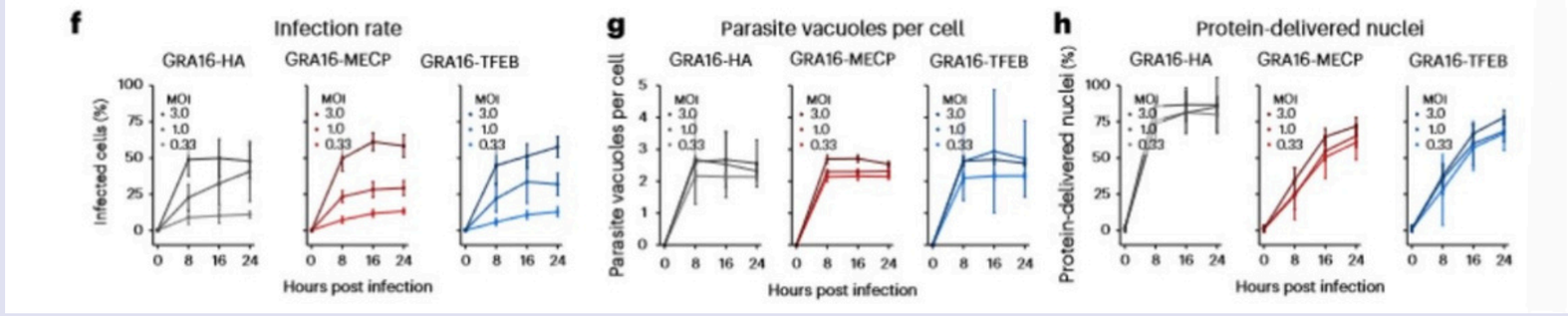


By trying proteins that have different molecule sizes, functions, and target positions in the cell, researchers observed High levels of intracellular delivery of several therapeutic neuroproteins. Then, using actins(TGME49_214080) and GRA16(TGME49_208830) as the two secretive systems that toxoplasma gondii can deliver effector proteins–Chromatoid body and Dense granule, and chose known function protein medicine to fuse.

Due to difficulty in exploring target proteins by immunostaining, researchers chose to test using easily detectable genome editing proteins such as zinc finger proteins and Cas9. Although they were both successfully expressed in the chromatoid body, no activity was detected in the cells. This could be due to low secretion levels, low nuclease activity, or insufficient gene induction time. Subsequent steps still require increasing the secretion or activity levels of the fusion proteins in the host cells.

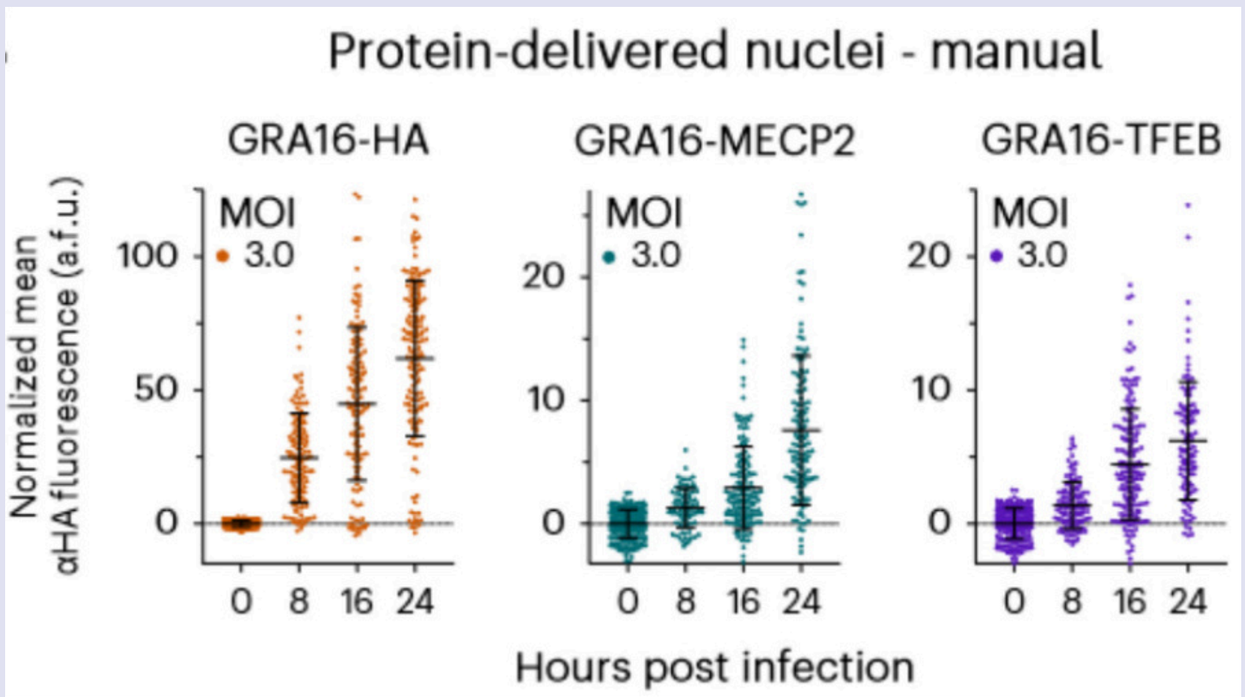


Fusion proteins locate on parasitic vacuoles and host nuclei(MECO2opt, SMN1, TFEBopt)



No significant differences in their abilities to invade, replicate, and deliver proteins to the host cell nucleus

Proving by the experiment, toxoplasma gondii can deliver between proteins in cells by dense granules. To deliver interested therapeutic proteins directional transfer to dense granules, researchers constructed fusion expression vectors of GRA16 with various fusion proteins, among which GRA16 fused with nuclear proteins TFEB and MeCP2 exhibited the most potent delivery and targeting capabilities. Especially, they are Mammalian Full-Length Proteins which sizes arrive 109kDa and 110kDa. Staining of mouse brain slices revealed that Toxoplasma gondii can deliver the MeCP2 protein to neurons in the brain without affecting the distribution and survival of the parasite. Furthermore, the study compared Toxoplasma gondii strains expressing different proteins and found no significant differences in their abilities to invade, replicate, and deliver proteins to the host cell nucleus.



The comparison of expression level in the nucleus of the host cell between fusion proteins and GRA16

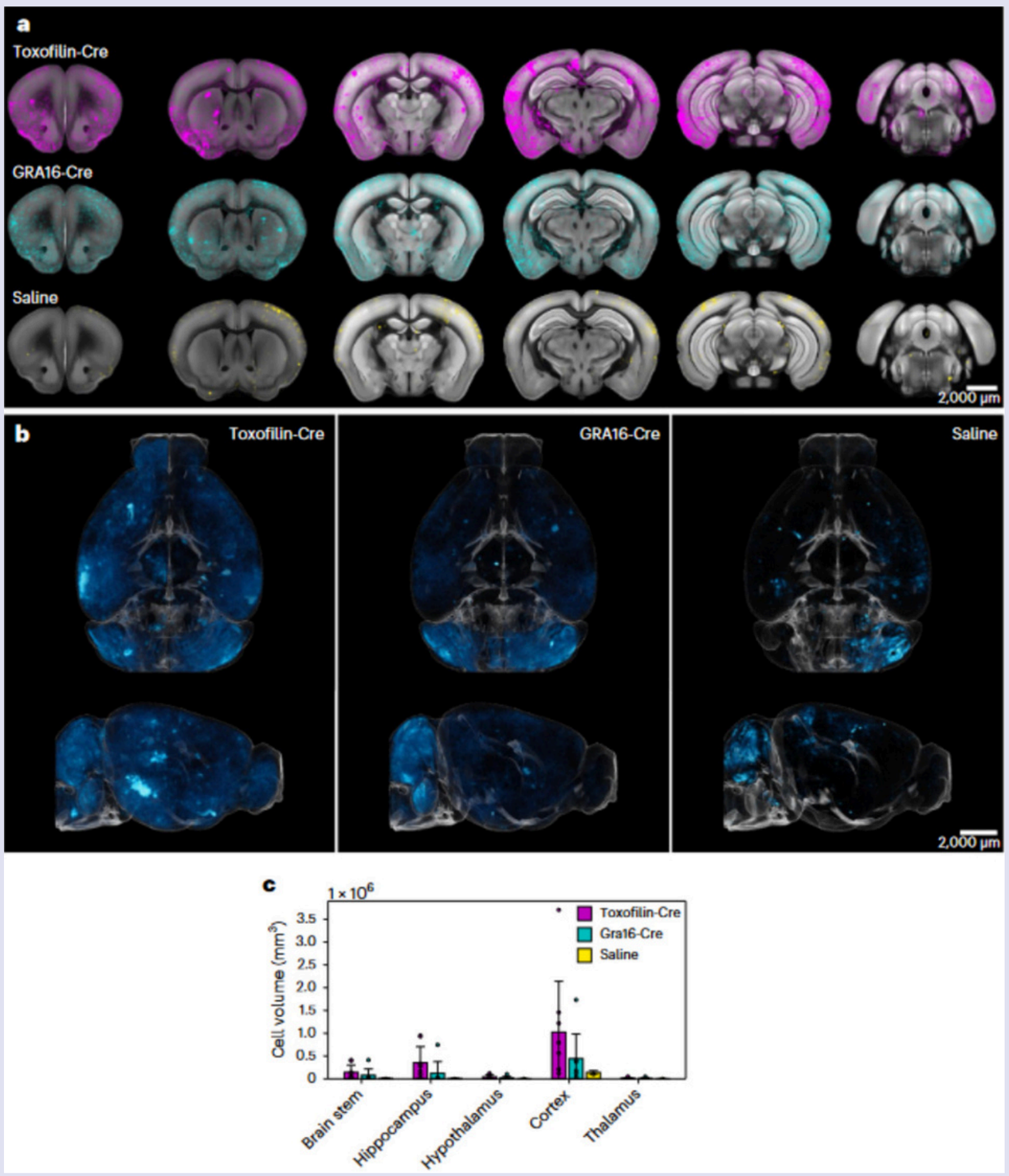
Conclusion:

This research indicates that Toxoplasma gondii can be the protein delivery system in cultured fibroblasts, in vitro differentiated neurons, human brain organoids, and mice, and suffer effects in different conditions that impact delivery ways. The chromatoid body system directly expels proteins into host cells through transient opening of the plasma membrane, avoiding cell invasion or persistent presence in these cells. In contrast, the secretion of dense granules needs to coexist with toxoplasma gondiis and cells, but it can provide a higher secretion of protein and a more lasting delivery. Samples do not observe the correlation between delivery efficiency and sizes of proteins; namely, the size of protein is not the limitation of delivery efficiency. With observing, whether it is rod protein secreted by granulosa cells or protein secreted by dense granules, protein delivery levels are highest in the cortex.

Although Toxoplasma gondii has no symptoms in most circumstances when they are infected, this still induces a series of negative impacts, hence it is necessary that further studies need to describe and improve the safety and efficacy of Toxoplasma gondii-based vectors.

Although fusion proteins' delivery efficiency is same as GRA16, but when entre into cells, these fusion proteins' cumulant significantly declines.

Researchers found that toxofilin-Cre has a significant advantage in delivery efficiency in 3D imaging. In this case, one explanation is that toxofilin-Cre may use certain mechanisms to pierce or entre into neutrons more efficiently instead of depending on the formation of intracellular parasitic vacuoles as GRA16-Cre.



3D imaging shows the average volume distribution of Zsgreen+ cells in each brain region

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SMART MAGAZINE AUTHOR: Evelyn

How Pregnancy Might Rewire Your Brain

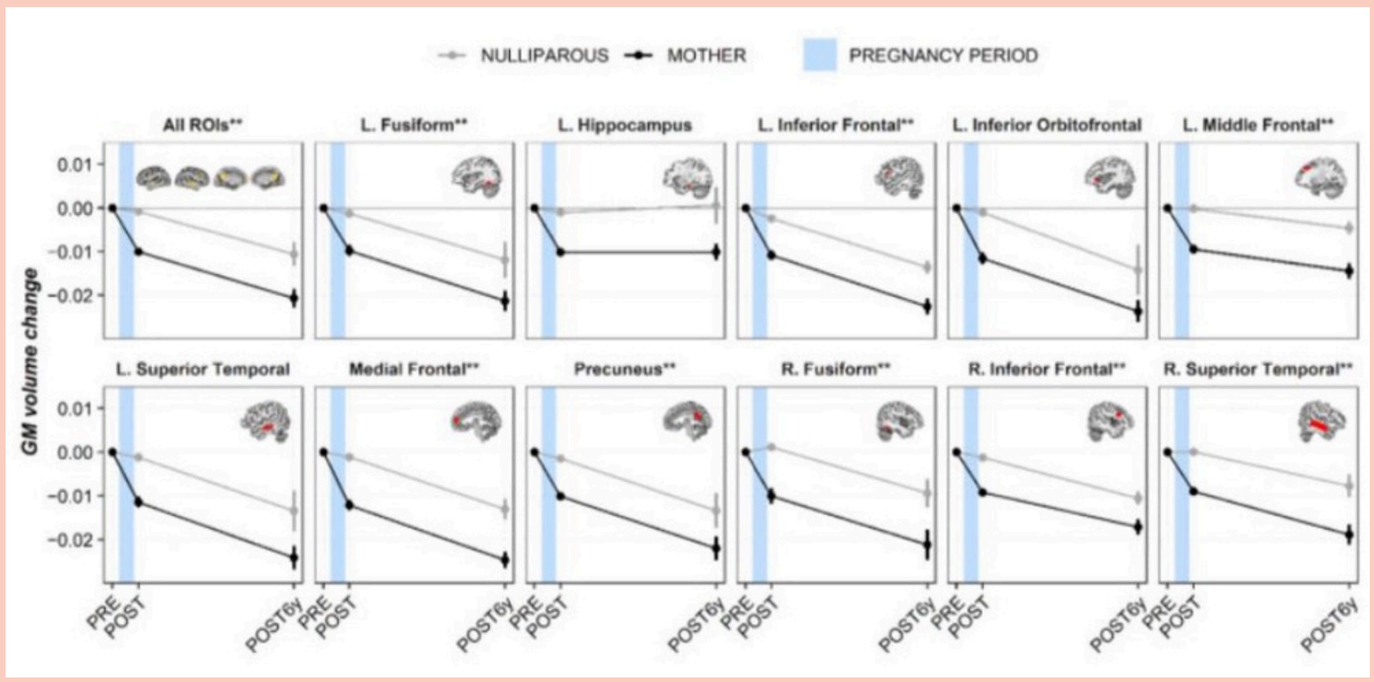
Keywords: pregnancy; maternal brain; cognitive deficits; gray matter; reproductive hormones

Introduction:

Pregnancy represents a tremendous transformation in both a woman's physical body and psychological state, due to a dramatic surge in reproductive hormones and subtle brain reformations. The prevalence of "pregnancy brain", for instance, referring to symptoms of forgetfulness, difficulty concentrating, and mental fogginess, speaks to the cognitive and neurological changes that a mother might undergo. Additionally, many women also reported increased empathy and emotional sensitivity during pregnancy and post-partum. By sensitizing the brain to key stimuli, these cognitive and neurological adaptations are speculated to serve as the evolutionary preparatory mechanism for parenthood. Yet there still exists a considerable gap in the scientific literature on pregnancy and post-partum neuroscience. It was not until the recent decade that science began to recognize the alterations that pregnancy produces in the human brain, with new studies emerging that observe lasting structural brain changes and effects of hormonal fluctuations during and after pregnancy.

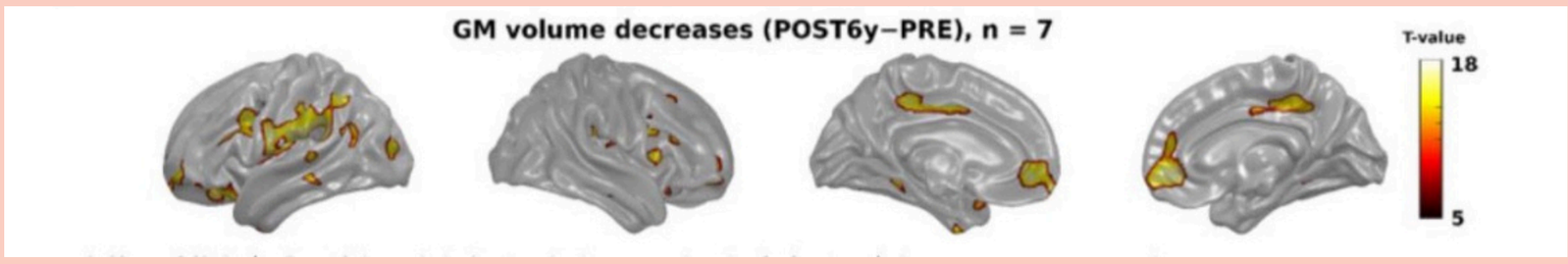
1.Effects on Cognition

Pregnancy tends to catalyze a series of shifts in memory, attention and concentration, executive function, and emotional and social cognition, among which the most notable are what is described as "pregnancy brain" or "momnesia". Despite ongoing debate regarding cognitive decline during pregnancy, an increasing body of research now corroborates its validity. In a prospective cohort study comprising 40 pregnant and 40 non-pregnant women, researchers found that non-pregnant women outperformed pregnant women in cognitive tasks such as Verbal Paired Associates (participants listen and remember paired words), Naming Objects and Fingers (participants name everyday objects and the fingers on their hand), and Digit Span (participants repeat back a series of numbers in the order they hear them or in reverse order). This demonstrates deficits in learning, memory, language abilities, and attention among pregnant women, which are associated with the involvement of brain regions such as the lateral, medial frontoparietal, occipital areas, prefrontal lobes, and inferior left parietal lobule (Barda et al.). In addition, the study suggests that impairment in cognitive functions may be attributable to hormonal changes, especially during the later stages of pregnancy.



2.Gray Matter Loss

Other cognitive shifts, particularly enhanced maternal caregiving and bonding, can be explained by changes in the brain structure. Studies have confirmed that pregnancy can induce pronounced gray matter volume reductions in brain regions associated with social cognition, empathy, reward processing, and emotional regulation. In a 2021 longitudinal study following a cohort of 25 first-time mothers and 20 nulliparous women, researchers found that most pregnancy-induced gray matter shrinkage persisted at least six years after parturition. Using MRI scans, researchers were able to classify women as having been pregnant or not with a 91.67% accuracy. Full brain analysis also showed gray matter volume changes in every region of interest in the study, including the medial prefrontal cortex(involved in social cognition, decision-making, and empathy); precuneus (involved in self-awareness, social processing, and perspective-taking); hippocampus(associated with memory and learning); inferior orbitofrontal cortex (involved in emotion regulation, reward processing, and decision-making); and superior temporal cortex (involved in auditory processing and language comprehension) (Martínez-García et al.). Lastly, to corroborate the relation between brain changes and motherhood, larger decreases in GM volume were associated with higher scores on the "Pleasure in Interaction", substantiating their relation to reinforced maternal bonding and caregiving behaviors.



Gray matter volume changes for every region of interest at every session (Martínez-García et al.) Gray matter volume decreases between the before conception (PRE) and the six years after parturition (POST6y) sessions in mothers (Martínez-García et al.).

3.Synaptic Pruning

The losses in brain mass, however, are not harmful but are akin to the similar decline in GM volume that occurs during adolescence, representing a process of pruning or streamlining of brain circuits. During this process, weak or excess neural connections are eliminated in order to optimize neural efficacy and tune the brain networks to more specialized functions. In pregnancy specifically, this process of synaptic pruning serves as an adaptive functioning, wherein essential cognitive functions take precedence to enable better caregiving behaviors, social bonding, parenting skills, and decision-making during and after pregnancy (Anderson & Rutherford).

4.Hormonal Influence

Closely interwoven with the body's neural network, hormones play a vital role in cognitive, emotional, and behavioral changes during gestation and after parturition. Hormones like estrogen, progesterone, oxytocin, cortisol, and prolactin orchestrate the reorganization of the brain's structure and function as well as underlie cognitive transitions and mood fluctuations.

Sex steroid hormones, primarily estrogen and progesterone, witness a dramatic surge during pregnancy, and peak in the third trimester. Estrogen is one of the principal triggers for pregnancy-related structural neuroplasticity and interacts with the brain's Default Mode Network (DMN). DMN is composed of brain regions that are active when the individual is engaged in self-referential thinking, autobiographical memory, and social cognition. For example, a prospective cohort study that follows nulliparous women over time noted that third-trimester estradiol (a type of estrogen) levels are closely linked to neuroplasticity by enhancing dendritic spine and synapse density, which can amplify functional connectivity and coherence in DMN. Increased DMN coherence, as a result, might lead to a shift in identity and cognitive focus from the mother to the child and augmented maternal responsiveness and capacity to interpret the infant's cue (Hoekzema et al.).

Other hormones, like the stress hormone cortisol, which increases to support fetal development and regulates immune response and metabolism, can impair learning and memory by damaging the hippocampus. High cortisol levels are associated with symptoms of forgetfulness and cognitive deficits, which can explain the phenomenon of "brain fog" or "pregnancy brain" during pregnancy. Cortisol, although critical to the development of the fetus, however, can also increase sensitivity to stress and anxiety, potentially contributing to prenatal depression.

Conclusion:

Historically, pregnancy has often been overlooked in scientific inquiry, with a lack of focus on neural changes spurred by pregnancy. While advancements in technology have enabled more precise equipment for investigating neurological landscapes, gaps remain in the understanding of pregnancy-induced changes occurring during gestation. Most research tends to focus on brain changes observed after childbirth as opposed to within its duration. Moreover, the long-term effects of these changes are also underexamined This oversight not only limits our understanding of maternal brain health but also impacts the quality of maternal healthcare practices. Addressing these gaps is essential not only in terms of academic interest; it is crucial for enhancing maternal healthcare practices and fostering a supportive environment for new mothers.

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Quinoxaline derivatives and their biomedical applications

Quinoline is a class of electron-deficient aromatic rings with multiple substitution positions, which can be utilized in the design of fluorescent materials. By introducing certain electron donors, the quinoline core can be modified to tune the photophysical properties of its derivatives. In recent years, quinoline has demonstrated broad application prospects in fields such as phosphorescent materials, donor-acceptor theory, and fluorescent probes, especially in high-sensitivity detection techniques in biomedical and chemical sensing applications. However, despite some progress in the development of quinoline-based luminescent materials, research on material structure design and response mechanisms remains insufficiently deep. Future studies need to further explore its potential applications and directions for performance optimization.

1.1 Pressure-Induced Luminescence

Pressure-induced color change (MCL) materials refer to a type of sensitive fluorescent material whose fluorescence color undergoes reversible changes in response to external stimuli, such as mechanical stress (e.g., grinding, pressing, crushing, scratching, and shearing), thermal treatment, and solvent vapor [1-2]. Research has shown that materials used for detection purposes exhibit higher sensitivity when their emission spectra are less affected by interference compared to their absorption spectra. Due to the responsive characteristics of MCL materials to external stimuli, they hold potential application value in various fields, including luminescent devices, fluorescent switches, mechanical force sensing, data storage, and security inks [2]. Most reports indicate that changes in molecular conformation, packing, and intermolecular interactions under external stimuli are key factors influencing MCL performance.

1.2 Donor-Acceptor (D-A) Theory

In the design of MCL materials, the donor-acceptor (D-A) theory is frequently employed to regulate the optical properties of the materials. The D-A theory is based on the interactions between donor and acceptor units, providing a foundation for molecular structure design and bandgap regulation. Quinoline, as a typical electron-accepting molecule, features a highly conjugated π-electron system and excellent electron-accepting capability, making it a common choice as the acceptor unit in D-A systems. According to D-A theory, by altering the electron donor and acceptor, it is possible to tune the energy gap and structural characteristics of the materials, leading to widespread applications in the field of organic optoelectronic materials [3-6].

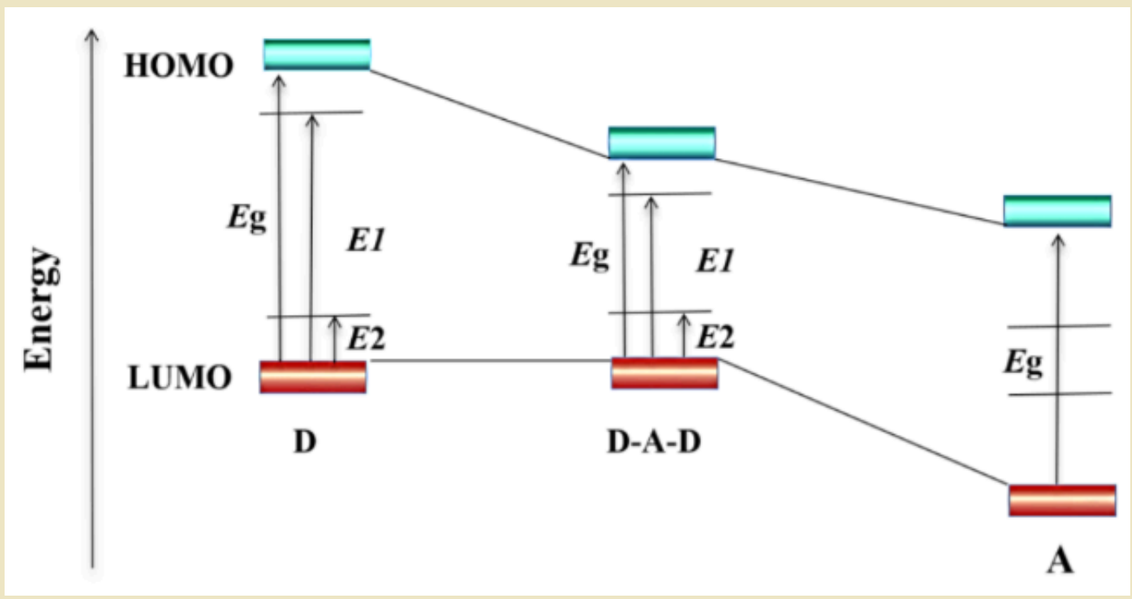

Figure 1.1 Donor-Acceptor (D-A) Theory

1.3 Fluorescent Probes

Fluorescent probe technology utilizes the photophysical and photochemical properties of specific substances to conduct qualitative and quantitative studies on research subjects at the molecular level [7]. This method is highly sensitive and offers a broad dynamic response range, making it widely applicable in various detection and labeling

scenarios. For example, various ions, amino acids, and biological enzymes present in living organisms play irreplaceable roles in maintaining physiological balance and coordinating physiological activities. Currently, researchers have developed different types of fluorescent probes to study physiological processes within organisms [8]. Fluorescent chemical sensors hold significant application value in fields such as molecular biology and clinical diagnostics, experiencing rapid development in recent years [9].

1.4 Research Progress on Quinoline-Based Luminescent Materials

Quinoline, also known as benzo[b]pyrazine, features an electron-deficient and rigid planar structure, making it suitable for the design of fluorescent materials [10-18]. Quinoline has multiple substitution positions, which can be modified by introducing electron donor groups to yield high-performance fluorescent materials [4-6]. Recently, researchers have also discovered that it shows strong responsiveness to specific metal ions, enabling its use in the creation of fluorescent probes or chemical sensors [19].

In 2016, Chen et al. [19] designed and synthesized a series of symmetrical cross-conjugated organic luminescent materials with different substituents. They systematically studied their intramolecular charge transfer (ICT), piezochromic fluorescence (PFC), and sensing properties. The results indicated that luminescent materials with the same conjugated backbone exhibited varying ICT interactions. Analysis by Lippert and Mataga revealed that the dipole moment difference between the ground state and excited state of the unsubstituted material 1 (as shown in Figure 1.2) was the largest. Furthermore, due to the phase transition between the crystalline and amorphous states, the target material exhibited reversible PFC characteristics. Material 2, with pyridine as a substituent (as shown in Figure 1.2), exhibited the most pronounced piezochromic fluorescence. A color shift of 40 nm was observed when the original sample was ground. Additionally, materials 1 and 2 showed selectivity and sensitivity to Fe^{3+}. Material 2 could also serve as a colorimetric and fluorescent chemical sensor for silver ions.

In 2018, Yu et al. [4] aimed to address the challenge of achieving both high efficiency and low efficiency roll-off in organic light-emitting devices (OLEDs) based on thermally activated delayed fluorescence (TADF) emitters. They meticulously designed and synthesized a series of novel emitters (3, 4, 5, and 6, as shown in Figure 1.2) by incorporating 9,9-dimethyl-9,10-dihydroacridine (DMAC) or 10H-phenoxazine (PXZ) as donor units within the quinoline framework. They discovered that by adjusting the electron-donating ability of the donor and the number of donor units, they could systematically tune the photophysical properties of the TADF-AIE emitters, allowing the emission range to span from green to red.

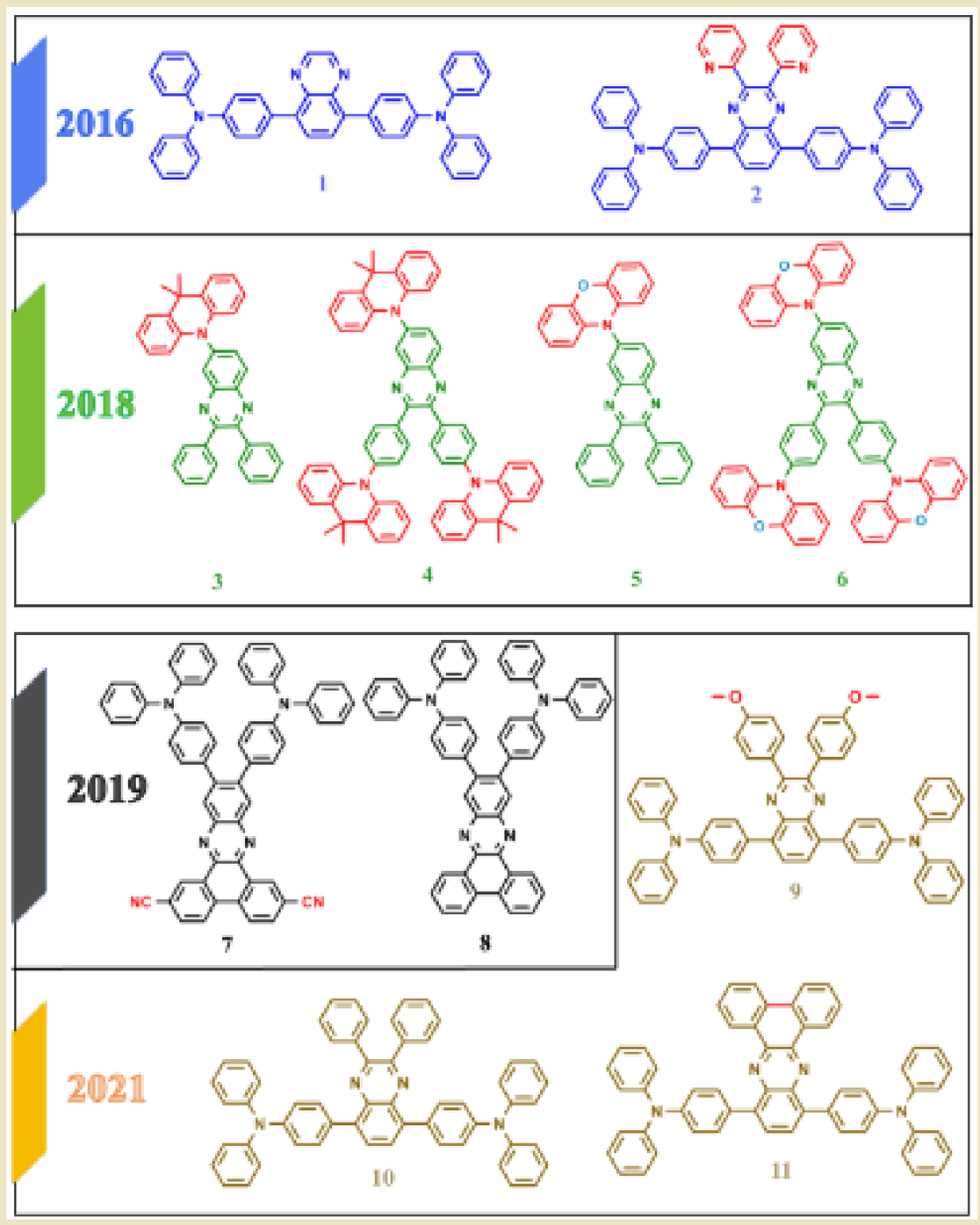

Figure 1.2 Recent Quinoline Derivatives

In 2019, Wang et al. [5] designed and synthesized two highly fluorescent emitting materials (7 and 8, as shown in Figure 1.2), where two adjacent triphenylamine (TPA) groups served as electron-donating units, and a dibenz[a,c]phenazine group acted as an electron-accepting group. In material 7, the introduction of two cyano groups connected to the dibenz[a,c]phenazine unit enhanced its electron-accepting ability. The results showed a significant red shift in the UV-vis absorption and photoluminescence spectra of 7 compared to 8. Additionally, the introduction of cyano groups in 7 resulted in significant separation of the frontier molecular

orbitals (FMOs), leading to a small singlet-triplet splitting energy (ΔEST) and a strong intramolecular charge transfer (ICT) state. Notably, material 7 exhibited a higher photoluminescence quantum yield (PLQY) and better device performance than 8. An OLED device doped with 10 wt% of 7 achieved a maximum external quantum efficiency (EQE) of 24.97%.

In 2021, Fu et al. [6] synthesized three novel donor-acceptor-donor (D-A-D) type molecules (9, 10, and 11, as shown in Figure 1.2) composed of triphenylamine (TPA) and substituted quinoline parts, which were further used in electrochromic devices. Derivatives 9 and 10, featuring two twisted substituents on the π-conjugated main chain, demonstrated effective electrochromic properties, including up to 70% high optical contrast, a short response time of less than 3 s, high coloring efficiency exceeding 200 $cm^2 C^{-1}$, and good cycling stability. However, derivative 11, which utilized a highly coplanar fused electron-acceptor unit, exhibited poor electrochromic performance and low stability.

1.5 Applications of Quinoline-Based Luminescent Materials in Biomedicine

Quinoline-based luminescent materials demonstrate extensive application potential in the biomedical field due to their unique structure and optoelectronic properties. Some compounds within this class possess aggregation-induced emission (AIE) characteristics, significantly enhancing fluorescence in the aggregated state, thus avoiding fluorescence quenching issues commonly encountered with traditional fluorescent dyes. This feature allows quinoline-based luminescent materials to excel in biomedical imaging, achieving efficient detection and diagnosis of cells, tissues, and living organisms. For example, fluorescent molecules based on the quinoline skeleton have been successfully applied for the specific detection of cell ferroptosis processes in vivo and in vitro.

Moreover, quinoline compounds have been widely studied and applied in the development of anti-cancer, anti-microbial, and anti-viral drugs. Through chemical modifications and structural optimizations, drugs with higher activity and selectivity can be designed. As fluorescent probes, quinoline-based luminescent materials exhibit high sensitivity and selectivity, enabling efficient recognition and detection of specific biomolecules, such as fluorescent probes for detecting explosives like trinitrophenol and specifically recognizing glutathione.

1.6 Current Issues

Currently, research on quinoline-based organic fluorescent materials has made certain progress, with some materials exhibiting high photoluminescence quantum yields and promising applications in luminescent devices; some quinoline-based materials respond to specific metal ions [19]. However, overall, the number of reported quinoline derivatives remains relatively small, with only a few dozen available. The regulatory role of electron acceptor/donor groups on the MCL performance of quinoline-based materials is still unclear, and the MCL mechanisms require further investigation. Additionally, the number of reported quinoline derivatives responsive to metal ions is also limited, and their response characteristics remain unclear, necessitating further development and exploration.

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SMART MAGAZINE AUTHOR: Teresa

Introduction and Applications of Molecular Markers– Case Studies in Africa

Key words: conservation genetics, molecular markers, genetic diversity.

Abstract

Molecular tools, the pivotal tools in molecular ecology and conservation genetics are introduced in this essay, along with their wide-ranged applications. Meanwhile, there will be parts focusing on discussing the consequences of implicating nuclear DNA markers, despite their differences and limitations, in the conservation of endangered animals in Southern and Eastern Africa.

Introduction

Biodiversity matters from many perspectives to both humans and nature. The loss of it is mainly caused by anthropological aggression to the rights of non-human organisms and can trigger a series of damage to both human civilization and the entire ecosystem. To maintain the vulnerable relationship between humans and the nature, to protect the global health and economy, it is the responsibility of humans to conserve and even helping to develop biodiversity across the borders (UNESCO, 2023).
As closely related interdisciplinary fields, molecular ecology and conservation genetics depend much on molecular and genetic studies to help designing strategies and thus tackling wildlife conservation dilemmas, with the molecular markers playing crucial roles in those studies (A. Rus Hoelzel, n.d.; Monsen-Collar & Dolcemascolo, 2010).

Fundamentals to the Topic

Defining Conservation
A definition of conservation or conservation efforts is the act of protection addressed to resources from the harms of anthropological activities thus to preserve the sustainability of society and nature and ultimately benefit all organisms (National Geographic Society, n.d.; Pimm, 1998, p. xx).

The Concept of Conservation Genetics
Conservation genetics aims at using genetic tools and disciplines to help identifying and protecting evolutionary significant units (ESUs), hence addressing biodiversity issues, although some teaching materials tend to refer to conservation genetics as a topic within molecular ecology (Van der Valk et al., 2024, p. 1-2; Supple & Shapiro, 2018, p. 1; Davinack, 2024, p. 4).

About the Molecular Markers
Within the genome of an organism, the special DNA sequences that help the identification of genes or loci, or the genotype are molecular markers; they include mitochondrial DNA (mtDNA) markers, ribosomal DNA (12S and 16S rDNA) markers, and nuclear DNA markers (Arif et al., 2011, p. 220-222; Jombart, 2008, p. xx).

The use of molecular markers can give information on the genetic diversity of the populations of threatened species (Arif et al., 2011, p. xx). Mostly devised in the early 21st century, new genetic techniques and molecular markers such as the random amplified polymorphic DNA (RAPD), amplified fragment length polymorphism (AFLP), shorter DNA sequences that surround a single base pair alteration (single nucleotide polymorphism, SNP), minisatellites and microsatellites (MSATs) were introduced to broader ranged ecological and evolutionary studies (Allendorf et al., 2010, p. xx; Davinack, 2024, p. 4; Al-Samarai & Al-Kazaz, 2015, p. 118).

An Overview of the Implications of Molecular Markers in Conservation Genetics

Molecular technologies are the laboratory techniques that are applied to studies and modifications ofe

biological molecules (The University of Kansas, 2024). The molecular markers can be classified depending on whether it is polymerase chain reaction (PCR)-based or what information it provides (Davinack, 2024, p. 7; Allan & Max, 2010).
In addition, innovation contributed much to the development of this field. The emergence of more advanced experimental techniques such as the restriction fragment length polymorphism (RFLP), PCR, and various DNA markers such as the microsatellites or short sequence repeats (SSR) allowed further genetics and ecology studies as the Earth steps into the Genomics era (Davinack, 2024, p. 3-4; Monsen-Collar & Dolcemascolo, 2010; Arif et al., 2011, p. 221).

The Application of Molecular Markers Impedes Biodiversity Loss
Overall, the use of molecular markers supports conservation efforts through several methods, despite there is not an optimal type of marker (Arif et al., 2011, p. 223). Two cases of successful conservation projects in Africa are supportive and promotive to existing and future conservation projects.
First, molecular markers help identifying populations that suffers from genetic crisis such as low genetic diversity and isolated populations (Western Ecological Research Center, 2017). The danger of genetic crisis gives rise to growth and reproductive disadvantages for the endangered species, because high genetic diversity maintains enough capacity for the population to develop mutations which could help them to adapt and evolve (Hoban et al., 2021, p. 965). To be specific, nuclear DNA markers can be used for DNA fingerprinting (or DNA profiling), which is to reveal the variable parts of the DNA sequence within a population through the isolation of DNA segments (Chadwick, 2023). This makes identification of organisms and phylogeny profiling more convenient for researchers. To elaborate, RAPD, AFLP, microsatellites or SSRs are markers that are frequently used for DNA profiling and genetic diversity analysis (and their differentiating power is arranged in descending order: SSR (co-dominant) > AFLP(dominant) > RAPD(dominant) (Arif et al., 2011, p. 221-222). Meanwhile, their dominance is measured by numbers of alleles per locus and the easiness to differentiate heterozygous and homozygous, and SSRs works better for differentiating (Arif et al., 2011, p. 222).

Second, mtDNA and rDNA markers help to deal with evolutionary complexity, poaching detection, and structuring populations (Arif et al., 2011, p. 220; Chafin et al., 2021, p. 1). Clarifying phylogenetic ambiguities and taxonomic uncertainties removes the confusion in coalescent histories of the species, simplifies the management and improves the effectiveness of the projects (Chafin et al., 2021, p. 2). Moreover, as a major cause of biodiversity loss, poaching aggresses the animal rights, and amplifies the existing ecological crisis, herein severely canceling out the conservation efforts (Hall, 2019). Early discovery of poaching brings people more time to react, like tracing and punishing poachers, rescuing animals, and developing defense methods against future poaching. Structuring populations benefits conservation by assessing the sustainability of the population's growth. For instance, population management of endangered animals which are put through in-situ conservation projects could be less economically and time costly by applicating newer markers (Hohenlohe et al., 2021, p. 63). The flaw of mtDNA markers is that they can only depict maternal inheritance, while each type of rDNA marker suits different categorical levels of phylogenetics studies (Arif et al., 2011, p. 223).

Case Study 1- Success in Conserving Southern African Cape Vultures
In 2021, the cape vultures (Gyps coprotheres), native to southern Africa, have been downlisted to "vulnerable" from "endangered" on the International Union for Conservation of Nature (IUCN) Red List of Threatened Species (Thompson & Du Toit, 2022). Using microsatellite markers (fig.1), a thorough genetic survey was run through, revealing the problem to be heterozygosity deficiency, increasing level of inbreeding, and a declining effective population size (Kleinhans & Willows-Munro, 2019, p. xx).

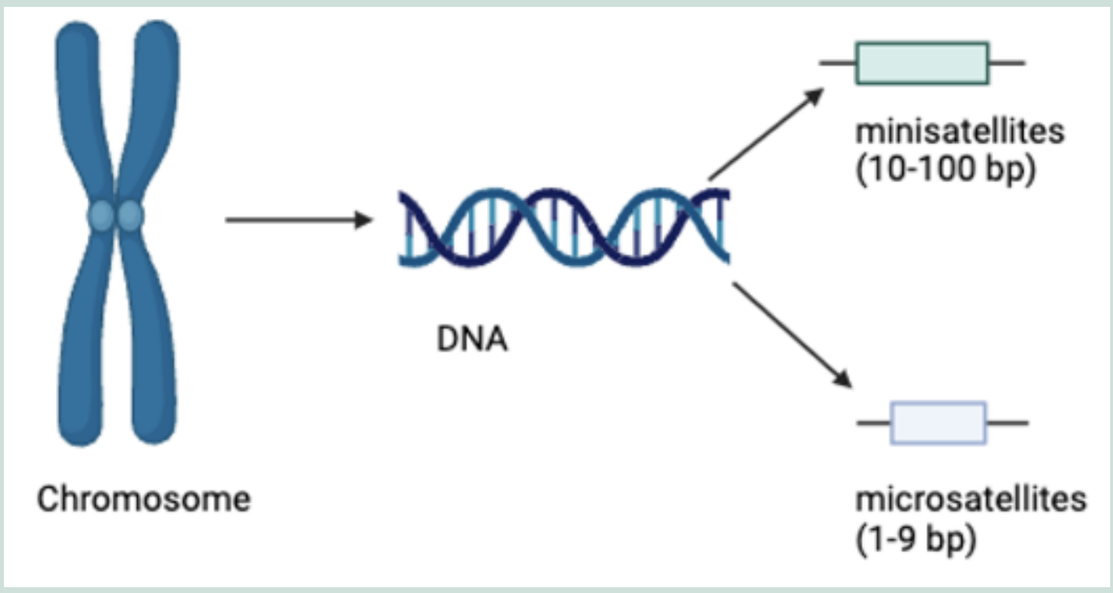

Figure 1 Differences between minisatellite and microsatellite, created with BioRender.com by Jingtong He.

Thence, the Multi-species Action Plan to Conserve African-Eurasian Vultures (Vulture MsAP) was carried out with three aims: first, termination of population decline; second, boost the population and bring favorable conservation status to the vultures; and last, provide legal protection and management of all species of vultures covered by the MsAP (SAFFORD et al., 2019, p. 5). Therefore, conservation strategies could be designed and targeted on improving the genetic diversity and optimization of population structure of G. coprotheres.

Case Study 2- the Achieved Continuous Progression of Conserving Black Rhinoceros in Eastern Africa
Although the black rhinoceros (Diceros bicornis) is “critically endangered” on the IUCN Red List, conservation efforts can prevent further decline of their population and contribute to their gradual and sustainable growth (World Wildlife Fund, n.d.; IUCN, 2020).

The direction of change in genetic diversity among populations of D. biscornis was determined through whole-genome resequencing (WGR), which are center prominence and peripheral degradation, thereby unmasking the evolutionary history of D. biscornis (Sánchez-Barreiro et al., 2023, p. 1; McGrath, 2023, p. 1). Also, WGR allows the discovery of more DNA markers, such as SNPs, making the design and devotion of more mature conservation strategies for the existing population (McGrath, 2023, p. 1; Xu & Bai, 2015, p. xx). Another marker used was the mtDNA markers, their diversity in D. biscornis in Tanzania shed light on future conservation implications (Mellya et al., 2023, p. xx)(A made-up model of mtDNA haplotype distribution is depicted in fig.2).

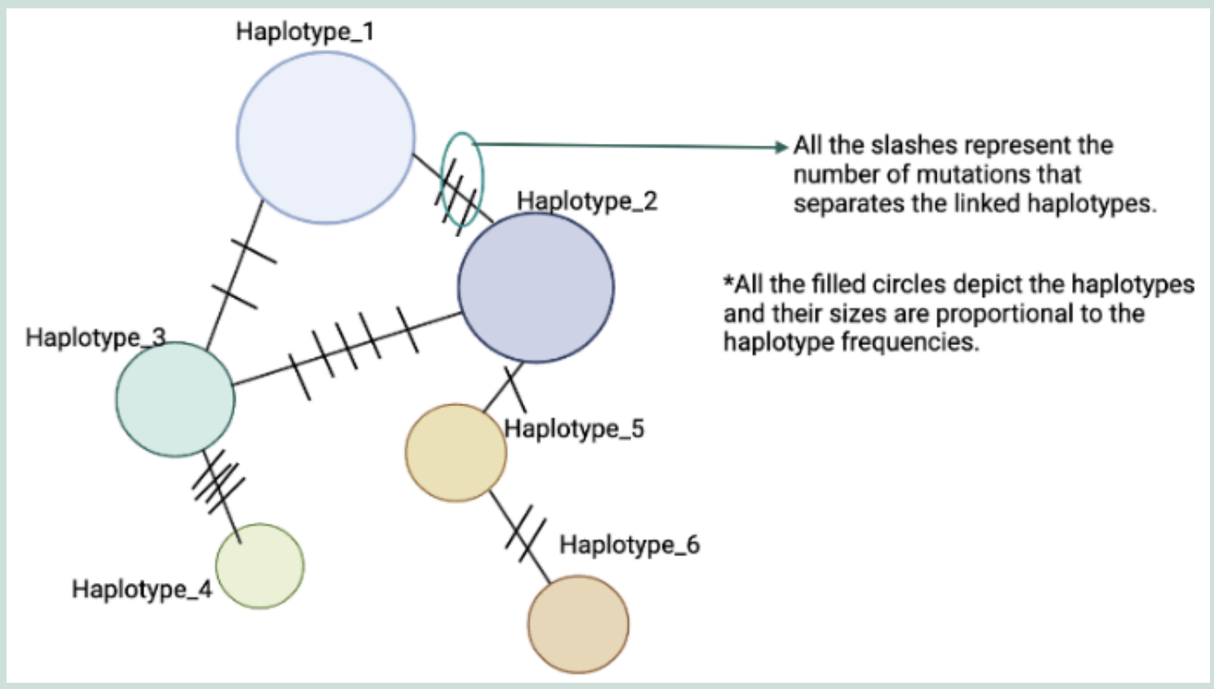

Figure 2 A simulated and simplified model of mtDNA haplotype distribution, created with BioRender.com by Jingtong He.

Conclusion

Molecular markers allow the detection of subtle changes or variations in populations, thus reprioritize conservation strategies to improve the efficiency and potentially the probability of success of the conservation project.
However, the evaluation of existing methods should be holistic. Although the molecular markers are versatile, imitations of current research methods are multi-perspective-wise. For instance, conservation genetics require genomic technologies’ assistance to make conservation plans suitable for other species of the same genus, or different populations of each species. Furthermore, there is not a kind of molecular marker that fits every occasion, so the choice of markers would affect the credibility of the results and repeatability of the surveys. Besides, the cost and efficiency must be considered before practicing any methods. To conclude, the prospect of conservation genetics is bright and molecular technology based.

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SMART MAGAZINE AUTHOR: Livana

I am Plastic Hero

Swish–A beam of bright light descended from the sky. "Plastic Hero" stood in front of a giant sphere composed of colorful, tiny particles. These particles twinkled like stars, yet they held hidden dangers. Plastic Hero held a magnifying glass, his brows furrowed, determination and wisdom in his eyes, as he firmly said:

"Hey, residents of Earth Village, listen up! Today, I, 'Plastic Hero,' am going to reveal a small secret hidden in your daily lives. It’s so small that it’s almost undetectable to the naked eye, yet it can disrupt the ocean’s tranquility, infiltrate our breath, and threaten the depths of the food chain–that is 'microplastics'! Don't be fooled by their 'miniature star' appearance. These are the invisible assassins of Earth's health!"

He raised the magnifying glass, like a detective searching for clues, and continued, "These tiny plastic fragments, although smaller than a grain of sand, but are like ghost, present everywhere. They dance with the wind, drift with the water, from city sewers to remote deep seas, from uninhabited glaciers to bustling cities–nowhere is spared." His gaze grew firmer, with a hint of concern between his brows.

"Do you know? Every year, millions of tons of plastic waste end up in the ocean, most of which break down into small particles and become microplastics. These microplastics are not only hard to degrade but also absorb various harmful substances, becoming 'invisible killers' for marine life. Sea turtles mistake them for food, seabirds use them to build nests, and even the smallest plankton cannot escape their grasp. In the Mariana Trench, considered one of the deepest and most mysterious places on Earth, some areas have microplastic concentrations of 200,000 to 2 million pieces per cubic meter. In this environment, a species of amphipod was discovered, and due to the plastic waste in its body, it was named 'Plastic Hook Shrimp.'"

As people stared in shock, a large screen slowly unfolded in the sky:

"Currently, the most common plastics are polyethylene terephthalate (PET), polystyrene (PS), polyethylene (PE), polypropylene (PP), and polymethyl methacrylate (PMMA). Among them, PET, PS, and PE account for 50%, 36%, and 23%, respectively. Microplastics are divided into two types: 'primary' microplastics, which are manufactured for industrial use and can be found in daily products such as cosmetics or cleaning products, like abrasives in toothpaste and exfoliating creams, as well as in textiles and synthetic clothing. These microplastics are discharged into rivers and other bodies of water through wastewater treatment plants. The other type is 'secondary' microplastics, which are plastic particles formed by the fragmentation and reduction in size of large plastic waste due to physical, chemical, and biological processes. They can directly enter from coastlines or through rivers and sewage systems into the ocean..."

"What should we do?"

"Yeah...what should we do..."

Worried voices emerged from the crowd...

"First of all, reducing the use of disposable plastic products is key. Choose reusable shopping bags, cups, and tableware to minimize plastic waste. Secondly, participate in beach cleanups to take action and help reduce microplastic pollution in our environment. Additionally, support environmentally friendly businesses and products to promote the development of a circular economy, ensuring plastic waste is more effectively recycled and reused."

People followed Plastic Hero's gaze and looked out towards the ocean, which was supposed to be pure and clean, lost in deep thought.

"Furthermore, raising public awareness about the microplastic issue is crucial. Through education and outreach, more people can learn about the dangers of microplastics and prevention methods, fostering a positive environment where society as a whole participates in environmental protection."

"My friends, Earth is our common home. Protecting it from microplastics and other environmental pollutants is our shared responsibility and obligation. Let us stand side by side, like 'Eco Heroes,' and contribute to the future of our planet. Remember, every small change can accumulate into tremendous power. Let us join together to protect this beautiful blue planet!"

The story of Plastic Hero continues, often featuring depictions of a future where humans are composites of synthetic materials–but we hope that day doesn't come because of the prevalence of microplastics. The food chain is the cycle of nature, and as the saying goes, "Big fish eat small fish, small fish eat shrimp." If humanity doesn't take action to control microplastic pollution, those at the top of the food chain–humans–will ultimately accumulate the highest concentration of microplastics in their bodies.

"Remember, everyone’s actions matter, because we are not fighting alone. The future of the Earth is in our hands. I am Plastic Hero, and I am taking action. What about you?"

SMART MAGAZINE AUTHOR: Derek

AIE Fluorescet Probe

I. Introduction

1.1 Overview of AIE Fluorescent Probe

As a new fluorescent detection material, AIE (aggregation-induced luminescence) fluorescent probe shows a wide application potential in the field of neuroscience because of its unique luminescence mechanism. Compared with traditional fluorescent probes, the luminous characteristics of AIE probes do not depend on the molecular dilution state, but are realized through the molecular aggregation state, which has a high fluorescent quantum yield and environmental sensitivity. This makes AIE fluorescent probes show superior performance in applications such as bioimaging, molecular detection and biosensors.
In neuroscience research, AIE fluorescent probes are widely used in the visualization of neurons. By accurately designing different AIE probes, such as modified polyethyleneimine, anhydride and benzothiophene, researchers can achieve selective labeling of specific neurotransmitters. Take a fluoride-based AIE fluorescent probe as an example, which can capture dopamine release events in neurons at a micron-level spatial resolution. The quantum yield of the probe can be as high as 90%, and the signal-to-noise ratio is significantly better than that of traditional probes.
The application of AIE fluorescent probes in disease models has also attracted attention. In the study of Alzheimer's disease (AD), AIE probes can effectively identify β-amyloid aggregates in the brain and promote the early diagnosis of the disease. Relevant experiments show that when the AIE probe is used for biological imaging, its detection sensitivity reaches the Pymore level, which can monitor molecular changes in the pathological state in real time.
AIE fluorescent probes also have good biocompatibility. By combining with biological macromolecules, such as phosphatidyl inositol and polylactic acid, stable marking and tracking can be achieved on the cell membrane to ensure the stability and durability of the probe in the body environment. At the same time, the chemical adjustability of the AIE probe gives it adaptability in different biological scenarios. Researchers can design the wavelength, luminous intensity and selectivity of the probe according to their needs, so as to improve the relevance and effectiveness of the experiment.
AIE fluorescent probes have shown many advantages in the biomedical application research of neuroscience, including high sensitivity, high selectivity and good biocompatibility. With the continuous progress of technology, AIE fluorescent probes are expected to play a more important role in the mechanism analysis of neurological diseases and the development of new treatment plans.

1.2 The importance of neuroscience research

The core of neuroscience research is to understand the structure and function of the nervous system, which is of great significance to explore the neurological mechanism, disease occurrence and treatment. In recent years, with the progress of technology, the research in the field of neuroscience has been continuously deepened, especially the revelation of neuronal activity, synaptic transmission and other basic biological processes, which has provided an important theoretical basis for clinical problems such as neurodegenerative diseases and mental disorders.
The emergence of AIE (enhanced internal electroluminescence) fluorescent probes has opened up a new horizon for neuroscience research. The application of these probes in biological imaging shows superiority, especially in living neuroscience research. AIE probes have excellent light stability and biocompatibility, and can achieve high-sensitivity imaging in complex biological environments. For example, the study confirmed that the use of AIE probes can achieve real-time imaging of neuronal activity in the brain of mice. When the probe concentration reaches 10 μM, the signal enhancement effect is significant. Through such research, the key role of specific neural circuits in behavioral regulation is revealed, thus providing a basis for neurological treatment interventions.
In understanding the mechanism of neurological diseases, AIE probes also show great potential. Many neuropsychiatric diseases, such as Alzheimer's disease, Parkinson's disease, etc., are characterized by damage or dysfunction of specific neurons. By marking the morphology and activities of these neurons, we can gain an in-depth understanding of the pathogenesis of the disease. Studies show that in the AD mouse model, the use of AIE probes can clearly observe the apoptosis process of neurons and quantify the changes in the number of
neurons in the pathological state, thus providing a new perspective for early diagnosis and intervention of the disease.

AIE probes can also play a role in intracerebral drug delivery. The treatment of cancer and a variety of neurological diseases usually faces the challenge of the blood-brain barrier. By binding to specific drug molecules, AIE probes can act as part of the drug delivery system to coordinate more accurate target drug release. In addition, the changes in the fluorescence characteristics of AIE probes under specific conditions can be used to monitor the dynamic changes of drugs in the nervous system and provide individualized treatment plans for patients.
Exploring neuronal interaction and network characteristics is the basis for understanding the advanced functions of the brain. In large neural networks, it is difficult to fully obtain information by relying on traditional electrophysiological technology alone, and AIE probes greatly enrich the data obtained by realizing synchronous imaging at multiple levels. This process is expected to reveal the neural basis of complex behaviors and cognitive activities, thereby promoting the development of relevant basic research and clinical applications.
The importance of neuroscience research lies not only in the promotion of basic scientific research, but also in its great impact on drug development and clinical application. The application of AIE fluorescent probes provides a new research direction for the future development of neuroscience, enabling scientists to have more efficient tools to explore more complex neural mechanisms, thus accelerating the panoramic understanding of the nervous system and ultimately promoting the research and development and practical application of new therapies.

II. Research the current situation

2.1 The development process of AIE materials

The research on AIE (active quenching fluorescence) materials began in the 1990s. Its core concept is to use the luminescence effect induced by aggregation to show significant fluorescence properties in the state of material aggregation. The key research breakthrough of AIE materials comes from the work of internationally renowned scholars Ding Zhongli and others, which reveals that traditional fluorescent materials usually show sudden extinction at high concentrations, while AIE materials can enhance fluorescence when aggregated, opening up new possibilities for them in biomedical applications.
With the deepening of research, the synthesis and improvement of AIE materials have gradually become a hot spot in the academic community. In 2001, researchers successfully synthesized group-based AIE probes, such as AIE-based benzothiazole, which showed their superiority in the application of biological imaging. Especially in in-vivo imaging, the high sensitivity and high selectivity of AIE materials make it an ideal choice for biomarkers. At the same time, the application of AIE materials in the field of cell imaging is also constantly expanding, such as real-time monitoring of calcium ions in neurons.
First, AIE materials adopt different groups in the design to regulate their photophysical properties. For example, by adjusting the proportion of the electron body and the receiver, AIE probes with different wavelengths can be obtained, so as to achieve multiple imaging. Second, in recent years, the combination of AIE materials and nanotechnology has formed AIE nanoprobes, which have shown excellent application potential in neuroscience research. For example, AIE nanoprobes can target specific neurotransmitters and monitor nerve activity at the molecular level, providing advanced experimental methods.
In terms of fluorescence imaging, AIE materials are not only widely used in nerve cells, but also show important practical value in the study of neurodegenerative diseases such as Alzheimer's disease. Specifically, AIE probes can be used to study the aggregation behavior of beta-amyloids, providing new biomarkers for the early diagnosis of diseases. In addition, in recent years, the adjustability and versatility of AIE materials have made them more widely applied in living imaging and drug delivery systems. These studies prove the important role of AIE materials in the field of biomedicine, especially in neuroscience, and promote the further development of this field.
By continuously optimizing synthesis methods and probe design, the application of AIE materials in biological imaging, drug delivery and disease monitoring continues to improve, showing broad development potential and application prospects. In the future, combined with advanced materials science and life science, the research of AIE materials may provide more effective technical support and treatment for clinical medicine.

2.2 Application of probes in the field of neuroscience

The application of AIE (aggregation-induced luminescence) fluorescent probes in the field of neuroscience has attracted wide attention, mainly because of its high sensitivity and selectivity to biological systems. The design of AIE fluorescent probes is usually based on small molecule materials, which can significantly improve the fluorescence intensity in the aggregate state, overcoming the problem of fluorescence quenching of conventional fluorescent probes in biological systems.
In the detection of neurotransmitters, a variety of AIE probes are developed to identify and image important neurotransmitters, such as dopamine, norepinephrine and acetylcholine. For example, a probe based on AIE characteristics can be used to monitor changes in dopamine concentrations in neurons, and its sensitivity is as high as Namole. The probe shows a stable fluorescent signal in the neuronal cell culture medium, which makes real-time imaging possible.

In the study of Alzheimer's disease, AIE probes are used to detect the aggregation of β-amyloid protein, and the concentration of the probe during operation is usually set in the range of 1 μM to 5 μM. The aggregation state of this probe enables effective imaging in a biocompatible environment, which provides an important tool for studying the mechanism of neurodegenerative diseases. In addition, some AIE probes can selectively bind to lipid vesicles to promote the conduction of intramembrane signals, which is conducive to the study of signal transduction pathways of nerve cells.
In neuronal activity research, AIE probes are often used in combination with calcium imaging technology to accurately monitor the dynamic changes of calcium ions in cells. In this regard, the response time of the probe is usually between more than a dozen milliseconds and tens of milliseconds, which can respond to changes in electrical activity of neurons in real time. For example, an AIE probe specifically for calcium ions shows a fluorescence enhancement of more than 10 times in cells, giving it the potential for extensive application in neuroactivity research.
The chemical modification of the AIE probe also improves its specificity. After modification, the affinity of the probe is improved, which can effectively control the reaction dynamics. Using this characteristic, researchers can optimize the performance of probes in different biological environments to adapt them to complex biological systems. In recent years, the research carried out using such probes is not limited to the establishment of disease models, but also extends to the regulation of neural network activities and the systematic observation of their impact on behavior.
With the advancement of technology, the application of AIE fluorescent probes in neuroscience will be further deepened in the future, which is expected to provide revolutionary methods and tools for the early diagnosis and treatment of brain diseases.

2.3 Current challenges and prospects

In the research on the application of AIE (aggregation-induced luminescence) fluorescent probes to neuroscience, there are many challenges that need to be overcome to promote its development. First, the problem of light stability is crucial to the performance of fluorescent probes. Although AIE probes have excellent fluorescence properties, they often face photobleaching and phototoxicity in biological environments, affecting long-term imaging capabilities. When applied in living organisms, the chemical stability and biocompatibility of AIE probes are also key challenges. The design of a new type of AIE probe needs to consider these factors to ensure the durability and safety of the probe in the biological system. In addition, the selectivity and sensitivity of the probes used are also important indicators. At present, the selectivity of some AIE probes for specific biomolecules still needs to be improved, and the sensitivity is insufficient in complex biological environments, resulting in the inability to achieve accurate detection of biomarkers.
The existing fluorescent probes are not flexible in intracellular imaging, which limits their application in different nerve tissues and cell types. For example, different combinations of probes may be required for different types of neurons or pathological states. How to achieve targeted design is still a difficult problem. The functional design of the probe requires fine regulation at the molecular level to ensure that it can maintain excellent optical performance and bioadaptability in different microenvironments.
In future research, improving the synthesis method of AIE probes and optimizing structural design is the key to meeting the above challenges. The exploration of new types of aggregation-induced luminescent materials, especially probes with functionalized molecules as precursors, helps to improve their performance in the field of biomedicine. In addition, by combining AIE probes with other imaging technologies (such as photoacoustic imaging and ultra-resolution imaging), it may expand its application potential in neuroscience. At the same time, the development of new sensors to realize real-time monitoring of neurotransmitters, ion channels and electrical activity will provide more quantitative analysis tools for neuroscience and support the study of complex neural network functions.
In the face of the above challenges, interdisciplinary cooperation will also be an important direction of future research. The deep combination of biology, materials science and engineering can promote the development of new technologies and the optimization of existing technologies, and finally realize the wide application of AIE fluorescent probes in neuroscience research.

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III. Design principle of AIE fluorescent probe

3.1 The relationship between molecular structure and properties

In the field of neuroscience, the relationship between the design of molecular structure and its optical properties is crucial for the development of new AIE (aggregation-induced luminescence) fluorescent probes. The molecular structure of the AIE probe is usually composed of multiple benzene rings and their derivatives, and the degree of stereochemistry and conjugation of these structures directly affect its fluorescence properties. For example, molecules with higher conjugation tend to show stronger fluorescence intensity and longer fluorescence life. Research shows that the non-radiational transition of molecules in the aggregate state is inhibited, thus enhancing their fluorescence performance.
In the design of AIE probes, the location and type of functional groups are key factors. The introduction of the donor-receptor structure can regulate the electronic properties of molecules and change their energy level distribution. For example, by introducing polar groups such as amino groups or carboxyl groups into molecules, the hydrophilicity of the probe in the biological environment can be improved and its distribution in the organism can be more uniform. Experimental data show that the fluorescence signal of AIE probes with polar groups in the cell is 1.5-2 times higher than that of non-polar probes.
The optimization of the guide structure is also an important way to improve the performance of AIE probes. By synthesizing polymers with different substituents, such as poly(styrene) materials, different luminous properties can be achieved and the photophysical properties of the probe can be effectively adjusted. At the same time, in the same aggregation state, different solvents are used to affect the luminous intensity of the probe, and its fluorescent quantum yield shows a significant difference, usually ranging from 10% to 90%. In addition, the particle size, morphology and other physical properties of the probe are also closely related to its fluorescence properties. The small-particle AIE probe has better penetration performance in cells, which greatly improves its wide application.
AIE fluorescent probes show excellent biocompatibility and targeting in neuron imaging. Research shows that the specific probe design for specific neurotransmitters, such as dopamine, optimizes the molecular structure so that it can be imaged on the cell membrane at a resolution of about microns. In addition, the application of AIE probes in living imaging has a broad prospect, and the sensing properties brought by different molecular designs can play an important role in the study of neuronal activity, transmission and pathological mechanisms. Due to the complex relationship between the above molecular structure and properties, future research should focus on improving the application potential of AIE probes in the field of biomedicine through diversified structural design and synthesis methods.

3.2 Research on fluorescence intensity and stability

In the application of neuroscience, the fluorescence intensity and its stability are the key parameters of AIE (aggregation-induced luminescence) fluorescent probes. Studies show that AIE probes show significant fluorescence enhancement effects in specific environments, which makes them have high sensitivity in biological imaging. Take a typical AIE probe as an example, its fluorescence intensity can reach several times that of the traditional fluorescent probe at the same concentration. Specifically, the fluorescence intensity measured at a wavelength of 520 nm is as high as 1500 RFU (relative fluorescence unit). Relying on the AIE special effect, after the probe adheres to the biological membrane, it shows a stronger fluorescent signal, which improves the resolution of neuronal cell imaging.
Stability is an important factor affecting the application of AIE fluorescent probes in biological samples. Many studies show that the AIE probe maintains a good fluorescence intensity in physiological saline with a concentration of 0.15 M of sodium chloride. After 72 hours of observation, the decrease in fluorescence intensity is only 10%. In addition, according to the conditions of different pH values, the fluorescence

intensity of the AIE probe is stable in the buffer of pH 7.4, and the change rate is maintained within 5%, which indicates its adaptability to the biological environment.
In order to enhance the stability of the AIE probe, the developer has designed a variety of modification strategies. The coating technology based on linear polymer effectively isolates the irradiation of the excited light source and avoids the phenomenon of light bleaching. The experimental data shows that the fluorescence intensity retention rate of the coated AIE probe at 520 nm is increased to 95%, which can ensure longer imaging under standard irradiation conditions (405 nm, 150 mW/cm²).
In terms of the temperature stability of the probe, the study found that the AIE probe maintains a high fluorescent signal in the range of 4°C to 37°C, and the impact of temperature fluctuations is negligible, usually no more than 7%. This feature provides the possibility for long-term in viviography. Therefore, for different experimental designs, the selection of appropriate AIE fluorescent probes and their optimization strategies is of great significance to improve the effect of fluorescence imaging and reduce damage.
Considering the fluorescence intensity and stability, AIE fluorescent probes show superior performance in both in vitro marking and living imaging, coupled with its good biocompatibility, which makes it have a broad application prospect in the field of neuroscience.

3.3 Multifunctional integrated probe design

Multifunctional integrated probe design has been an important development direction in neuroscience research in recent years, especially the application of aggregate emission (AIE) fluorescent probes in the field of biomedicine is constantly expanding. The design of the probe usually involves the selection and modification of probe materials to achieve specific bioimaging, drug advantage release and biomarker capture and other functions. Probes based on AIE characteristics have excellent fluorescence intensity and low background signal, which are suitable for high-contrast imaging in complex biological systems.
First, the embedded polymer substrate is often used in the design process, so that the probe has stronger biocompatibility and stability. For example, through the combination of polymer carrier and AIE luminous material, the light stability of the probe can be effectively improved and its service life in cells can be extended. Relevant studies show that AIE probes using polymer substrates show more than 80% light stability in living cell imaging.
Second, in terms of probe functionalization, specific target groups are usually introduced to enhance the target recognition ability of the probe. Commonly used target groups include nucleic acid sequences, peptide chains and antibodies, etc., and their dose is regulated at the Namor level by chemical cross-linking technology. Taking the AIE probe targeting tumor cells as an example, the experimental results show that its selective binding rate in tumor cells can reach more than 95%, which significantly improves the specificity of imaging.
Third, the design of the multi-functional probe can also achieve multiple marking through the fluorescence resonance energy transfer (FRET) mechanism. By combining AIE probes of different wavelengths, a variety of biomolecules can be detected at the same time. For example, using two different wavelengths of AIE probes to image neurotransmitters and receptors can provide dynamic information on intercellular signal transmission, and then gain an in-depth understanding of the function of neural networks.
The optimization of the physicochemical properties of the probe, such as particle size, hydrophilicity and targeting ability, is a key design consideration. Studies show that probes with a particle size of 10 to 30 nanometers can effectively penetrate the cell membrane and enter the cell interior, thus improving the clarity and resolution of intracellular imaging. Hydrophilicity is usually achieved through surface modification and functionalization, which enhances dispersion in the biological environment and reduces non-specific binding.
By comprehensively considering and optimizing these design elements, the multifunctional integrated design of AIE fluorescent probes shows great potential in neuroscience research. It can not only realize cell imaging, but also carry out drug delivery and biomarker detection, providing new solutions for precision medicine and personalized treatment.

IV. Biomedical Application Analysis

4.1 Nerve cell imaging technology

Neural cell imaging technology is one of the core methods in neuroscience research, which can observe the activity of neurons and their interactions in real time. In recent years, AIE (aggregation-induced luminescence) fluorescent probes have been widely used in this field due to their unique optical properties. The AIE probe has a significant fluorescence enhancement phenomenon in the aggregation state, which makes it show an excellent signal-to-noise ratio in cell imaging. This technology can achieve high-resolution imaging at the single-cell level by combining spectral imaging and microscopic technology.
In specific applications, AIE fluorescent probes are suitable for living cell imaging with their good biocompatibility and low toxicity. The selective carrying and signal amplification mechanism of the probe enables it to directly mark neurons in the body. Taking the "thiophene-based AIE probe" as an example, the study found that it has the highest fluorescence intensity at λem= 580 nm, is extremely sensitive to changes in calcium ion concentration, and can be used to monitor changes in the excitability of nerve cells.

Through strong laser irradiation, the AIE probe in the cell can be effectively excited to achieve instantaneous imaging. Imaging systems are usually combined with advanced image processing software to post-process signals to extract intracellular structure and functional information. In addition, with the application of FRET (fluorescence resonance energy transfer) technology, the combined use of AIE probes with other fluorescent probes further improves the sensitivity and accuracy of imaging.
In terms of technical parameters, the quantum yield of AIE probes is usually higher than 30%. By changing the chemical structure of the probe, its emission wavelength can be adjusted and imaging can be carried out for specific biomarkers. For example, in the study of Alzheimer's disease, the specific AIE probe for β-amyloid protein successfully realized the visualization of lesion nerve cells, and the optimal concentration of the probe was 10 μM.
With its unique performance and wide applicability, AIE fluorescent probe has promoted the development of nerve cell imaging technology and provided a powerful tool for neuroscience research. Dynamic observation of complex events in neurobiology is conducive to an in-depth understanding of the basic mechanism of the nervous system and the pathogenesis of its related diseases.

4.2 Diagnosis of neurological diseases

In the diagnosis of neurological diseases, AIE (aggregation-induced luminescence) fluorescent probe, as a new imaging tool, shows its unique advantages. Specific AIE probe design can effectively recognize changes in pathological characteristics in neuronal cells, such as amyloid plaques, tau protein aggregation, etc. The high sensitivity and specificity of these probes in fluorescence imaging make it an important means for early diagnosis of neurodegenerative diseases.
Specifically, studies show that some AIE probes can identify amyloid plaques in brain tissue at a nanometer-level resolution in the Alzheimer's disease model, and the fluorescence intensity can reach 108 counts/s, which is much higher than that of traditional fluorescent dyes. In addition, the confocal microscope imaging ability of the AIE probe can provide cell-level resolution, which has a strong application prospect in the diagnosis of neurological diseases. Relevant studies found that the optimized AIE probe showed excellent targeting and low toxicity in both lung cancer cells and Alzheimer's disease mouse models, and its IC50 value was at the micromolar level.
In the study of a variety of neurological diseases, AIE probes can not only achieve specific recognition of target molecules, but also perform in living imaging in biological samples. For example, by injecting AIE probes into the brain of mice, combined with real-time fluorescence imaging technology, researchers can monitor the changes of calcium ions in neurons, which is of great significance for analyzing the functional state of neurons and various conduction mechanisms. In addition, for the early biomarkers of Parkinson's disease, scientists have adopted targeted AIE probes, which can accurately locate and quantitatively analyze relevant neurotransmitters, further improving the accuracy of early diagnosis of the disease.
During the development of the AIE probe, a variety of chemical modification methods are also used to enhance its water solubility, targeting and biocompatibility. By changing the molecular structure and functional group of the probe, researchers can effectively improve its biological interaction ability, so as to achieve accurate diagnosis of specific neuropathy. For example, in the rat model, neuronal damage can be identified at the pathological level by using a specific AIE probe, and the fluorescent signal of the probe is significantly enhanced in the damaged area, showing its potential in clinical application.
AIE fluorescent probes show superior characteristics and application prospects in the diagnosis of neurological diseases. By accurately identifying pathological changes, these probes not only promote the progress of basic research, but also provide new possibilities for clinical diagnosis. With the development of technology, it is expected that AIE probes will play a broader role in more disease models and clinical samples in the future.

4.3 Neurological intervention treatment monitoring

The application of AIE fluorescent probes in nerve intervention treatment monitoring has attracted more and more attention. Due to its excellent optical properties and biocompatibility, this kind of probe can monitor neural activity and its response in the body in real time. Through the intensity change of fluorescent signals, researchers can evaluate the effectiveness of neural interventions. In application, the design of AIE probes is usually based on the strategy of combining polymers and small molecules to ensure significantly enhanced fluorescence emission in a specific environment.
For neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease, AIE fluorescent probes are used to monitor biomarker changes during treatment. By calibrating specific biomolecules, such as β-amyloid and α-synaptic nucleoprotein, combined with imaging technology, AIE probes can provide high-resolution biological imaging results. This process often involves a specific excitation wavelength, usually set in the range of 400-480 nm to ensure the best fluorescence signal.
Under laboratory conditions, the sensitivity of AIE probes is usually higher than that of traditional fluorescent probes, and the detection limit can be as low as nM level. For example, some studies show that the sensitivity of neurotransmitters released by neurons released by AIE probes has increased to 10^(-9) M, which is far higher than that of conventional probes. In addition, the response time of the probe is generally a few seconds to a few minutes, which can capture important moments of neural activity in real time, which is of great significance for studying the immediate effect of neural intervention measures.

In preclinical trials, AIE fluorescent probes have been used to monitor the activity of nerve cells after drug intervention. The results show that under the action of drugs, the fluorescence intensity of nerve cells changes significantly, indicating the effectiveness of the intervention measures. At the same time, this kind of probe can be combined with other imaging technologies such as MRI, PET, etc. to enhance the effect of multimodal imaging and make the monitoring of neural intervention more comprehensive.

With the progress of technology, the research on the biological distribution and metabolic path of AIE probes has gradually deepened, providing theoretical support for its clinical transformation. By optimizing the chemical structure of the probe and improving the adaptability of its internal and external environment, AIE fluorescent probe has shown great application potential in neural intervention treatment monitoring in terms of simplicity and accuracy of operation. In the future, personalized medical monitoring schemes based on AIE probes are expected to become a new direction for neuroscience research and neurological disease treatment.

V. Conclusion

The biomedical application research of AIE (aggregate-induced luminescence) fluorescent probes in neuroscience has shown its great potential in living imaging, neuronal signal transmission and pathological state monitoring. With the deepening of neuroscience research, the requirements for probes are becoming more and more demanding, requiring high sensitivity, selectivity and biocompatibility and other characteristics. In recent years, multiple AIE probes have been synthesized and evaluated, such as composites based on different fluorescent monomers, showing excellent optical properties and good biocompatibility. In this regard, the use of modified polymers as probes for fluorescent substrates, such as the use of polyvinyl alcohol (PVA) and polylactic acid (PLA), shows low toxicity and excellent intracellular imaging ability.

For neuron-specific authentication, the synthesized AIE probe is often combined with target markers through molecular design to achieve high selectivity. For example, some probes specifically target ceramide to detect changes in the activity of small glial cells, indicating that probes show extremely high sensitivity when identifying specific intracellular signals (the detection limit can be as low as nM level). In pathological states such as chronic pain or Alzheimer's disease, the AIE probe can accurately reflect intracellular Ca2+ ion changes and ROS levels with its real-time imaging ability, helping researchers analyze the mechanism of the disease.

The research on the optical stability and imaging depth of AIE probes has also been strengthened. The improved polymer matrix effectively improves the light stability and can maintain a stable fluorescent signal under long-term excitation irradiation, which greatly improves the feasibility of in vivo imaging. For example, the newly developed AIE probe achieves more than 100 hours of stable imaging in small animal models, promoting the ability to observe dynamic biological processes.

Compared with traditional fluorescent probes, AIE probes have higher tolerance and a wider range of applications, especially in multiple imaging and real-time tracking. The progress of this technology will bring new opportunities for the basic research and clinical application of neuroscience. For example, the application of AIE probes is gradually expanding to the real-time monitoring of neurotransmitters, which responds to the interaction between neurons in real time, providing a new perspective for understanding complex neural networks.

Future research needs to focus on the specific application of AIE probes in different neurological diseases to explore its potential in disease progress monitoring, treatment effect evaluation and individualized medical care. At the same time, the design strategy of the probe should continue to be optimized to improve its biocompatibility and targeting, so as to achieve a wider range of clinical transformation applications. On the whole, the research and development prospects of AIE fluorescent probes in the field of neuroscience are broad and need to be explored in depth.

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The CHINESE VERSION

English Version in the Front

SMART MAGAZINE AUTHOR: Aseria TRANSLATOR:Yaqi

胰腺癌

简介：

胰腺癌是一种可怕且通常具有侵袭性的疾病，起源于胰腺细胞。胰腺是位于胃后方的重要器官。该类癌症因其晚期发现、快速进展和低生存率而闻名。胰腺癌可以以多种形式表现，最常见的是胰腺导管腺癌 (PDAC)，它起源于胰腺导管内壁的细胞。胰腺癌的症状在初期可能比较隐蔽，导致早期诊断非常困难。因此，了解胰腺癌的风险因素、症状及现有的治疗方案对于改善该病症患者的预后至关重要。

风险因素

有几种不可改变的风险因素：年龄、性别、血型和糖尿病。随着年龄的增长，患胰腺癌的风险增加，大多数患者年龄都超过55岁。性别方面，女性通常比男性更不容易患胰腺癌。血型方面，O型血患胰腺癌的风险低于其他血型。这可能与不同ABO血型在炎症调节上的差异有关，炎症调节影响了癌细胞转移的过程。此外，糖尿病患者患胰腺癌的风险较高。

还有一些可改变的风险因素，包括吸烟、饮酒和肥胖。一项研究表明，吸烟者患胰腺癌的风险增加了74%。香烟烟雾及其成分能够增强胰腺细胞的干细胞特性，使其能够自我更新并分化为不同的细胞类型。关于酒精，研究表明每天饮酒超过30克的人，患胰腺癌的风险显著高于不饮酒的人。而且，肥胖也会增加患癌风险。因为对于快速增殖的癌细胞来说，脂质氧化和生物合成对细胞生存至关重要。肥胖中的KRAS突变也促成了胰腺癌的形成。

症状

胰腺癌通常表现出模糊且非特异性的症状，因此它常被称为“无声的杀手”。早期症状可能包括腹痛或背痛、不明原因的体重减轻、黄疸（皮肤和眼睛发黄）以及消化问题如恶心和排便习惯改变。这些症状通常较为轻微，容易被误认为是其他不太严重的疾病，这可能导致诊断和治疗的延误。

随着胰腺癌的进展，症状可能会加重，患者可能会出现疲劳、食欲不振、新发的糖尿病，甚至血栓。疾病的晚期阶段可能引发更严重的并发症，如肠梗阻、腹水（腹腔积液）和剧烈疼痛。识别这些症状并及时寻求医疗帮助，对于早期发现和改善胰腺癌患者的预后至关重要。

治疗选择

胰腺癌的一种治疗方式是手术。是否适合手术取决于肿瘤的位置。位于胰腺头远端的肿瘤可以通过远端胰腺切除术切除。然而，大多数肿瘤位于胰腺头部，可以通过胰十二指肠切除术（PD）进行切除。PD手术最早出现在1889年，其死亡率在几十年间居高不下，但如今其死亡率已从约30-45%降低至1-3%之间，现代报道中的术后五年生存率中位数约为20%。

尽管手术成功率不断提高，但总体复发率仍然较高，约为70-80%，这可能是由于手术时存在微转移。 因此，有必要对患者进行新辅助化疗。这种治疗方法能够更有效地针对组织，并解决微转移问题，能提高切缘阴性切除率，还可以将不可切除的患者转为可切除的患者。
另一种可能的治疗方法是放疗。它可以在手术前（新辅助放疗）或手术后（辅助放疗）使用，通过高能X射线或其他形式的辐射来破坏癌细胞及缩小肿瘤，损害其DNA，从而抑制癌细胞生长和分裂。在胰腺癌中的应用需谨慎，以避免损害胰腺周围的健康组织。精确的放疗技术帮助最大化治疗效果并减少副作用。

未来展望

胰腺癌的未来前景充满希望，研究和治疗策略不断进步。努力可以集中在改进早期检测方法上，以便在更易治疗的阶段诊断出疾病，同时个性化治疗方案也在被探索，以根据个人的基因特征量身定制治疗计划。免疫疗法和靶向疗法正作为潜在的治疗选项，旨在增强免疫系统对癌细胞的反应，并靶向肿瘤生长的特定分子通路。这些进展为胰腺癌的治疗带来了乐观前景，未来将为患者带来更好的治疗效果和生活质量。

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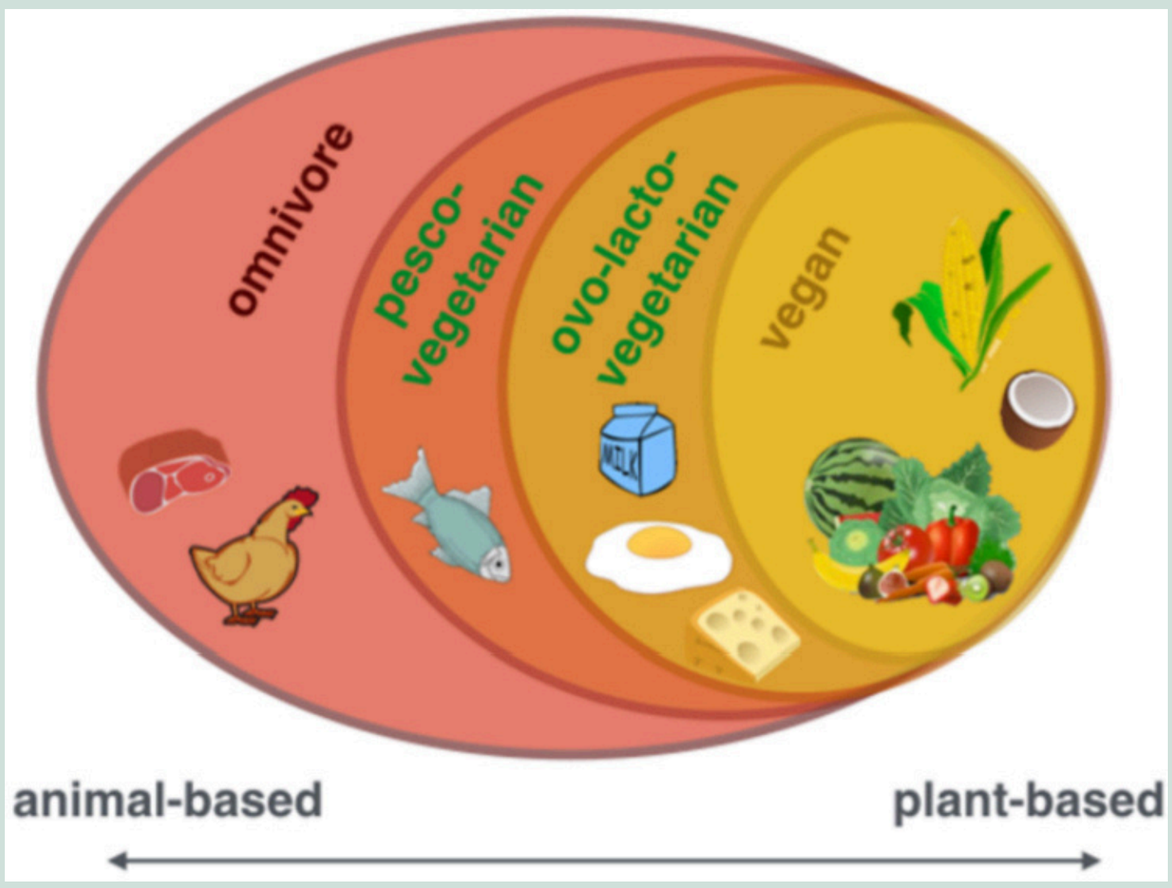
素食是否健康?

关键词:素食，营养缺乏，心血管疾病，2型糖尿病，癌症

简介:

近年来，极端素食主义的兴起在公众中引发了广泛的争议，导致人们开始质疑素食是否真正健康。有人认为，长期以植物性食物为主可能导致营养不足，使身体无法摄取维生 素B12、维生素D和铁等主要来自动物性食物的必需营养素。然而，与此同时，另一种截然 不同的观点也在大众媒体中广泛传播——即“所有素食都是健康的”。

但这两种看法其实都忽略了事实的复杂性。植物性饮食涵盖了多种不同的饮食方式 ，每一种都可能对个人健康产生不同的影响。比如，素食并不总是意味着更健康的饮食。毕竟，薯条、蛋糕等许多“垃圾食品”虽然也是素食，但它们却富含脂肪、糖分和精制碳水化合物，几乎没有什么营养价值可言。



素食主义的分类

素食是一种总称，涵盖了多种不同的饮食方式。通常，这些饮食方式都避免食用肉类、家禽和海鲜，但在乳制品和鸡蛋的摄入方面可能存在差异:

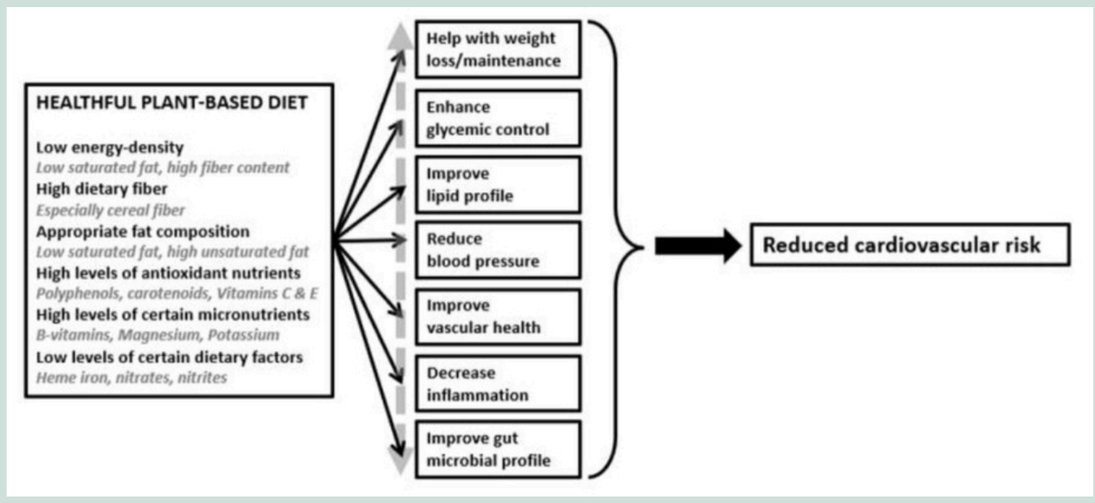
- 严格素食者:避免所有动物产品，包括肉类、家禽、鱼类、奶制品、蛋类，通常还包 括蜂蜜，以及任何从动物身上提取的产品(如明胶和凝乳酶)。
- 乳蛋素食者:允许食用奶制品和蛋类，但避免肉类、家禽、鱼类和海鲜。
- 乳类素食者:食用乳制品，但避免肉类、家禽、鱼类、海鲜和蛋类。
- 卵生素食者:食用蛋类，但避免肉类、家禽、鱼类、海鲜和奶制品。
- 部分素食者:避免食用红肉，但偶尔会食用家禽和鱼类。

健康益处

尽管有观点认为植物性饮食可能导致营养缺乏，从而对健康产生负面影响，但实际上，各种素食性饮食通常是保持健康的有效途径之一，甚至往往比以肉类为主的饮食更具 健康益处。主要以未经加工的植物性食物为基础的饮食通常热量较低，饱和脂肪和低密度 脂蛋白(LDL)胆固醇含量较低，而膳食纤维、维生素、矿物质、抗氧化剂和植物化学物质 的含量则较高。大量研究通过测量心脏病、癌症、糖尿病及血压等风险指标，证实了植物性饮食对健康的积极影响。

心脏病

大量研究表明，植物性饮食与心血管疾病的关系密切，对心脏健康大有裨益。在一项大规模研究中，研究人员考察了素食与缺血性心脏病风险之间的关系。这项研究纳入了 48188名无心血管疾病史的参与者，经过18年的跟踪调查，发现素食者的缺血性心脏病发 生率比肉食者低22%。



健康植物性饮食对心血管影响的潜在机制”(Satija 和 Hu)

健康的植物性饮食以谷物、水果、蔬菜和坚果为主，通常具有较低的能量密度，这主 要归因于其低饱和脂肪和高纤维含量。高纤维饮食能够通过促进胃部充盈感来减少总体能 量摄入，从而有助于体重管理。此外，高纤维饮食还能通过限制胆固醇吸收和胆汁酸合成来 降低低密度脂蛋白胆固醇水平。

植物性食物(如坚果)富含多酚和抗氧化剂，这些成分能够减少氧化应激，支持血管 健康并降低炎症。植物中常见的营养素，如钾和镁，也有助于调节血压和降低中风风险，从 而改善心血管代谢健康。

相对而言，动物产品中的某些成分被发现可能增加心血管疾病的风险。例如，肉类 中的血红素铁会提升氧化应激水平，而氧化应激与炎症和血管损伤密切相关。此外，红肉中的胆碱和左旋肉碱等化合物会转化为TMAO，TMAO水平升高可能影响胆固醇代谢、引发炎症，并促使动脉粥样硬化，从而增加心血管事件的风险。

2 型糖尿病

饮食在糖尿病预防中也起着重要作用。多项研究证实，素食有助于降低2型糖尿病的风险。基督复临安息日会健康研究2(AHS-2)对素食对健康的影响进行了大规模调查，参 与者约96,000人。研究发现，素食饮食“与较低的体重指数、较低的高血压发生率、较低的 代谢综合征发生率、较低的糖尿病患病率和发病率以及较低的全因死亡率相关”(Orlich 和 Fraser)。具体而言，素食者的糖尿病患病率为2.9%，发病率为0.54%，而非素食者的糖尿病患病率为7.6%，发病率为2.12%。

这种效果可能归因于素食者的高纤维摄入。膳食纤维能够减缓糖分的吸收，从而帮 助调节血糖水平，提高胰岛素敏感性。增强的胰岛素敏感性意味着身体对胰岛素的反应更 有效，能够更好地利用葡萄糖作为能量，从而降低胰岛素抵抗的风险，胰岛素抵抗是2型糖 尿病的前兆。此外，植物性食物通常具有较低的血糖生成指数(GI)，这意味着它们导致血 糖水平上升的速度较慢且更稳定，有助于维持血糖水平的稳定，从而减少糖尿病等代谢性疾病的风险。

癌症

在AHS-2研究中，初步结果表明，素食可能有助于降低多种癌症的风险，尽管这种风险降低的幅度并不显著。总体危险比(HR)为0.92，表明素食者罹患癌症的风险比非素食者 低8%。特别是在胃肠道癌症(如胃癌、结肠癌和直肠癌)的预防方面，素食显示出特别的效 果。这种效果可能与素食者的饮食特点有关，即植物性饮食通常富含纤维、维生素和抗氧 化剂，这些成分有助于降低癌症风险。

健康问题

尽管植物性饮食对健康有诸多积极影响，但人们仍然担心这种饮食是否能满足一些重要营养素的需求，如蛋白质、维生素B12、锌和欧米伽-3脂肪酸。

● 蛋白质:尽管有些人认为素食者可能缺乏蛋白质，并且运动员不适合植物性饮食，但 这种说法并不准确。植物性饮食可以通过豆类、坚果和种子、豆制品及谷物等富含 蛋白质的食物来获得足够的蛋白质。研究表明，植物蛋白在支持肌肉力量方面与动 物蛋白同样有效。

● 维生素B12:维生素B12是一种对红细胞生成和DNA合成至关重要的营养素，只存在 于动物产品中。对于包括奶制品和鸡蛋的素食者来说，维生素B12的缺乏不是问 题。然而，对于完全避免动物产品的素食者来说，补充维生素B12是必要的，以防止缺乏症。

● 铁:虽然研究显示肉食者和非肉食者的铁摄入量相似，但动物来源的血红素铁比植 物来源的非血红素铁更易被人体吸收。因此，素食者需要摄入比肉食者多1.8倍的铁 来弥补这一不足。

● 欧米伽-3脂肪酸:不吃鱼和蛋的饮食通常会导致EPA和DHA(两种主要的欧米伽-3脂 肪酸)含量较低。然而，素食者可以从核桃、亚麻籽、奇亚籽、大麻籽、毛豆、海藻和 藻类以及补充剂中获取这些欧米伽-3脂肪酸。

结论

植物性饮食确实为健康带来了显著的益处，如降低心脏病、癌症和2型糖尿病的风险。然而，这并不意味着每个人都必须完全转变为素食者。重要的是在饮食选择中保持平 衡，并提高对植物性食物的认知。并非每个人都需要完全避免动物产品，而是应有意识地增 加植物性食物的摄入。通过将饮食重点放在更多未经加工的植物性食物上，人们可以享受 素食带来的健康益处，同时实现更可持续的生活方式。这样的饮食调整不仅能显著改善个 人健康，还有助于保护环境，促进长期的生活质量。

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原来鸟叫也有方言

关键词: xxxxxxxxxxxxxxxxxxx

俗话说“三里不同调，十里不同音”，人类世界的方言多姿多彩，构成属于每个地界的特色符号，纵使“少小离家”，也依旧“乡音难改”。然而，方言不仅存在于人类世界，而是存在于广泛的动物界。鸟类作为动物界的“歌唱家”，其觅食、自卫、求偶等行为都要借助鸣叫来沟通，因此，鸟类语言的多样性往往超过了大部分动物，据统计，在全世界已知的9000多种鸟类里，就有近3000种风格迥异的语言。除不同种的鸟类语言不同外，同种鸟在不同地区的语言也会随之变化，这就是鸟类的“方言”。

“方言”究竟是怎么形成的呢？这要从鸟的发声来讲起。按照长度、复杂度、上下文为标准区分，鸟的发声包括啼唱和鸣叫两种，在鸟类学和观鸟中，啼唱代表的是相对更复杂的发声，而鸣叫则指的是相对简单的发声，而啼唱更长、更复杂，并且与领地、求爱和交配相关；而鸣叫则一般是为了警示或与同胞联系。对于复杂的啼唱而言，由于各个区域内有较为稳定的鸟群，各个群体之间就独自发展出了不同的唱法，在同一个“方言区”内，鸟的唱法就会有高度的一致性，而在不同“方言区”内，鸟叫声的长度、音节、音色等方面都有差别。

鸟类自己会意识到本地鸟的语调和外地鸟不同吗？这个验证实验其实非常简单，观鸟爱好者只需提前录制好外地鸟的叫声，再将外地“方言区”的鸟叫声放给本地鸟听，就可以观察本地鸟的行为。人们发现，领地意识更强的雄鸟会先飞近声源，寻找这个潜在的竞争对象，然后想方设法把对方驱逐出去，也就是说由于地域的分隔，鸟类已经将讲方言的鸟判定为外来鸟，纵使他们所持的语言体系仍是同一套，而叫声中细微的差别就是他们分辨异己的线索。

鸟类的“方言”和人类“方言”一样，也是可以传承下去的。鸟类和人类语言都是通过发声学习将文化传递给下一代。由于地理上的分隔，同种鸟类的不同族群久而久之也会产生啼唱声的细小差异，最终发展成为一种新的方言--这和人类发展出不同口音、方言和语言的过程类似。

然而，鸟类的“方言”也昭示了环境污染。在城市中的鸟叫声往往频率更高，这是因为城市里充斥着嘈杂沉重的噪音，为了更好地与同伴交流，城里的鸟只能以更高频率的声音来应对噪音污染。

随着社会对噪声污染的关注度逐渐提高，从2025年1月1日起，全国将建立起统一的声环境质量自动监测网络。但是自动监测设备在监测噪声同时，也会将附近的鸟叫、虫鸣、蛙声以及风、雨、雷电声等同步记录下来，影响对实际噪声情况的判断。这一举措不仅有利于噪声污染整治，还为野外记录鸟鸣种类丰富度提供帮助，在对自然声进行筛选、甄别的过程中，工作人员同样发现了鸟声的“方言”，他们记录到同一种类型的鸟声存在着地域上的差异，而且通过听声，不仅能够识别鸟的种类，还能知道它来自哪片区域，甚至能分辨出它们的状态和情绪，这为进一步研究鸟类间的信息交流提供了丰富信息。

古语有言：“蝉噪林逾静，鸟鸣山更幽”，在广袤的大自然中，鸟儿的歌声清脆嘹亮，点缀着草木花树，丰富了人们的生活。鸟叫的“方言”为我们研究鸟类群体行为提供了特别的视角，相信随着噪音污染的整治，更多鸟儿将与我们相伴相生，我们将真正生活在鸟语花香的世界里！

SMART MAGAZINE AUTHOR:Rosy TRANSLATOR: Yaqi

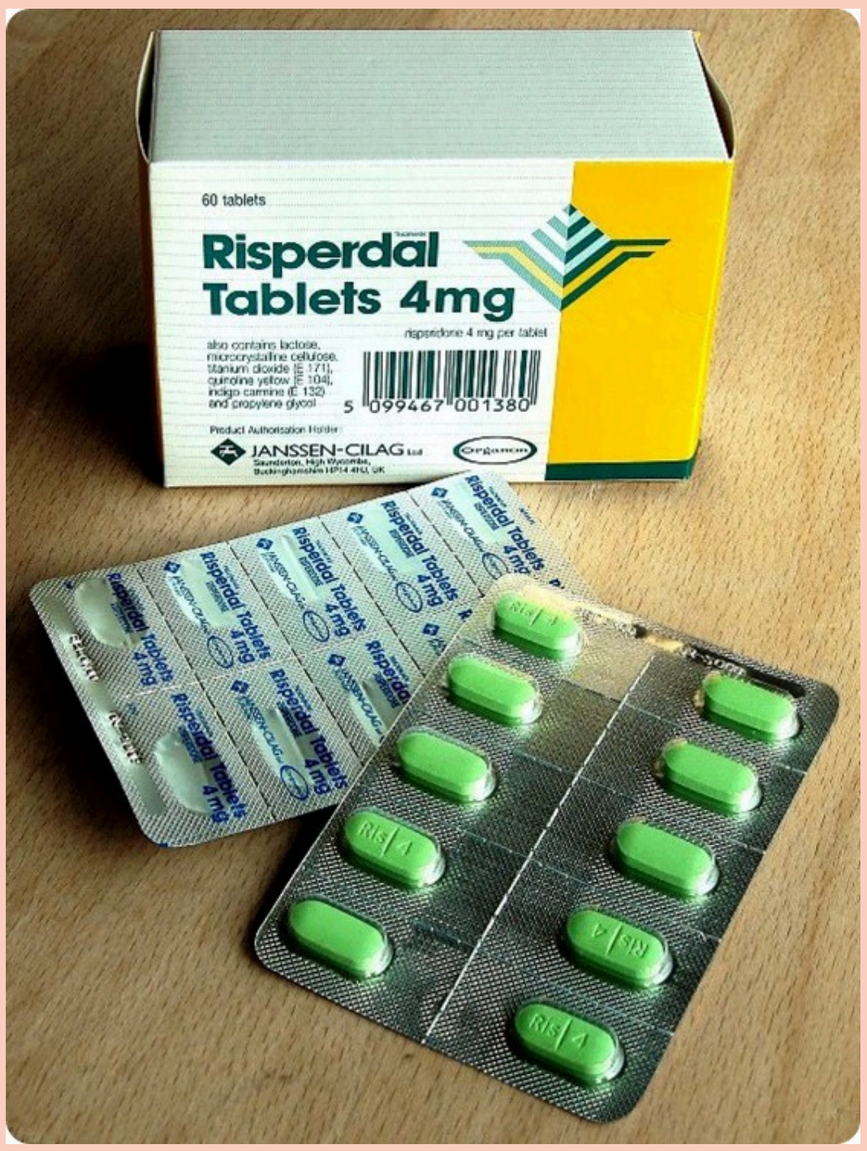
关于治疗精神分裂症主要药物氯丙嗪与帕罗西汀联合用药的研究进展

关键词：精神分裂症、氯丙嗪、帕罗西汀、联合用药

1. 精神分裂症

精神分裂症(Schizophrenia)是一种异质性疾病，同时具有阳性症状和阴性症状。阳性症状表现为妄想、幻觉、思维障碍，阴性症状表现为快感缺乏、厌倦、社交退缩、认知功能障碍等。目前，尽管有许多抗精神病药物可用于精神分裂症的治疗，但这些药物的治疗效果低于预期，起效缓慢，且常产生严重的副作用。虽然精神分裂症的病因仍然知之甚少，病理学家们主要集中在多巴胺和谷氨酸上，但许多神经递质和神经调节剂，包括 5-羟色胺 （5-HT）、γ-氨基丁酸（GABA）、甘氨酸、D-丝氨酸和神经活性类固醇等都与其有关[1]。

目前，已确定的与精神分裂症相关的基因位点有108个，许多基因已被用于生成精神分裂症的动物模型[1]。例如，细胞粘附分子神经调节蛋白1（NRG1）及其受体ErbB4的基因突变会增加患精神分裂症的风险，NRG1在中枢神经系统突触中表达，在神经递质受体（包括谷氨酸受体）的表达和激活中具有明显的作用。NRG1或其受体ErbB4杂合子的突变小鼠显示出与精神分裂症小鼠模型重叠的行为表型，从而证明NRG1与ErbB4基因与精神分裂症相关[2]。

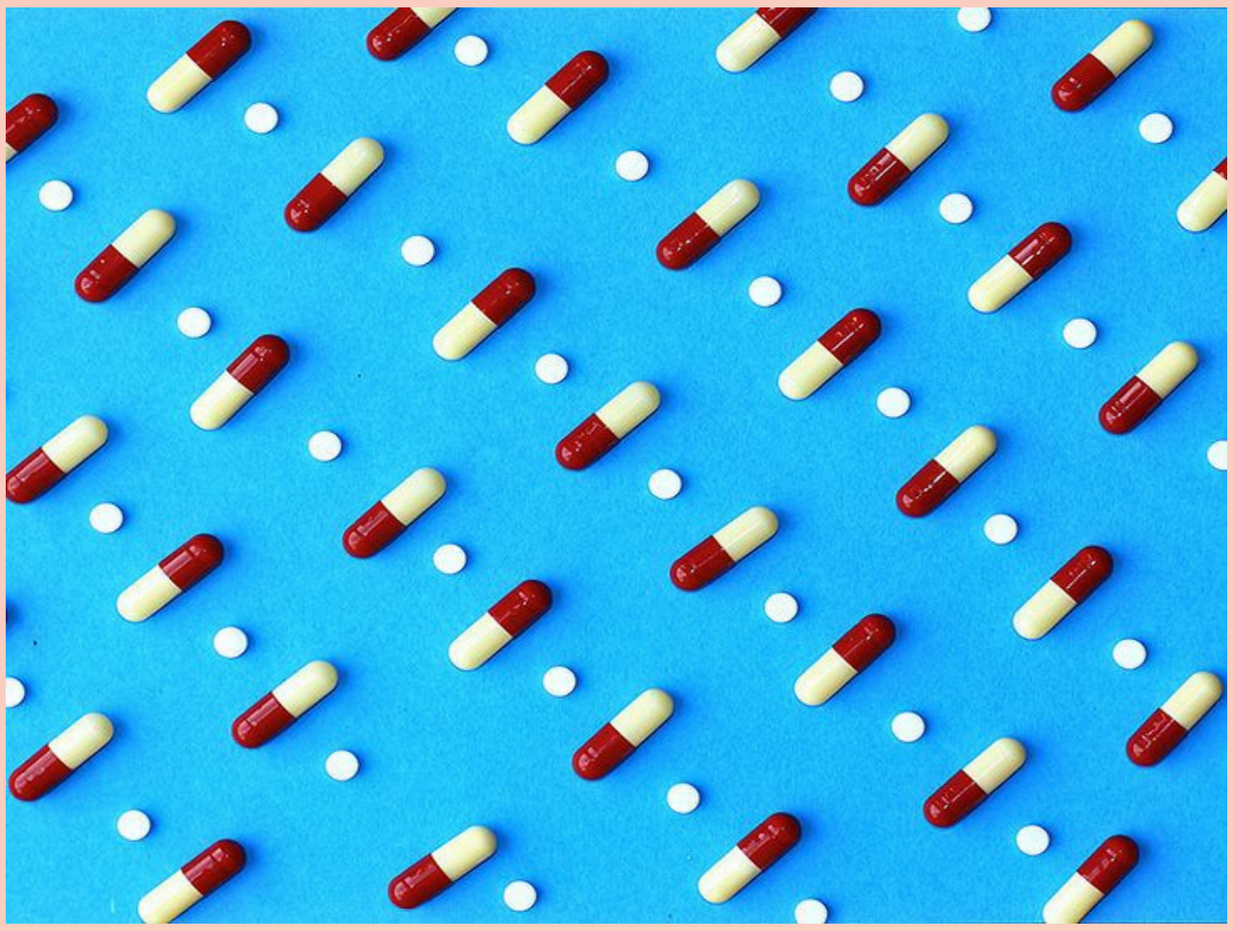


2. 氯丙嗪的作用机理

氯丙嗪是治疗精神分裂症最广泛使用的药物之一。氯丙嗪主要对DA受体有阻断作用，另外也能阻断α受体和M受体等。抗精神病方面，氯丙嗪的作用机制未定。目前认为精神分裂症的临床症状是由于脑内DA功能过强所致，且脑内D2受体密度特异性增高。吩噻嗪类是D2受体的强大拮抗剂，因此认为吩噻嗪类抗精神病的作用是通过阻断中脑-边缘叶及中脑-皮质通路中的D2受体而发生的。临床上主要应用氯丙嗪治疗各型精神分裂症，对急性患者疗效较好，但必须长期服用以维持疗效，减少复发 [3] 。

3. 氯丙嗪与帕罗西汀的联合用药

氯丙嗪安全范围大，但长期大量应用，不良反应较多。常见的不良反应分为一般不良反应、锥体外系反应、过敏反应。一般不良反应有嗜睡、无力、视力模糊、鼻塞、心动过速、口干、便秘等中枢神经及植物神经系统的副作用。锥体外系反应有帕金森综合征，急性肌张力障碍，迟发性运动障碍或迟发性多动症等。过敏反应常见皮疹，光敏性皮炎，急性粒细胞缺乏等。



帕罗西汀是治疗精神疾病的常用药物之一，是一种苯基哌啶衍生物，能够与 5- 羟色胺转运体发生相应反应，从而降低突触前膜对5- 羟色胺的再摄取能力，进而减缓患者的抑郁情绪，而且能够在一定程度上增强机体活力，在精神分裂症的治疗当中为取得良好的治疗效果 , 可以采用帕罗西汀联合抗精神类药物进行治疗。刘萍等 [4] 探究在精神分裂症中选用帕罗西汀、氯丙嗪联合治疗的临床效果，参照组患者采取单一氯丙嗪治疗，观察组采取帕罗西汀、氯丙嗪联合治疗，结果显示治疗后，观察组抑郁情绪、焦虑情绪评分均低于参照组 。观察组不良反应发生率也明显低于参照组。因此，氯丙嗪与帕罗西汀联合用药是一种相对有效且温和的治疗方案。

4. 展望

虽然帕罗西汀与精神病药物相结合可以提高精神分裂症在临床的中的治疗效果，但由于该治疗方式在临床中的使用时间较短，机制尚未彻底明确，临床经验相对匮乏， 因此， 需要医师在临床治疗中不断总结经验，为今后类似疾病的治疗奠定基础。在此过程中，医院应该为精神分裂症的诊疗医师提供一个相互交流的平台，通过进行案例分析的方式，总结帕罗西汀药物在治疗精神分裂这一疾病中的经验，使医师在治疗精神分裂症这一疾病的过程中，可以更加详细的了解帕罗西汀的药性，合理掌握帕罗西汀药物在临床应用中所需要使用的剂量，从而使帕罗西汀药物可以在治疗过程中将药物疗效发挥到最佳。

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SMART MAGAZINE AUTHOR: Zeke TRANSLATOR: Zeke

从头设计具有氢键网络介导的模块特异性的蛋白质同质异构体 (double check title)

文献背景：

蛋白质电路的发展历史可以追溯到上个世纪90年代。最早的研究主要集中在通过基因调控来构建分子电路，例如使用基因调控元件如启动子、转录因子和反应器等来控制基因表达。然而，传统基因电路受限于转录和翻译的时间尺度以及固定的调控因子，不能实现快速和精确的信号处理。

随着对蛋白质和蛋白质相互作用的深入理解，研究人员开始将注意力转向蛋白质电路的设计。蛋白质电路的主要优势在于其能够快速响应，通过多种化学修饰实现更为复杂的信号处理和动态调节。这种快速反应机制使得蛋白质电路在复杂环境中具有更高的灵活性。基础研究主要关注蛋白质电路的设计、构建和功能鉴定，旨在揭示蛋白质相互作用和信号传导的机制。应用研究则将蛋白质电路应用于生物医学和医药领域，例如将蛋白质电路应用于肿瘤治疗、分子诊断和药物释放等。

这篇文章是2016年刊登在science杂志上的，PI陈子博在后续持续在这个方向进行研究，在18年在cell上发表了综述Programmable protein circuit design。在蛋白质的相关研究中，David Baker实验室及RosettaDesign系统发挥了非常重要的角色。

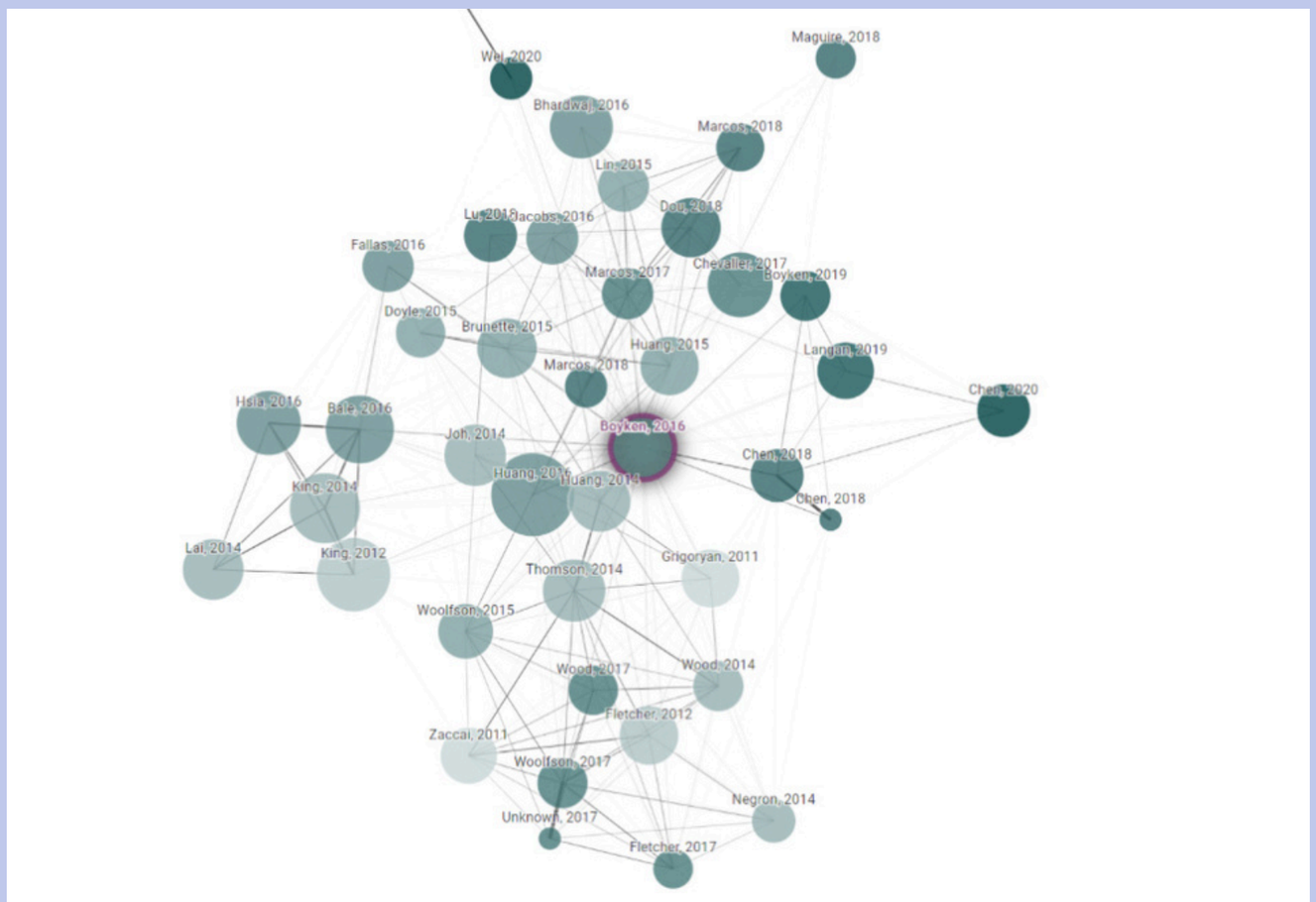


Fig1. Research Network Diagram

背景知识介绍：

蛋白质电路设计是建立在分子计算概念上的新兴交叉学科，蛋白质具有多样的结构和功能，可以通过相互作用、修饰和调控实现与其他蛋白质以及细胞内外路径的耦合。这样的特性使得蛋白质成为设计和构建复杂分子回路的理想组分。然而，蛋白质的多样性也给蛋白质电路的设计和控制带来了挑战，因为需要解决如何选择适当的蛋白质组分、调控蛋白质相互作用和保持回路的稳定性等问题。

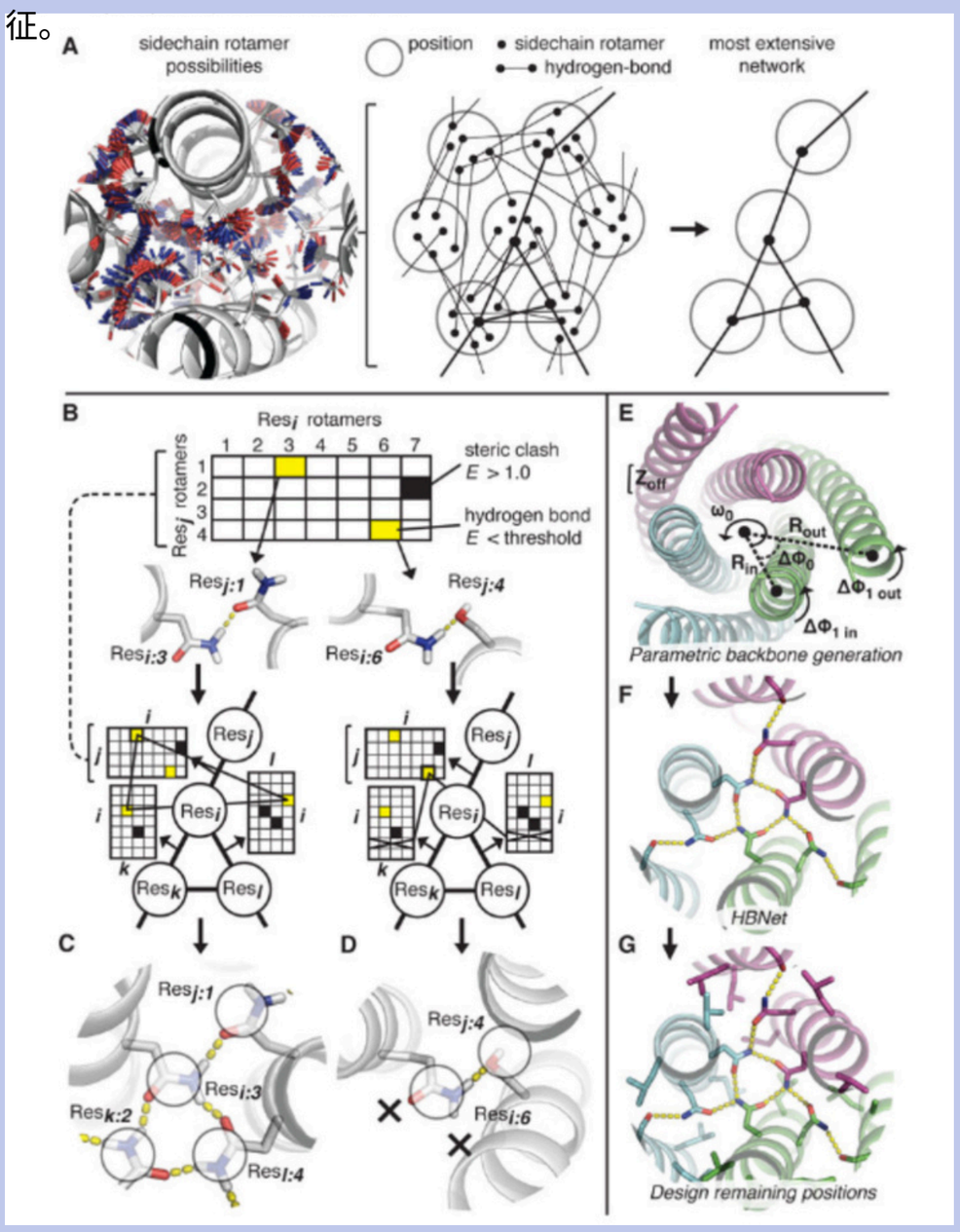
近年来，研究人员通过关注正交性和可组合性等原则，努力解决蛋白质电路设计的挑战。正交性指的是回路中的组分相互作用不会与细胞内其他分子相互作用，以保持回路的独立性。可组合性指的是可以使用一组有限的工程蛋白质组分构建多样的回路级功能。利用这些原则，研究人员已经成功设计和构建了可以感知、传递和处理信息的蛋白质电路。这些电路可以实现动态控制细胞行为，发展出新的治疗策略，并为编程生物学提供了强大的工具和范式。

创新性：

设计方法创新：研究人员开发了一种名为HBNet的计算方法，可以快速列举出输入的背骨结构中可能存在的所有氢键网络。这种方法可以在原子级别精确地设计大规模的氢键网络，为蛋白质设计领域提供了重要的突破。通过该方法，可以实现对蛋白质寡聚体的特异性编程，为合成生物学应用提供了新的可能性。

结构拓扑创新：研究人员利用HBNet方法设计了具有模块化氢键网络的蛋白质同源寡聚体，并通过RosettaDesign进行优化。研究设计了包括三角形、正方形和超螺旋等以前未见的拓扑结构的二聚体、三聚体和四聚体。这些新颖的结构展示了设计蛋白质寡聚体的多样性和灵活性。

实验验证创新：设计的蛋白质同源寡聚体通过循环二色光谱、解析蛋白质结晶结构和小角X射线散射分析进行了进一步的结构表征。



HBNet 通过 极性侧链对的所有构象（旋转态）之间的氢键和立体排斥之间的相互作用 做为起点 。 这个方法能够高效识别低能量氢键网络，从而优化蛋白质的结构设计。 这些能量存储在图数据结构中，其中节点是残基位置，空间中接近的位置通过边连接，并且对于每条边，都有一个矩阵表示两个位置的不同旋转态之间的相互作用能量。HBNet 遍历此图，以识别所有由低能氢键连接的三个或更多残基组成的网络，且立体排斥较小。在C中，展示了 在指定的蛋白质骨架结构中，HBNet识别并保留了能量最低且覆盖最广泛的氢键网络，这些网络在后续的设计优化中被用于稳定蛋白质的整体结构。 D显示了被拒绝的氢键网络，这些网络具有不满足的埋藏供体和受体。在设计过程中，这些未满足的氢键可能会导致不稳定或不合适的蛋白质结构。因此，这些网络被识别并排除在设计考虑之外。

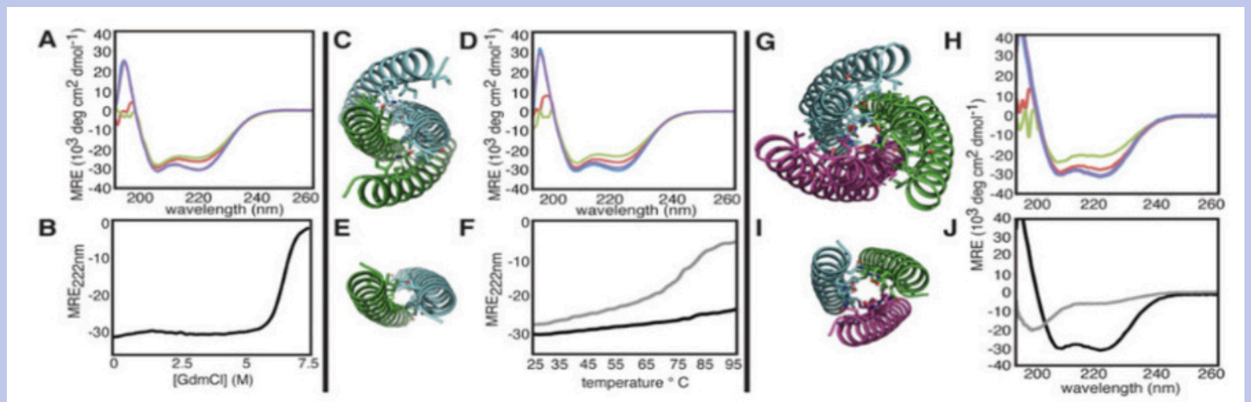


Fig. 2. The outer ring of helices increase thermostability and can overcome poor helical propensity of the inner helices

Fig.3 螺旋外圈结构增强热稳定性

使用共螺旋（coiled-coils）作为蛋白质寄主结构，因为共螺旋具有重复的几何横截面，并且可以通过参数化生成。他们构建了具有两个同心环的寄主结构，每个环由螺旋发夹单体亚单位组成，包括 外螺旋通过短连接环与内螺旋连接，这种设计不仅确保了蛋白质整体结构的紧密性，还增强了其热稳定性和功能性。 。通过系统地对内外螺旋的半径、螺距、内外螺旋之间的 z 偏移和整体超螺旋扭转进行采样，生成了广泛范围的骨架。之后，在骨架中搜索跨分子界面的网络，并使用RosettaDesign优化剩余残基位置的旋转体，实现有复杂氢键网络的设计。

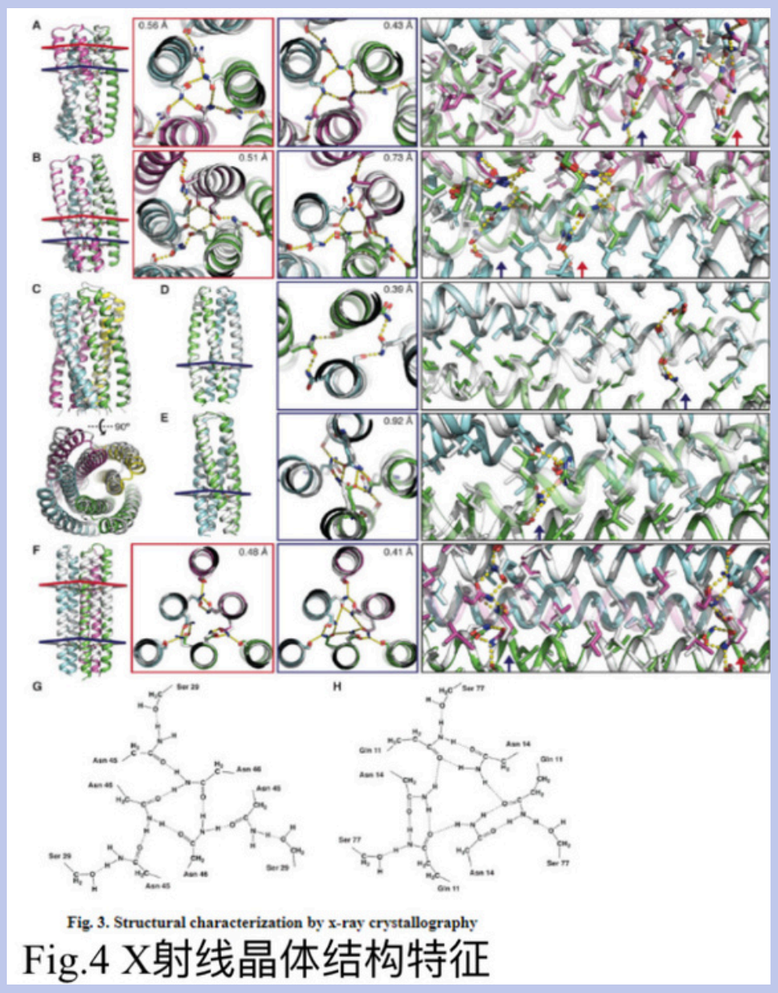


Fig. 3. Structural characterization by x-ray crystallography

Fig.4 X射线晶体结构特征

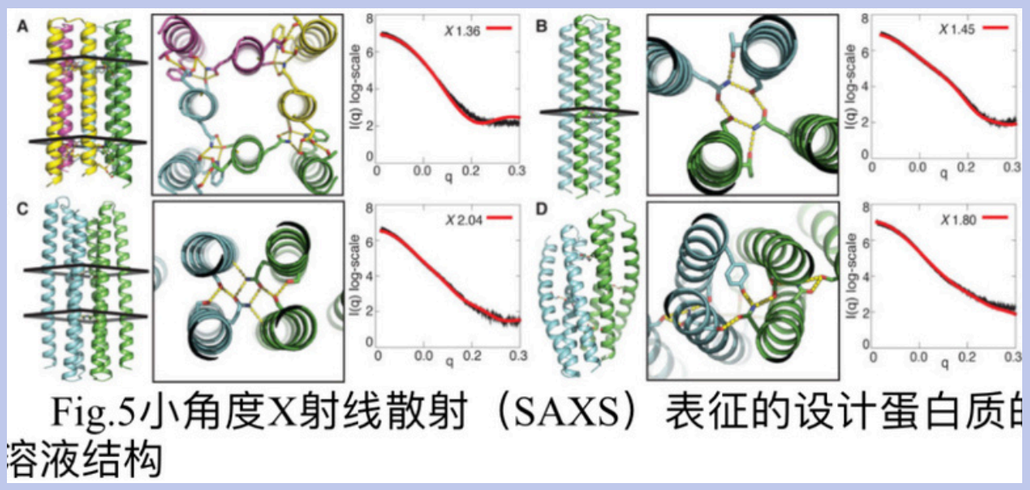


Fig.5小角度X射线散射（SAXS）表征的设计蛋白质的溶液结构

他们的研究对设计蛋白质稳定性和结构特性的全面分析，显示了这些设计在CD光谱和热稳定性方面的典型特征，并且通过比较两环设计和仅内环设计的结果，揭示了外环对蛋白质稳定性和组装的重要性

溶液结构：

通过SAXS，观察到了方形的未扭曲四聚体和二聚体的形态（A&B），以及六螺旋二聚体的形态，其中有右旋（C）和左旋（D）两种超螺旋几何形状。通过SAXS的实验数据，这些设计模型的结构与实际情况非常吻合，表明在溶液中，设计的蛋白质能够形成预期的多聚态。

结果表明，具有将疏水界面区域划分为相对较小区域的氢键网络设计比具有大面积连续疏水斑块的设计具有更高的特异性。最好划分疏水区域的设计具有跨越整个寡聚体界面的网络，每个螺旋至少贡献一个侧链。结果显示，组合设计表现出了相当高的特异性，尽管它们具有相同的骨架和高度相似的序列，而全疏水控制则相对杂乱。中央的氢键网络清楚地起着介导特异性的作用。\ "

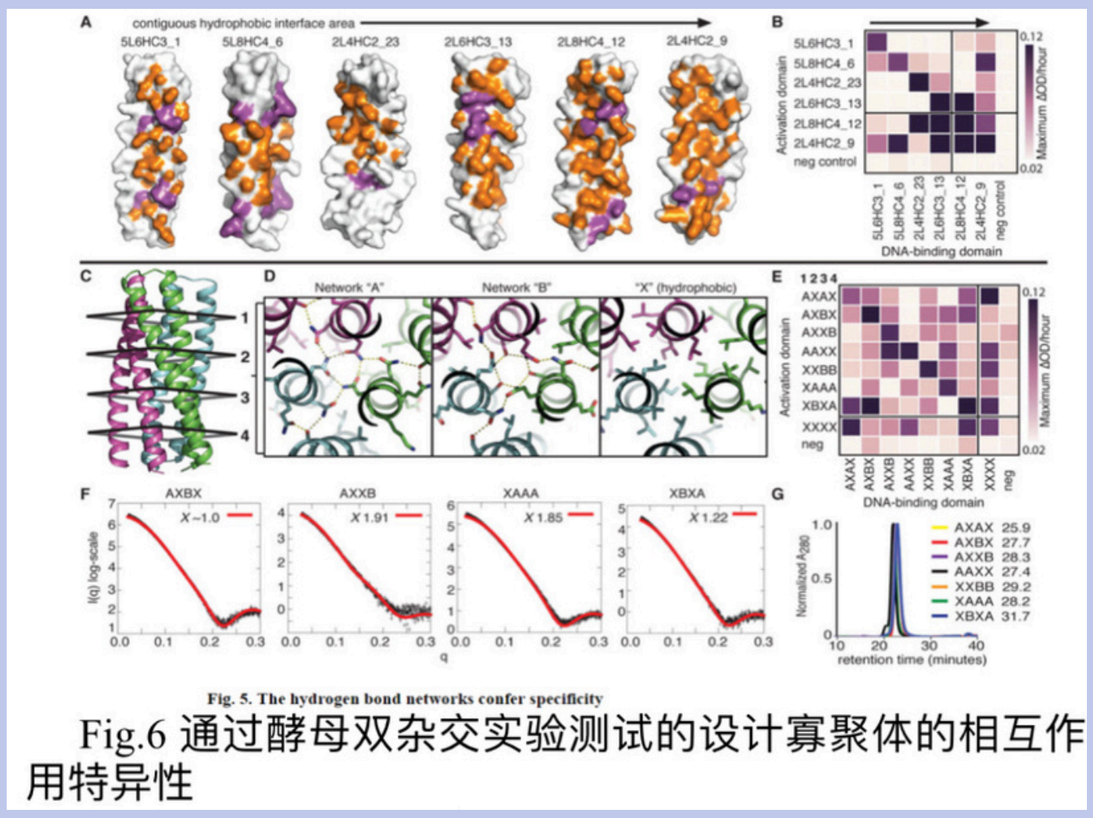


Fig. 5. The hydrogen bond networks confer specificity

Fig.6 通过酵母双杂交实验测试的设计寡聚体的相互作用特异性

启发和感想：

研究中提出的HBNet方法在蛋白质结构设计领域有创新型，可以快速高效搜索骨架结构中的氢键网络，其设计的模块化氢键网络寡聚体拓扑结构新颖，也充分展现了蛋白质作为电路设计环节中的优势。研究中设计的氢键网络寡聚体拓扑结构各具特定的几何形状和相互作用模式。这些寡聚体可以作为不同逻辑门的模块化组件，通过组装构建具有不同计算功能的生化逻辑电路。

相比于基因回路，基于蛋白质的电路反应迅速，可以实时检测细胞内外条件变化并做出相应响应。这使得可以构建闭环反馈电路实现对细胞过程的准确调控，如控制细胞增殖、分化和凋亡。蛋白质电路可以架设在细胞内或跨细胞之间，协调组织和器官层面的活动。这为构建类似电信号的多细胞调控网络提供可能。

蛋白质电路的设计原理如模块化和正交性为合成生物电路的设计提供了全新的思路，有助于标准化和系统化地构建生物系统。基于蛋白质电路的传感和执行模块，可以实现对各种信号精确和动态的检测及对行为的可编程控制。

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SMART MAGAZINE AUTHOR: Nox TRANSLATOR: Rick

科幻照进现实？体外构建器官的魔法！

关键词：类器官、器官芯片

简介：

类器官和器官芯片是两种快速发展的3D细胞培养技术，它们的出现弥补了传统的体外2D细胞培养和动物模型之间存在的差距。今年7月，多伦多大学的研究人员在Nature Reviews Bioengineering期刊上发表了一篇题为“Integrating organoids and organ-on-a-chip devices”的综述性论文，该文章首次对这两种新兴技术进行了明确定义，探讨其发展所面临的问题，并展示了其目前在医疗领域中的应用。文章最后还讨论了通过整合这两种技术，以实现集成设备的要求与限制。

3D细胞培养的意义

在药物研发过程中，常用的传统体外模型有动物模型和2D细胞培养模型，动物模型不仅价格昂贵，其使用也存在巨大的道德争议。但传统的体外2D细胞模型无法准确反应药物在体内发挥的作用，通过体外模型筛选的药物仍有很大可能在临床实验中失败。而3D细胞培养技术则能更好地模拟体内生理环境，从而提高药物体外筛选的成功率。
(2D细胞培养：在塑料或玻璃表面培养，无法准确再现复杂的生理结构
3D细胞培养：细胞像在体内一般，被其他细胞和细胞外基质(ECM)包围，能更好地再现体内细胞的生理结构。3D细胞培养技术包括球状体、类器官、器官芯片(OoC)以及依靠水凝胶或聚合物支架的组织工程。)

首次给出明确定义

类器官（Organoids）：类器官是一种自组织结构（即可由细胞自发组织形成）。通常由人类多能或成体干细胞增殖分化而来。其包含多种细胞类型，具有与特定器官区域相似的细胞结构和功能特征，一些类器官(如肠道或肾脏类器官)在组织学上与天然器官几乎没有差别。但类器官缺乏与其他器官和组织的互动，常常没有血管和免疫系统。为了克服这些限制，研究人员已经开发了组合体（assembloids），这是一种通过融合不同类型的类器官而形成的自组织细胞系统。
器官芯片（Organs-on-Chips，OoCs）：器官芯片是一种工程化或微加工培养系统，可支持细胞组装成类似组织结构，以用于测量模拟器官的功能特征。OoCs虽然不完全再现整个器官，但能够提供更精确的3D细胞培养，以模拟一个或多个组织的生理反应。器官芯片可在单个设备中整合多种细胞类型，使用膜或柱阵列促进营养物质和氧气的运输，以及通过组织固定来控制几何形状和多轴拉伸，这些功能在传统2D细胞培养中通常都不能实现。

3D细胞培养的应用

类器官和器官芯片可用于组织工程和再生医学应用，通常器官芯片的规模比类器官更小。组织工程是指集成使用细胞、生物材料支架和生物反应器，以创建可以探测疾病病因、药物疗效和发育机制并替代或增强本体组织结构的组织。再生医学则是用多能或成体人类干细胞和相关技术（如基因编辑）来替代或修复损坏的组织和器官。通过诱导干细胞形成类器官后，可将类器官移植入体内修复或取代原有受损器官（如肝脏和肠道）。再生医学和类器官研究都使用定向分化方案，这种方案依赖细胞因子来激活发育过程中负责器官发生的途径，从而实现高度特异性的细胞分化。

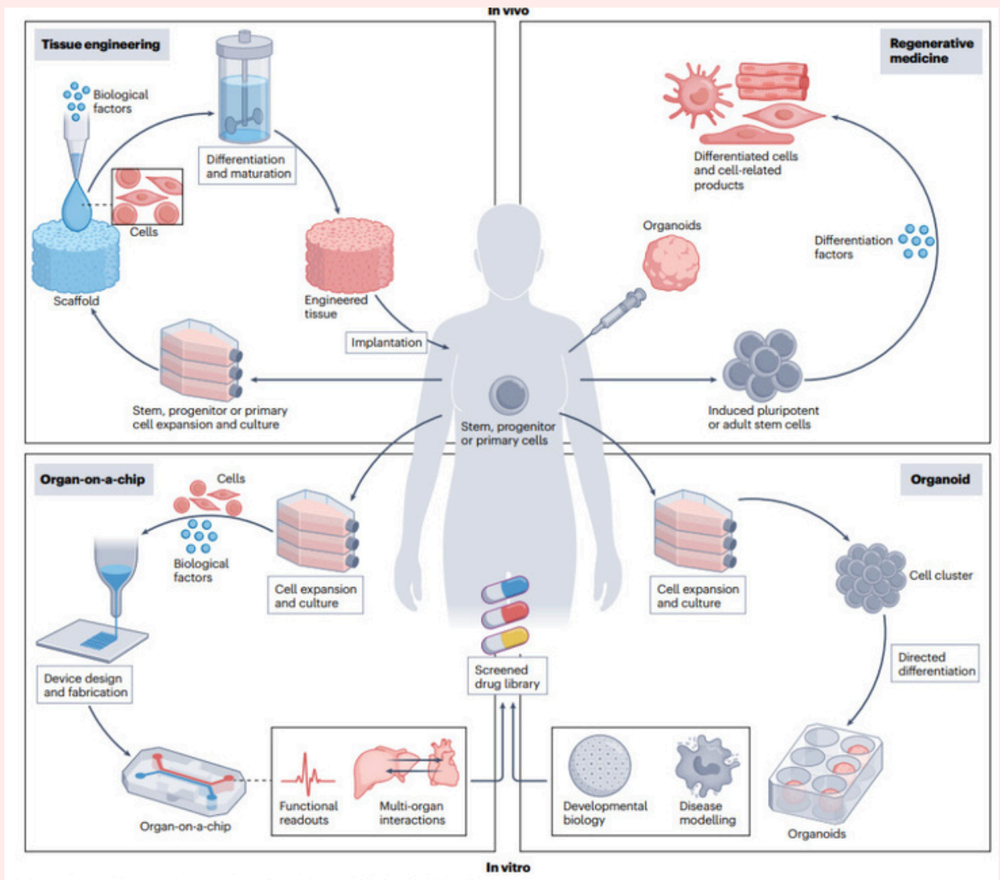


图 1 类器官和器官芯片的方法

SMART MAGAZINE AUTHOR: Nox TRANSLATOR: Rick

发展所面临的问题

虽然3D细胞培养技术，可以模拟目标组织的某些生物过程，但目前仍然存在许多问题，包括有关血管化、药代动力学和药效学的常规评估、药物耐受性机制和脱靶效应的识别等方面的缺陷。并且在尺寸和保真度方面，它们的工作尺度往往在几百微米到1厘米之间，无法完整再现人体器官。例如，心脏器官芯片虽然能通过提供心肌细胞束来再现心肌的收缩功能，但它们不能复制心脏的四个腔室，甚至也不能复制心室壁。

类器官与器官芯片的整合

整合类器官和器官芯片旨在结合两者的优势：一方面，类器官可提供复杂的细胞组成，增强器官芯片的功能。另一方面，器官芯片的精确几何和微观特征有助于引导类器官发育，提高一致性和成熟度，并通过内置传感器实现现场功能读数。但把类器官整合在器官芯片中，会由于类器官被限制在一定边界中从而影响其生长特性和细胞谱系的确定。而且整合后会使对于类器官的成像更为困难。

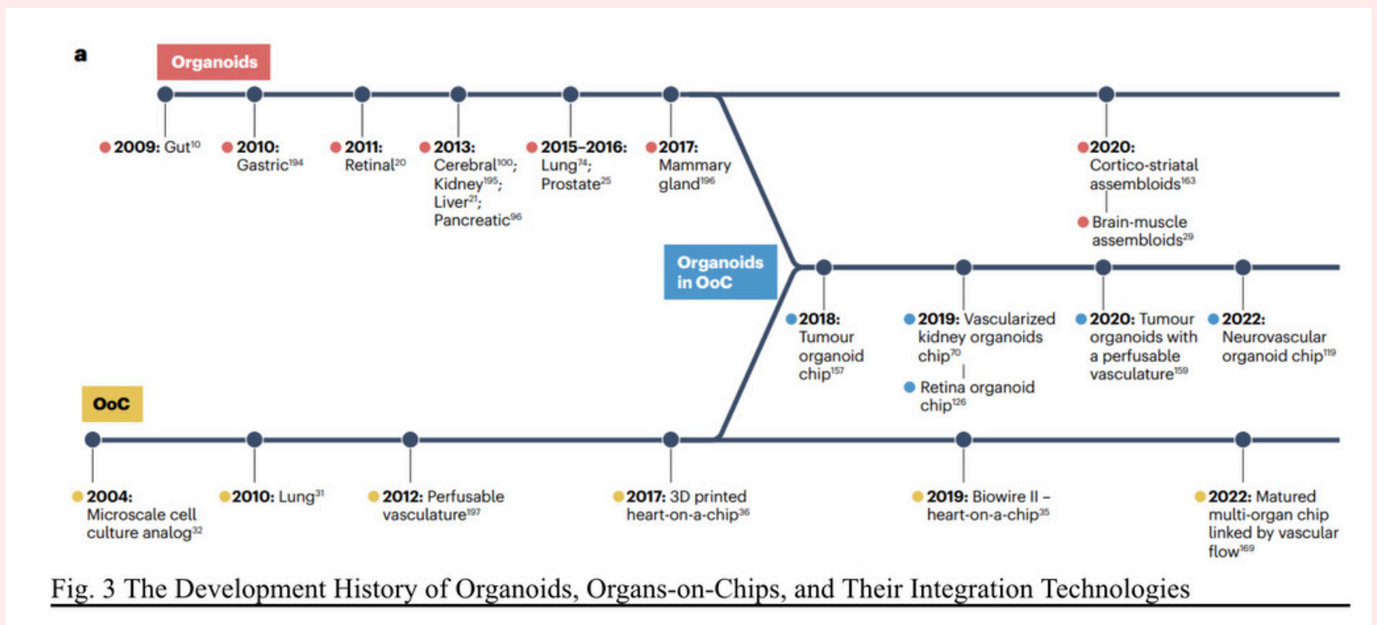
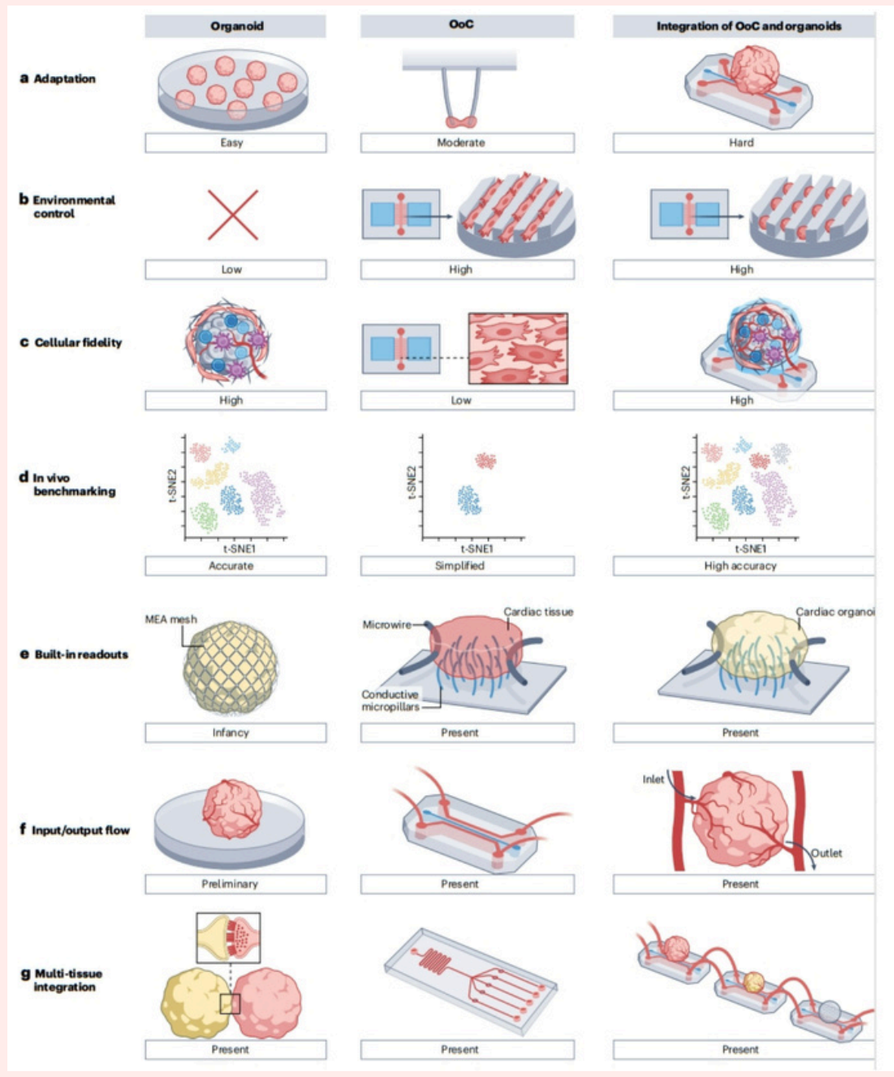


Fig. 3 The Development History of Organoids, Organs-on-Chips, and Their Integration Technologies



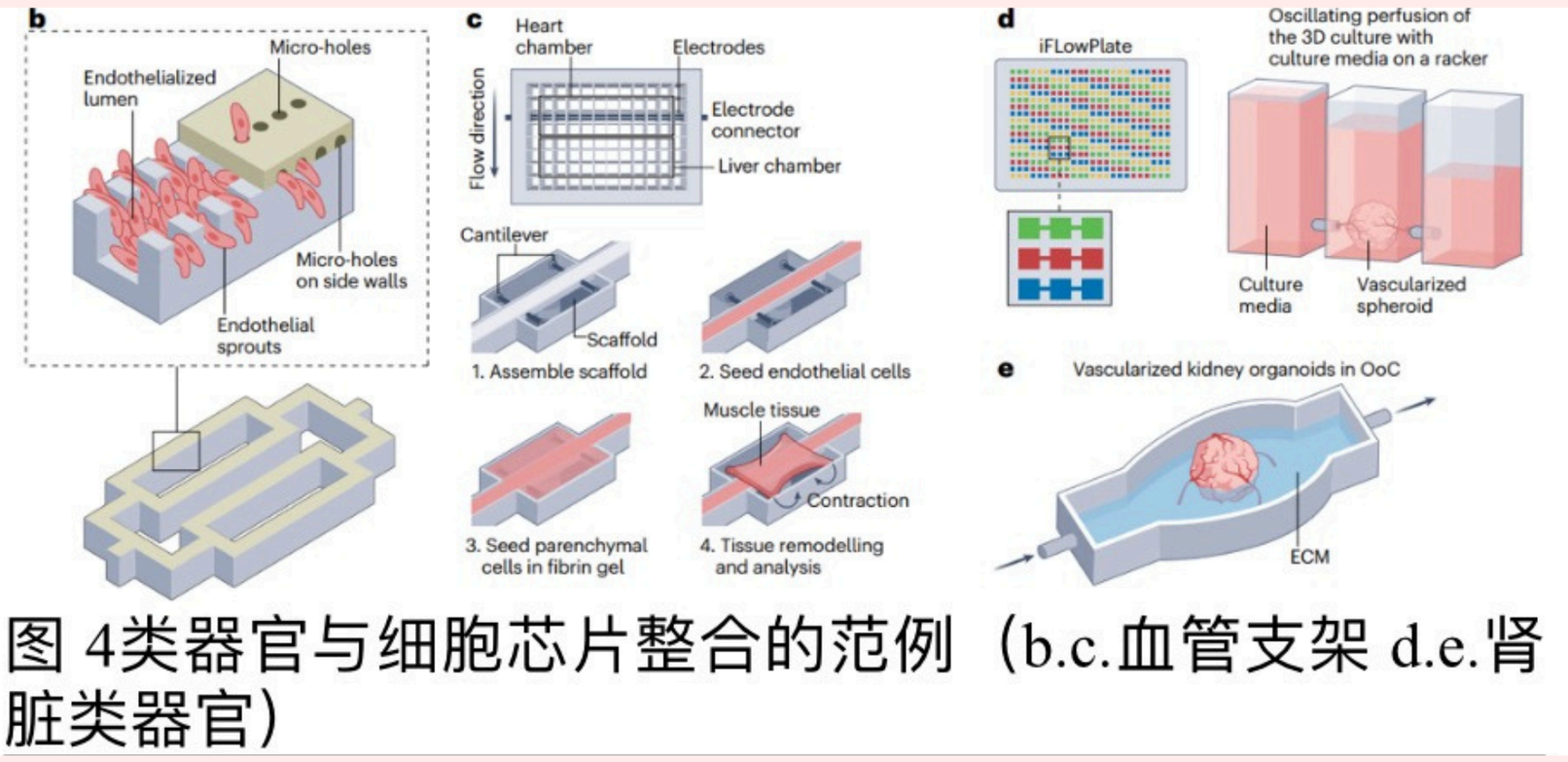


图 4类器官与细胞芯片整合的范例（b.c.血管支架 d.e.肾脏类器官）

目前通过整合类器官和细胞芯片，人们已初步搭建了包括肠道、肾脏、肺部、肝脏、胰腺、神经系统、心脏和肿瘤方面在内的多种生理模型。以肾脏为例，目前通过在3D打印的可灌注芯片上诱导培养多能干细胞，已经成功制造出具有一定经上皮转运功能的肾脏类器官。

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SMART MAGAZINE
AUTHOR: Molly TRANSLATOR: Zona

糖友应该怎么吃蛋白质

Key words: diabetic nephropathy, protein, old age

简介

肾病是糖尿病的常见并发症之一，约40%糖尿病患者受到肾病的困扰。除了日常锻炼和减少吸烟外，控制饮食也是改善预后的重要手段。美国肾脏病基金会（NKF）肾脏病预后质量倡议（KDOQI）推荐糖尿病和不依赖透析的慢性肾病患者采用低蛋白饮食，即每日蛋白质摄入量为0.6-0.8克/千克体重。低蛋白饮食已被证实能够减缓肾损伤进程和蛋白尿的进展，但这可能导致营养不良、蛋白质代谢紊乱、碳水比例增加等问题，不利于控制血糖水平，影响患者预后。

研究方法与设计

研究人员利用全国健康和营养检查调查（NHANES）数据库中1999-2018年的数据，剔除缺少数据的个体后，按照《肾病：改善全球预后（KDIGO）2022指南》对2901名研究对象的数据进行了分层分析。

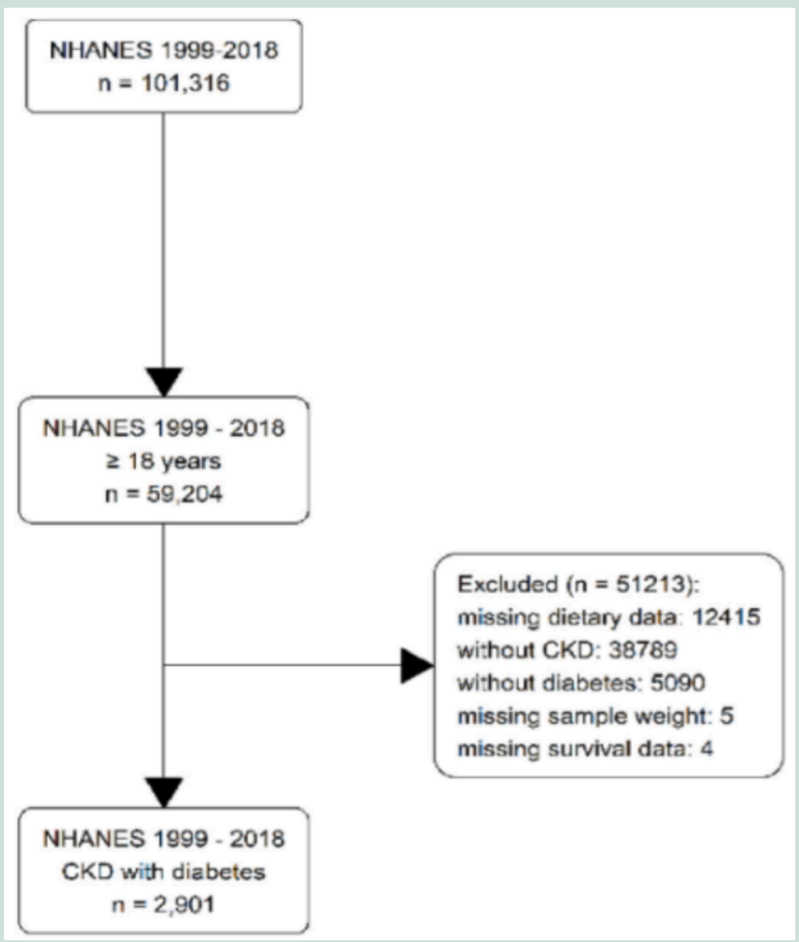

图1
基于1999-2018年NHANES的数据的筛选流程图

结果与讨论

结合分析结果和随访结果，膳食蛋白质的适度增加与降低糖尿病肾病患者死亡率有关。

那么究竟应该吃多少蛋白质呢？与KDOQI指南的建议摄入量不同，分层分析结果显示，每日保持0.6-1.2克/千克体重的蛋白质摄入量对60岁以上的患者有益，且能够一定程度上降低死亡率。其中，1.0-1.2g/kg的膳食蛋白质摄入与所有原因的糖尿病患者死亡风险降低显著相关。当然，对于患有其他慢性病或具有特殊情况的老年人，这个数值会有所变化，如对于血液透析的患者而言，考虑到蛋白质在透析过程中的损失，患者需要更多的营养摄入；对于患有高血压的老年人来说，每日0.8-1.0克/千克体重的蛋白质摄入与更低的死亡风险相关；但对于糖尿病肾病预后不良的极高风险患者而言，这个数值为每日0.6-0.8克/千克体重。

然而进一步分析数据发现，动物蛋白摄入量增加与升高的死亡率有关。

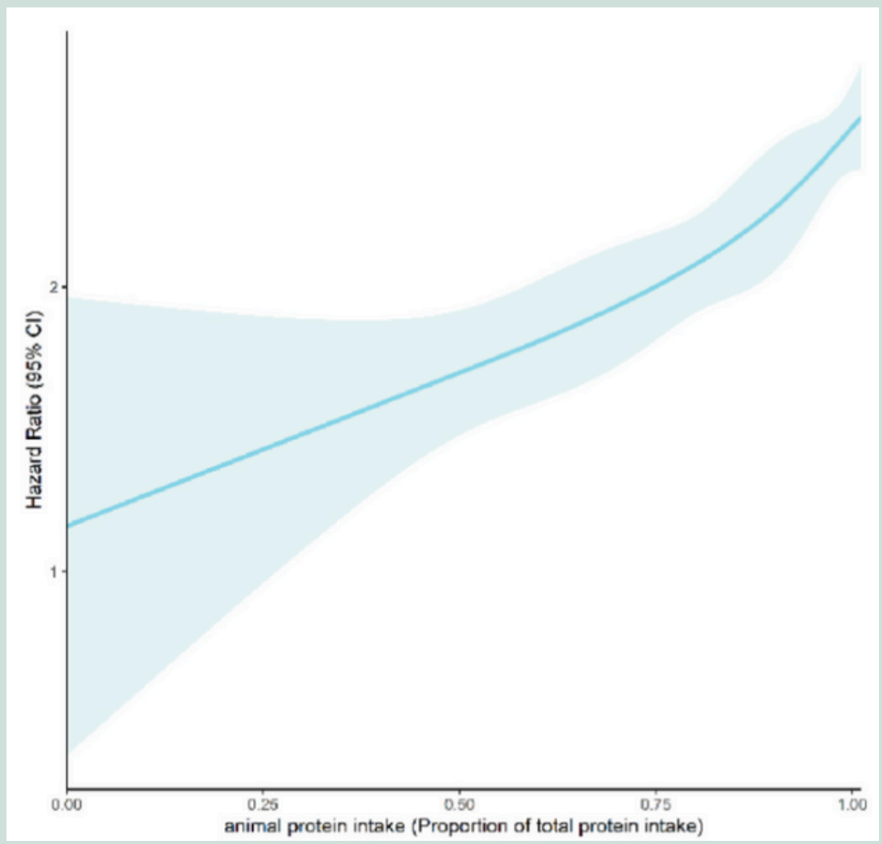

图2
对于动物蛋白摄入比例以及全因死亡率的rcs分析

相关研究数据表明，相较于植物蛋白，食用动物蛋白时肾脏负荷更大。动物蛋白中含有更多的甲硫氨酸和丙氨酸，水解后生成更多氨气和硫化合物，会扰乱肠道菌群稳定性、提高心血管疾病的发病几率，还可能导致炎症的发生。摄入大量的红肉，尤其是预制肉，会增加患高血压的风险，对肾功能同样有所损害。对此，其中一种说法是甲硫氨酸作为半胱氨酸的前体，能增加非对称二甲基精氨酸水平，抑制一氧化氮（NO）发挥降血压作用。另一种说法是蛋白质和脂肪在高热状态下发生美拉德反应时产生终末糖基化产物（AGEs），刺激血管张力素II的产生，诱导血管收缩，最终导致血压上升。通俗的说，煎烤烹炸的高脂肪肉蛋制品可能具有升高血压的作用，高血压及肾功能障碍人群都要少吃。

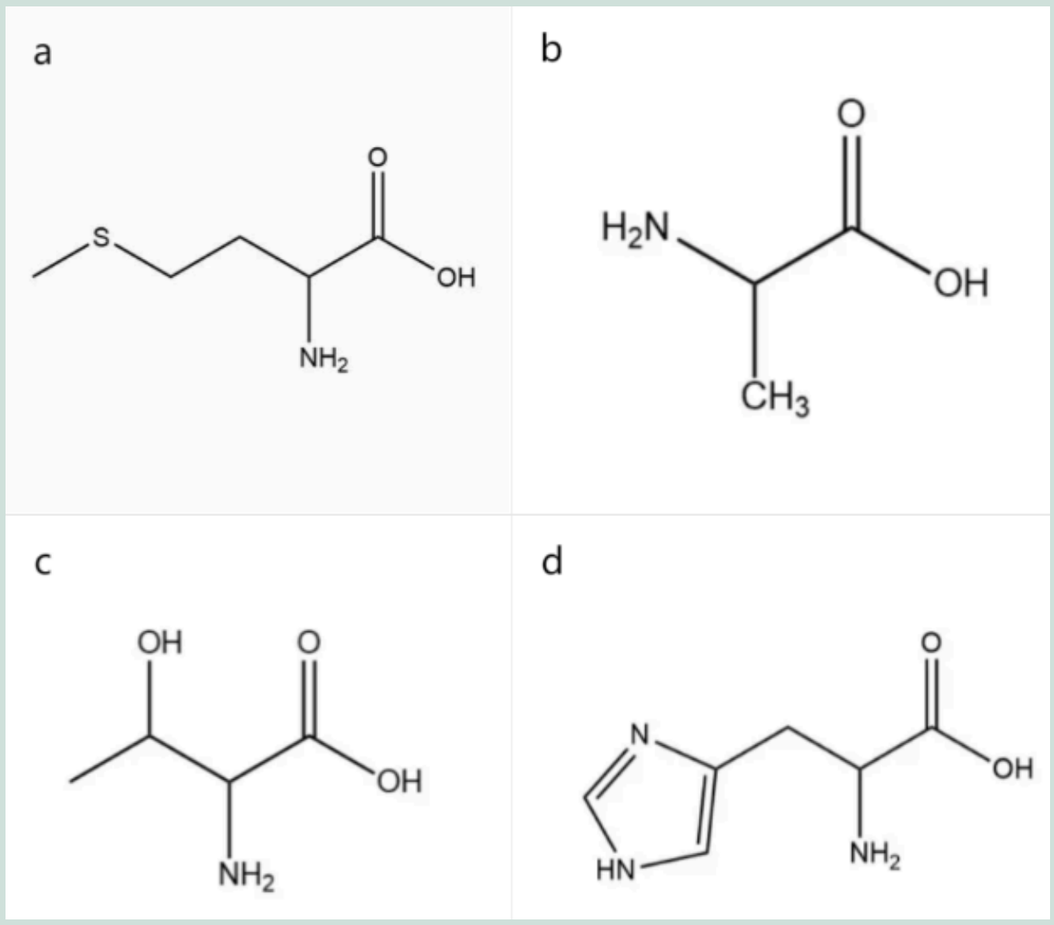

图3
部分氨基酸结构简式（a：甲硫氨酸；b：丙氨酸；c：苏氨酸；d：组氨酸）

植物蛋白和动物蛋白富含的氨基酸不同，植物蛋白中丰富的苏氨酸和组氨酸已经被证明能降低血压，保护肾脏。此外，植物蛋白能影响胆固醇代谢，减少氧化低密度脂蛋白胆固醇和尿酸水平，对肾功能受损患者十分有益。因此对于肾功能受损的患者而言，摄入更高比例的植物蛋白对肾脏有益。

总而言之，推荐糖尿病患者适当摄入更多的蛋白质，其中多吃植物蛋白制品更有利于肾脏健康。

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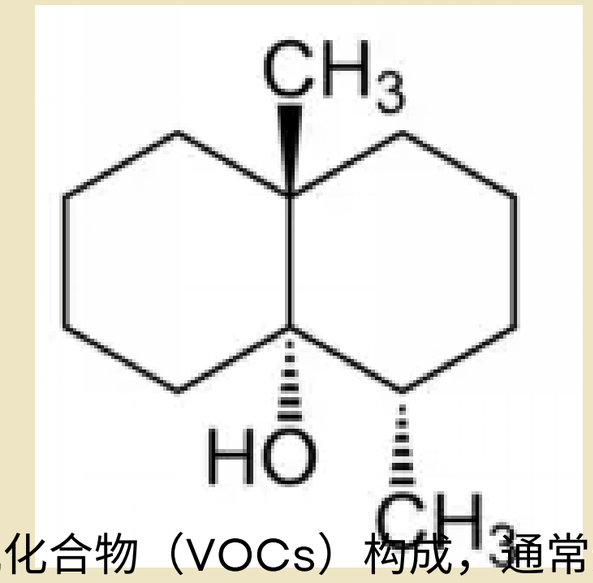
SMART MAGAZINE AUTHOR:xxx TRANSLATOR: xxx EDITOR: xxx

雨后泥土的清香？其实是土壤菌类的“气味陷阱”

关键词:植物学；微生物学；土壤菌类；跳虫

简介：

炎炎夏日，几场大雨无疑是上天最好的恩赐。大雨过后，走在路上，我们发现树叶更绿了，花更鲜艳了，连空气中都弥漫着泥土的清香。不过这“泥土的清香”到底从何而来呢？其实这是土壤菌类布下的“气味陷阱”，今天我们就一起揭开清香气味后的秘密吧！



1 土壤菌类排放的挥发性物质

土壤中含有大量放线菌、粘细菌、蓝细菌和以及丝状真菌散发的具有挥发性有机化合物（VOCs）构成，通常这类化合物包含土臭素（Geosmin）和 2-甲基异茨醇（2-MIB）。[1]内容有点少，可以考虑一下增加一些后续段落的内容移植到这个段落或者将其合并到其他段落

2 “泥土清香”从何而来?

关于雨后泥土香气的探寻最早可以追溯到1881年，Berthelot 和 Andre 发现“泥土的清香”可以通过蒸馏的方式提取出来。而后，部分科学家发现培养基中的粘细菌也会产生类似的气味，于是推测这种气味与土壤中的菌类有关。

直至1964 年，澳大利亚研究者 I. J. BEAR 和 R. G. THOMAS 对该气味作出了解释，并将该气味命名为“潮土油（petrichor)”。学者指出，这种气味来源于存在于土壤中的一种特殊物质--土臭素（Geosmin)。当雨水落到土壤中时，会把这种气体包裹住，形成许多小气泡。当雨停后雨水蒸发时，这些气味就随水蒸气一起释放到空气中，我们就会闻到泥土的清香了。

值得一提的是，约翰英纳斯研究中心（John Innes Centre）的分子微生物学主任 Mark Buttner 教授曾向 BBC 记者表示：“人们闻到的潮湿土壤味实际上那是某种细菌产生的分子。这种分子名为土臭素，由链霉菌产生。大多数健康的土壤中都存在链霉菌，它们也被用于制造抗生素。撞击地面的水滴使土臭素释放到空气中，阵雨之后的土臭素浓度远高于下雨之前。很多动物对它都很敏感，尤其是人类。”人类为什么对他感到敏感?

如果可以查到相关资料的话，可以适当添加一些以及敏感的原因

“气味陷阱”又是什么?

实际上，土臭素的味道不仅存在于土壤中，在日常生活中也十分常见。只不过当这些气味存在于饮用水或食物中时，你感受到的就会是“水嗅味”或者是“馊味”了。也就是这些水或食物已经被微生物感染了。[2]

本次研究发现，土壤菌类挥发的这种气味不仅能被人类感知，还可以吸引一些小型动物，其中就包括跳虫（Collembola)。这是一种小型节肢动物，喜欢潮湿的环境，以土壤中的放线菌、粘细菌等真菌为食。所以土臭素的味道对于跳虫来说无疑是“开饭啦！”的信号。可以说说跳虫对合成土臭素的中间素的生理反应是什么吗 以及这些信号如果有表现，他大概表现出来的是什么呢

图 3. 跳虫的形态外观

不过，既然土壤菌类是跳虫的食物，那“陷阱”这一说法又从何而来呢?

为了进一步研究，学者们在实验中分析了土壤中的一种放线菌--天蓝色链霉菌（Streptomyces coelicolor)。链霉菌属于革兰氏阳性细菌的一种，当它准备繁殖时会产生孢子，这些孢子可以传播新生的细菌。这种链霉菌产生孢子的过程中的代谢产物就是土臭素和2-甲基异莰醇，这种味道吸引着跳虫的同时，又成功让跳虫帮忙传播了孢子。

由此，我们就不难理解“气味陷阱”这一形容啦！土壤菌类用香气布下一个陷阱，其实为的是利用跳虫帮助自己传播孢子。

值得一提的是，研究人员观察了跳虫对挥发性气味的反应发现，跳虫不仅能被土臭素吸引，且合成土臭素的中间产物 germacradienol 以及副产物大根香叶烯-D 也能诱导跳虫的触角产生电生理反应。[3]

4 跳虫与土壤菌类的互利关系

有了上文的介绍，相信你也意识到了，跳虫与土壤菌类之间并不是单向的利益驱动，而是一种特殊的互利关系，那么我们就来看看这种互利关系是如何表现的吧!

4.1 链霉菌是跳虫的食物

链霉菌会产生一些有害的代谢产物，不利于无脊椎动物食用。但对跳虫而言，链霉菌是其唯一的食物来源，这主要归功于跳虫基因组中含有的多个解毒机制相关的基因簇。另外，链霉菌能够产生多种抗生素，帮助跳虫杀死体内的病原体。所以，链霉菌宿命般地成为了跳虫的食物。

4.2 跳虫帮助链霉菌传播

虽然链霉菌是跳虫的食物，但跳虫同样对链霉菌的传播有很大的帮助。跳虫能够帮助真菌孢子的扩散，帮助链霉菌完成生命周期。

跳虫帮助孢子传播的方式主要有两种：

1.体表粘附

研究指出，跳虫体表覆盖了一层疏水的蜡质层，具有一定的抗粘性，大部分真菌无法吸附在跳虫的体表，不过孢子却是可以的。研究数据显示，在接触链霉菌的跳虫体表上，存在 1 万~10 万个链霉菌孢子，主要吸附于跳虫的刚毛上。

2.通过排泄物传播

研究发现，在跳虫排泄物中，有 70.8% 的跳虫粪便颗粒含有活的链霉菌孢子。这一发现证实了孢子能够在跳虫的肠道中存活并通过排泄再次进行传播。[3]

5 雨后清香的其它可能

实际上，在雨后我们闻到的除了泥土的气息，同样还混杂着许多其它的清新气味。就比如雨后植物挥发的精油产生的气味，或者空气中的氧气分子被电离成正氧离子和负氧离子，也会让我们感觉空气更加清新。

所以，在下一场雨后，请走出家门，大口地呼吸新鲜空气吧!

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SMART MAGAZINE AUTHOR: Dora

有关动物实验中的伦理问题浅析

实验动物是医学实验中不可或缺的一部分，但是有关于实验动物的伦理与福利问题一直是社会争论的焦点。

补充：实验动物是指经过人类长期驯化，按科学要求定向培育，对其携带的微生物实行控制，遗传背景明确或者来源清楚的生物。，用于教学、生产、检验及科学研究的动物，被称为“活的试剂”

对于实验动物来说，牺牲与奉献似乎已经成为它们的天职，那么我们是否不是因此就可以无视实验动物的生命属性，而按照人类的意愿任意使用和处置它们？如果不可以，在具体的使用过程中，实施者的边界又在哪里？随着实验动物使用数量和使用领域的增加增多，在审查世界范围内，这些命题显然已不只受到科学科研界的关注，而是引起了社会各界更广泛的讨论和争议。

在西方国家，关于动物保护主义的萌芽最早可以追溯到古希腊和古罗马时期哲学家关于非人类存在的法律思考。然而，随着基督教的兴起，人类中心主义思潮开始占据主导地位，动物被视为由上帝创造并受人类支配的从属品物品。直到文艺复兴时期以及思想启蒙时期，仁慈主义慢慢成为了主流思潮。 强调对动物的关爱和同情，这一时期，人们对动物福利的关注逐渐增加，并开始呼吁保护动物的权益限制对动物的残忍行为。

最近几年，动物实验占所有科学实验中的比例越来越大，据估算，仅 2015年一年全球用于科学研究的实验动物数量高达 1.921亿只；2021年，全球实验动物市场规模约达200亿美元，仅2017-2018年间，美国实验动物的使用量可能高达10亿只。近几年我国实验动物需求量
逐年持续攀升，在2015年，我国实验动物年使用量为1159.54万只。

一些由动物实验引发的伦理伦理问题引发的争议也愈加受到关注越来越多。例如：2011年，来自麻省理工学院、哈佛医学院和Broad研究所的研究人员在《Nature》杂志发表了一篇题为《Selective killing of cancer cells by a small molecule targeting the stress response to ROS》的研究论文，该论文报告一种小分子的荜茇酰胺（piperlongumine） 可以选择性杀死小鼠体内的癌细胞。2015 年9月，《Nature》发表勘误表，以该研究中部分小鼠体内的肿瘤体积超出允许的最大直径1.5 cm为由，撤销了论文中的部分数据。最后处理方式为：论文作者向公众道歉，《Nature》杂志社要求以后涉及动物实验的论文需作者列出动物使用委员会所允许的最大肿瘤尺寸，并声明这一尺寸不会在试验期间被超过。

中国在实验动物的伦理福利方面虽然相较于欧美国家起步较晚，但在很多相关立法上已经有所进展是相对来说发展较快，不过目前还存在以下问题：

1. 从业人员对实验动物福利伦理的内涵及其意义认识不足，意识不强。
　　现实工作中发现很多医学科研人员对实验动物福利伦理的认知仍然都相对比较肤浅，只是泛泛认为实验动物福利伦理就是为对实验动物提供较好的照料，但具体怎么做似乎仍为未可知，甚至有些人员粗浅地认为实验动物福利伦理审查只是表面形式，没有实际价值。

1. 实验动物福利伦理委员会的建设尚待加强和完善

在实际工作中，很多机构对实验动物福利伦理的认知认识仍然不足，重视程度不够，伦理委员会委员亦缺乏相应专业知识培训。，甚至有些伦理委员会的委员对于实验动物伦理问题漠不关心，因此对实验动物的伦理与福利讨论问题进展较慢，没有达到预期目标。科学研究过程中，难以预料的问题层出不穷，是否能遵循实验动物福利原则大都要依赖使用者的职业素养和职业道德，所以如何在进行过程中管理和项目、终结管理到位是我们应该考虑的一个重要环节，这也是避免动物福利流于形式，实现动物福利的关键所在。

2. 实验动物科研平台软硬件建设不足，不能满足需求。

实验动物的饲养和繁殖要求有相应的环境和设施及专用饲料和垫料，实验动物平台建设的规模和质量将直接影响着实验动物相关科研项目的进展、进度。、质量和实验动物福利实现的程度。但实验动物平台建设相对于当今医学科研发展的需求，存在着滞后性和地区不平衡性。这些无一不影响和制约着实验动物福利伦理的实现、科研质量的提高及科研成果的转化。

综上所述，为保障实验动物的伦理福利，以下方面值得被改进：

（1）保证动物生理需要，使动物免受饥渴之困，提供保持动物生长发育所需要的营养等；
（2）保护动物心理需要，使动物免除恐惧和压迫，避免遭受精神痛苦；
（3）提供环境条件保障，包括适当的房舍或安逸的栖息场所，让动物能够躲避极端天气
等自然危害；
（4）提供卫生健康条件，预防和减少动物伤、病与疼痛，使患病动物能够得到及时的治疗；
（5）保障动物天性表达，通过提供足够的活动空间和条件，满足群体互动等正常动物行为需求。

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SMART MAGAZINE AUTHOR: Nox

沉默的高压社会-- 小胶质细胞介导的社交障碍

关键词：小胶质细胞；小胶质I型干扰素；突触丧失；社交障碍

引入：

在各种反乌托邦及现实主义影视作品中，我们常常能通过镜头感觉到人与人之间的疏离、无助以及社会整体的麻木--写字楼中面无表情的员工、贫民窟中眼神失焦的孩童、流水线中失去思考的工人.....

在科学技术迅速崛起的今天，人的异化愈发严重，冷漠和疏离仿佛成为了时代的通病。在这个高压锅般的社会中，慢性压力导致的抑郁症、精神分裂症等精神疾病与沉默疏离的社会现状如影相随，其中社交障碍正是这些疾病的核心病症之一。这种症状此前已被证明与大脑前额叶皮层（prefrontal cortex, PFC）的突触功能障碍和树突棘的丢失有关[1]。今年8月份，一项由美国德克萨斯大学休斯顿健康科学中心Anilkumar Pillai研究团队发表于Molecular Psychiatry期刊的研究指出，小胶质细胞中的I型干扰素受体（type I IFN receptor，IFNAR）在调节突触可塑性和与慢性应激条件相关的社会行为缺陷方面起着关键作用。[2]

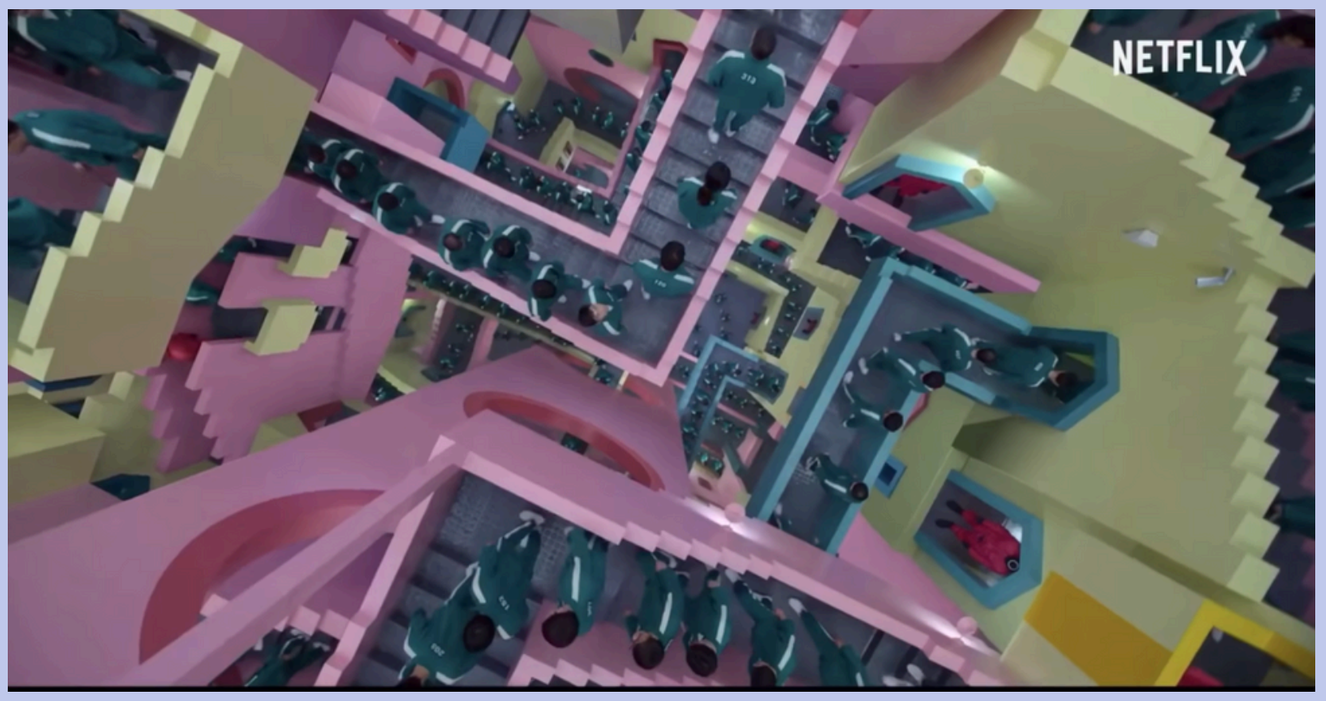


图1. 《鱿鱼游戏》剧照

图2. 三室测试（Three-chamber test）示意图

研究内容与结果:

慢性不可预测压力(Chronic unpredictable stress，CUS)是指反复出现、持续时间较长的压力事件，并且个体无法预测该事件何时会发生，这种不确定性加剧了焦虑和紧张感。

研究人员首先证明了CUS导致I型血清干扰素（IFNβ) 水平降低。随后通过动物行为测试，研究人员发现与无压力(no stressed, NS) 小鼠相比，在三室测试（Three-chamber test）和社交互动测试（Reciprocal social interaction test）中，CUS小鼠在的社交意愿更低。但通过Y迷宫测试（Y-maze test），并未发现两组小鼠在空间记忆能力上有明显差异。

三室测试（Three-chamber test）： 评估小鼠对陌生小鼠的社交偏好。实验装置分为三个相连的隔间，两个侧室和一个中间室。实验开始时，一只小鼠被放在中间室，两个侧室各放置一只陌生小鼠或一个空的隔间。通过观察实验小鼠在各个隔间停留的时间，可以评估它对社交互动的偏好。

社交互动测试（Reciprocal social interaction test）：评估小鼠与陌生小鼠之间的物理互动。将两只小鼠放在同一个环境中，通常是一个开放的测试盒。记录两只小鼠之间的接触、追逐、嗅探等互动行为，以及它们的反应时间和频率。

Y迷宫测试（Y-maze test）： 评估小鼠的空间工作记忆能力。小鼠被放置在其中一个臂中，允许小鼠自由探索迷宫，记录它进入不同臂的顺序和频率以评估小鼠的空间学习和记忆能力。

此后研究人员通过检测了一些促炎和抗炎细胞因子的mRNA水平，发现其在CUS小鼠PFC中有明显增加，这说明CUS促进了神经炎症。之后再通过骨架化分析，发现CUS小鼠与正常小鼠相比，PFC中突触密度明显降低。由于发现PFC中血清IFN β水平和小胶质细胞激活程度显著增加，研究人员接下来研究了小胶质细胞IFNAR在介导cus诱导的社会行为缺陷中的作用。在敲除了小胶质细胞的IFNAR后，慢性压力导致的小鼠社交障碍和突触丢失情况均有所减轻。

这项研究进一步阐明了小胶质细胞在介导慢性压力导致的社交障碍中的重要作用。研究结果表明，暴露在慢性不可预测压力(Chronic unpredictable stress，CUS)下小鼠PFC中的炎症因子表达量会大幅上升。其中炎症因子IFN会与小胶质细胞上的IFNAR结合，从而激活小胶质细胞中突触丧失相关基因的表达。而PFC中突触的丢失，则会进一步导致生物体的社交功能障碍。

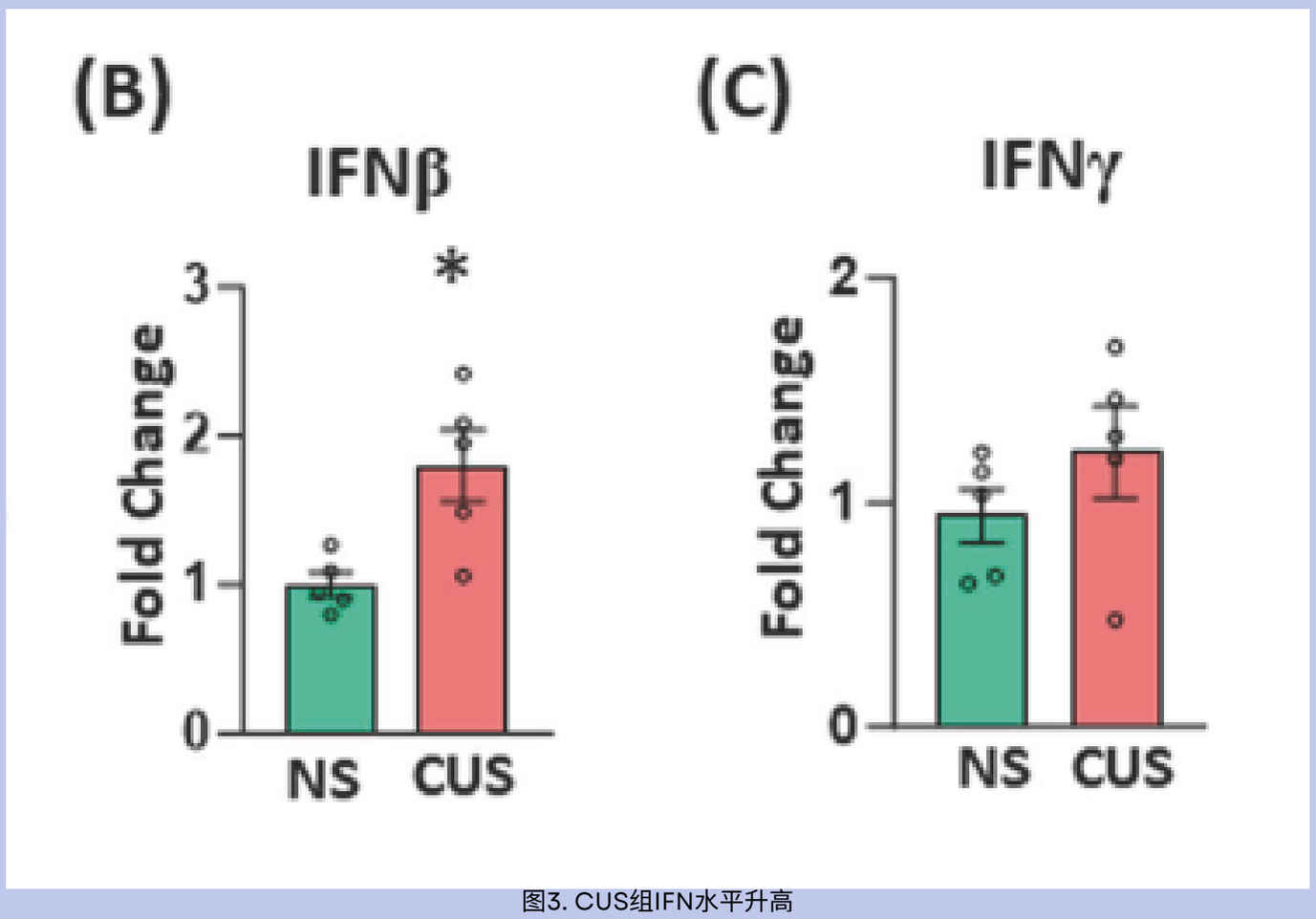


图3. CUS组IFN水平升高

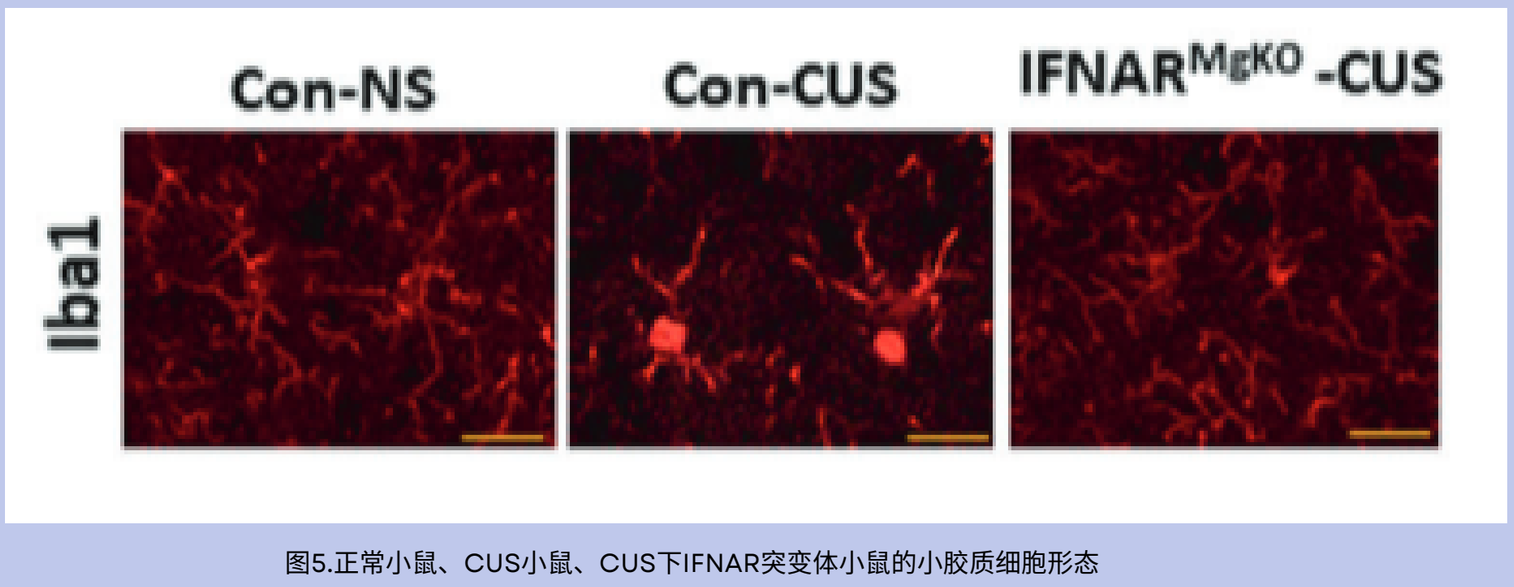
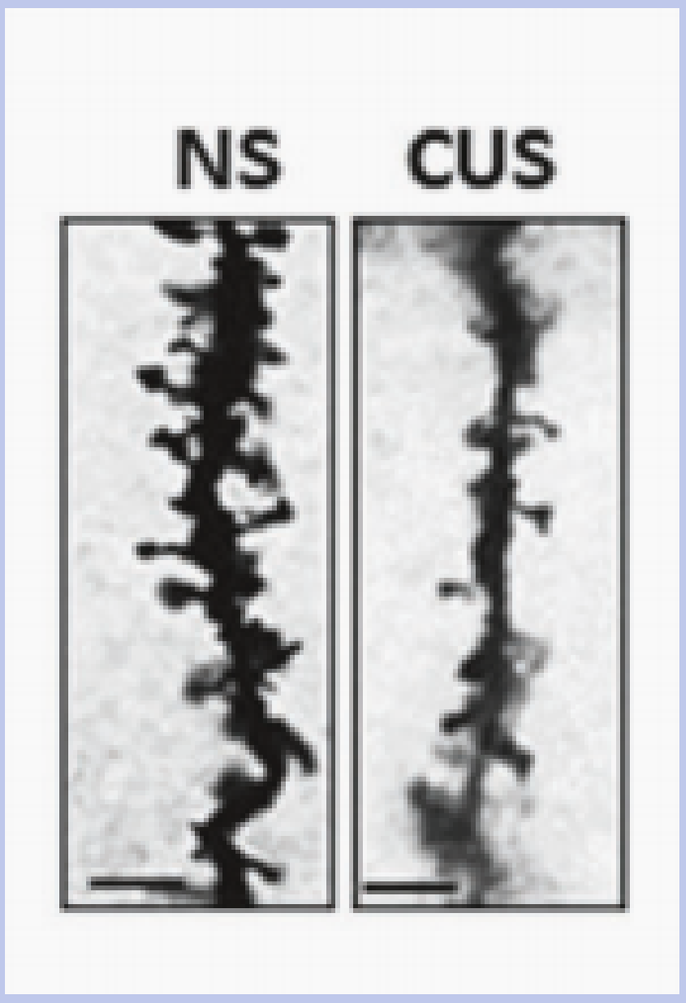


图5.正常小鼠、CUS小鼠、CUS下IFNAR突变体小鼠的小胶质细胞形态

研究意义

该研究发现慢性压力暴露会诱导小胶质细胞中IFNAR表达增加，并且小胶质细胞特异性IFNAR缺失的小鼠免受慢性应激诱导的突触密度和社会行为损伤。在此前使用IFN治疗已被证明会加重有抑郁史的多发性硬化症患者的抑郁症状[3]，而该研究进一步证明了IFN的神经毒性作用。不仅如此，此项研究还为治疗慢性压力相关的行为缺陷提供了以IFNAR为靶点的潜在治疗策略。

图4. CUS组突触减少



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颠覆认知！食盐居然可以帮助抗癌？！

关键词: 高盐饮食 过继性免疫疗法 CD8+ T细胞 谷氨酰胺代谢

研究简介：

近年陆续有研究发现氯化钠（食盐）在不同的背景下都能调节免疫，凸显了它在细胞激活、分化和效应功能方面的多方面免疫调节作用。这就不免让人好奇：氯化钠对抗癌有何影响？

最近，由意大利Enrico Lugli领衔的团队发现，氯化钠可以增强T细胞治疗在小鼠身上的抗癌效果。这一发现意味着，CAR-T和TCR-T等基于T细胞的细胞免疫疗法的疗效，有望通过简单的处理进一步增强，快速转化到临床应用中去。尤其值得一提的是，他们还在小鼠身上证实，仅通过高盐饮食就能增强T细胞的抗癌能力，抑制肿瘤的生长。

据了解，这也是科学家首次发现氯化钠可以增强人CD8+ T细胞的活化状态和效应功能，进而增强其肿瘤杀伤能力，因此可作为抗肿瘤免疫的正向调节因子。该研究揭示了氯化钠助力抗癌的潜在机制，有助于提升过继性免疫疗法的效率，让更多肿瘤患者从该疗法中受益。

实验过程及结果

研究人员先用高盐（80mM）处理CD8阳性幼稚T细胞，还用尿素和甘露醇处理另一组T细胞，模拟高盐带来的渗透压变化作为对照组。

与对照组相比，实验组颗粒酶B基因的表达显著增加，说明高盐诱导出了活化的效应记忆T细胞。RNA测序结果进一步显示，与对照组相比，高盐诱导了转录组水平的广泛变化，与效应或细胞毒性相关和与干性相关的转录本均上调。

他们还发现，诱导T细胞代谢重编程的主调节因子、编码质膜谷氨酰胺转运体以及与糖酵解相关的基因表达也上调。这说明，高盐还会重塑T细胞的代谢。

原本的作用和高盐导致的影响 重塑代谢有什么好处和变化

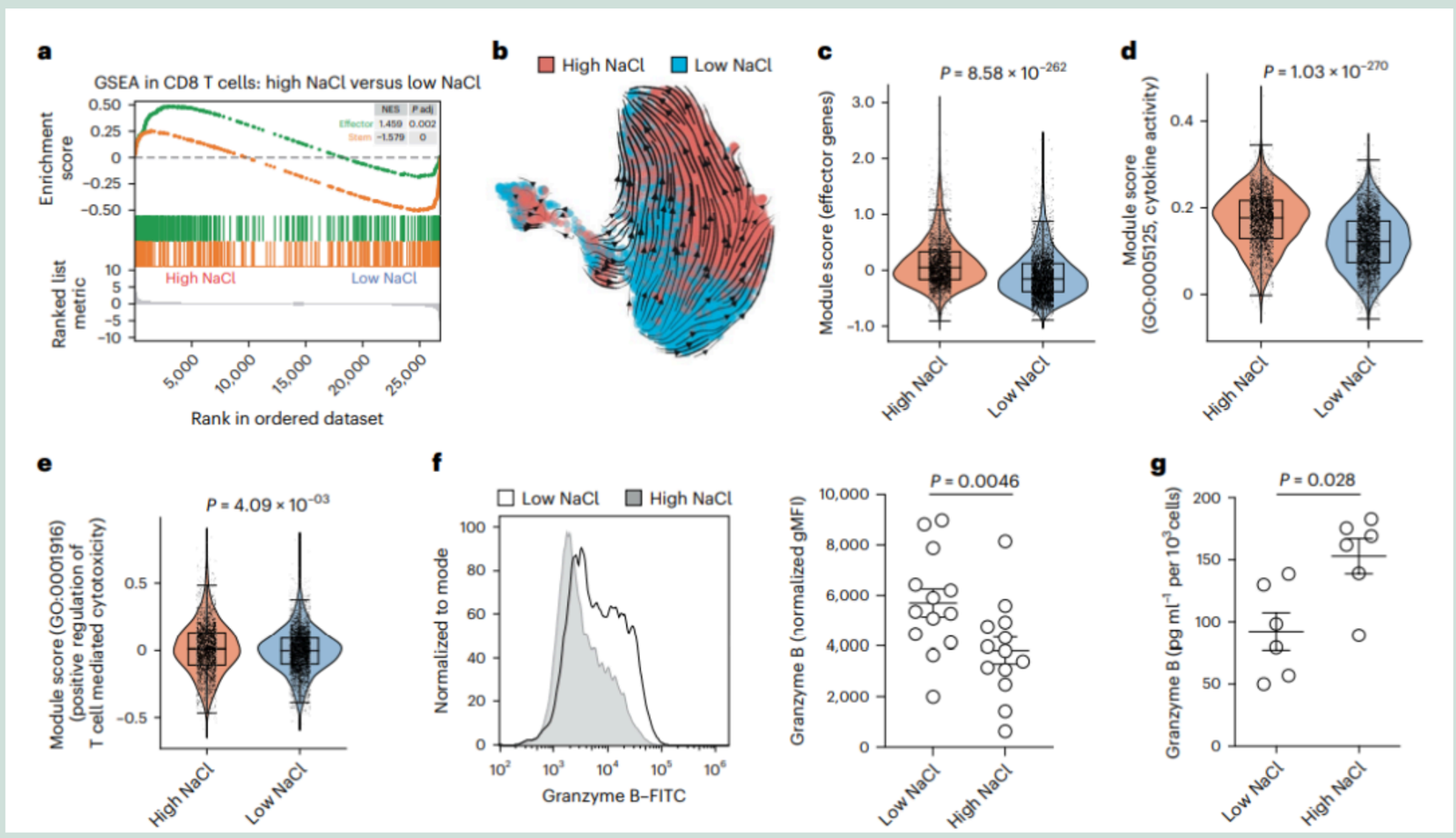

图1：氯化钠可以让T细胞活性更强

从细胞功能的变化来看，与对照组相比，高盐处理使干扰素-γ和脱颗粒标志物增加。体外细胞毒性试验结果显示，高盐处理过的T细胞杀死黑色素瘤细胞的效率更高。此外，他们还注意到T细胞受体（TCR）信号转导增强；且高盐要发挥作用，必须得结合TCR的激活刺激。

建议：在实验过程及结果一模块中可以解释一下T细胞

基于以上研究结果，他们认为高盐会促进人CD8阳性T细胞的效应分化。随后，他们大胆地将研究延伸至体内环境，探究高盐饮食对小鼠抗肿瘤免疫的影响

他们给小鼠安排了高盐饮食（食物含盐量为4%，水的含盐量为1%），让小鼠自由进食。在高盐饮食（HSD）开始两周之后，他们再给小鼠移植MC38结肠腺癌细胞，发现高盐饮食会导致氯化钠在肿瘤中蓄积抑制了肿瘤生长，而其他器官中蓄积较少，且不会影响小鼠的总体健康状况。

从抗肿瘤效果来看，与正常饮食（NSD）相比，高盐饮食能显著抑制肿瘤的生长。不过，在使用抗CD8单抗清除小鼠CD8阳性T细胞后，高盐的抗肿瘤效果就会完全消失。说明CD8阳性T细胞是高盐饮食表现出抗肿瘤作用的关键。

分析小鼠肿瘤中的免疫细胞变化后，科学家发现高盐饮食组的肿瘤中CD8阳性T细胞、自然杀伤细胞和CD4阳性T细胞的频率增加，是对照组的两倍有余。

具体到CD8阳性T细胞来说，与对照组相比，高盐饮食组中与终末分化和衰竭相关的转录本减少了，而编码细胞毒性分子的转录本或与活化和效应分化相关的转录本增加了。

不难看出，高盐饮食在促进免疫激活的同时还消除了免疫抑制。值得注意的是，他们还发现高盐饮食诱导的CD8+T细胞的转录谱发生积极变化，表现为终末分化和衰竭相关基因的下调和细胞毒性、活化及效应分化相关基因的上调，与PD-1抑制剂诱导的相似。高盐饮食增强了CD8+ T细胞的效应作用，抑制了T细胞的终末分化，也加速了CD8+ T细胞清除肿瘤的过程。

接下来，研究人员探索了高盐饮食重塑CD8阳性T细胞的机制。他们发现NaCl介导的重编程在很大程度上依赖于从微环境中摄取的谷氨酰胺的增加，简单来说，高盐饮食通过促进CD8阳性T细胞对谷氨酰胺的摄入，从表观遗传的层面实现对T细胞的重编程，增强T细胞的抗肿瘤活性。

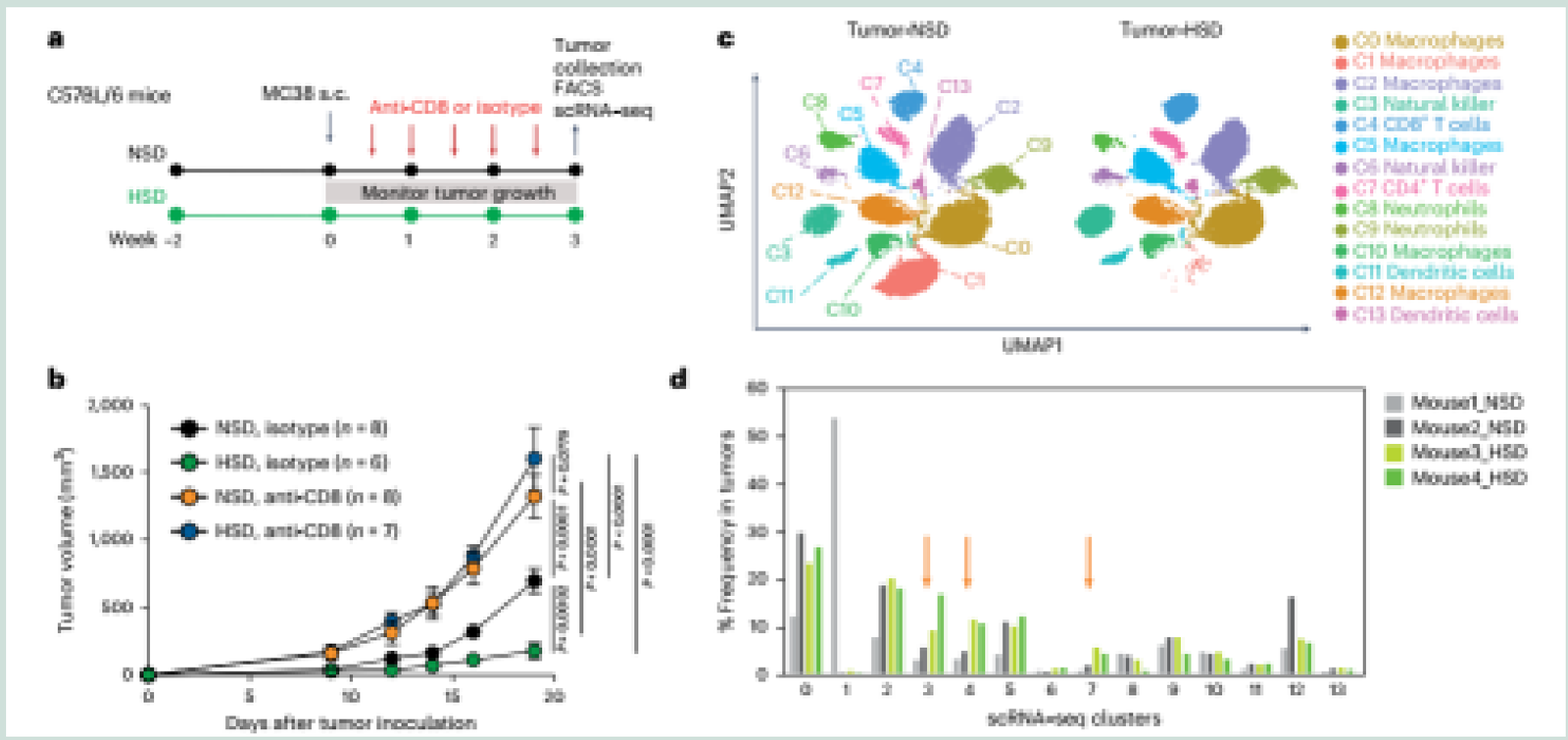

图2：体内实验的设计示意图（a）；喂食正常盐饮食（NSD）或高盐饮食（HSD）的雄性B6小鼠在接受抗CD8抗体或对照抗体处理后的MC38肿瘤平均体积（b）；喂食NSD或HSD的小鼠在肿瘤接种后第19天采集的单细胞RNA测序（scRNA-seq）数据（c）；小鼠中每一个簇的细胞频率条形图，箭头标出了在喂食高盐饮食的小鼠中发生变化的簇（d）

生物学机制

在CD8+ T细胞培养期间，NaCl补充剂诱导效应细胞分化、干扰素γ（IFN-γ）产生和细胞毒性，同时保持负责干细胞样可塑性的基因网络，因此，在人源化小鼠模型中，对采用特异性肿瘤T细胞移植产生了更优越的抗肿瘤免疫反应。在小鼠中，高盐饮食（HSD）以CD8+ T细胞依赖的方式抑制了终末分化，增强了CD8+ T细胞的效应能力，从而抑制了肿瘤生长。

从机制上来讲，NaCl增强了谷氨酰胺的消耗，这对于转录、表观遗传和功能重编程至关重要。简单来说，这是一个谷氨酰胺依赖过程。高盐处理CD8阳性T细胞之后，谷氨酰胺转运体的编码基因表达上调，促进CD8+T细胞对谷氨酰胺的摄入；谷氨酰胺的代谢产物会提高去甲基化酶的活性，提升CD8阳性T细胞特定基因位点的染色质可及性。

而在人类中，在肿瘤中进行抗原识别并预测对免疫检查点阻断疗法（ICB）有良好反应的CD8+ T细胞与由NaCl诱导的CD8+ T细胞相似。因此，NaCl代谢是CD8+ T细胞效应功能的调节剂，对癌症免疫疗法具有潜在影响

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前景展望

这一发现揭示了NaCl潜在的免疫保护作用，并为免疫反应的代谢重编程提供了新见解，这对免疫疗法具有深远影响。需要提醒大家的是， 虽然研究证明氯化钠可以增强抗肿瘤免疫，但是这一结论目前仍处于临床前探索阶段，仍需严谨的人体临床试验来验证其有效性与安全性。且高盐饮食是多种严重健康问题的主要诱因。因此，我们不能基于这两个研究得出高盐饮食能抗癌甚至是防癌的结论，更不能尝试实验提及的方法。

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个人认为太多的用于强调关键词和关键句的颜色和对小标题不充分的强调会让整篇文章看起来观感不太舒服，很乱，看起来有点难受。格式不太好，建议减少一些颜色，并对小标题进行下划线或者加粗的强调

高盐饮食在增强免疫的同时会造成的后果可以适当举例，且本文可以对一些专业名词进行解释

SMART MAGAZINE AUTHOR: Molly TRANSLATOR: Anaya

仅需“雕虫小技”即可药到病除

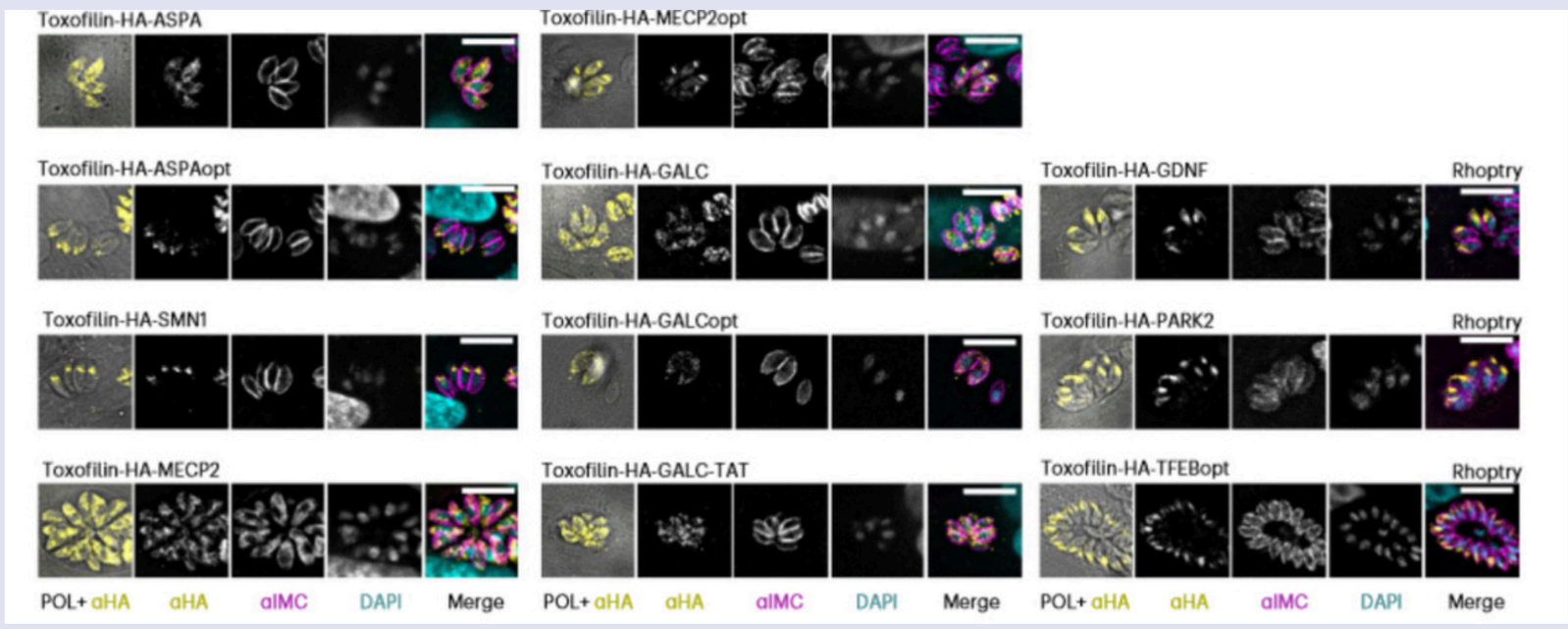
关键词:弓形虫，蛋白质药物，神经元，药物递送

简介:

通过血脑屏障等生物屏障递送大分子有一定的难度，限制了其在体内的应用。弓形虫(Toxoplasma gondii)是一种从人类肠道自然传播到中枢神经系统(central nervous system ， CNS)的寄生虫，可以将蛋白质递送到宿主细胞。在本研究中，我们利用弓形虫的内源性分泌系统- -棒状体和致密颗粒，通过与肌动蛋白结合蛋白和GRA16的翻译融合，将多个大的(> 100 k Da)治疗性蛋白递送到神经元中，并证明了药物递送的有效性。

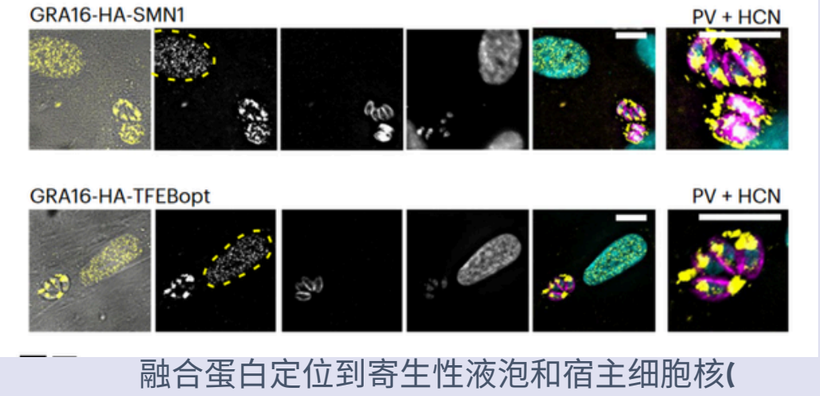
研究方法与设计

研究人员使用弓形虫作为蛋白质递送的载体。弓形虫几乎无处不在，他们能主动迁移到中枢神经系统中，通过与宿主协同进化、适应调整形成的复杂形式通过血脑屏障，随后基本上持续存在于中枢神经系统中。



在尝试了具有不同分子大小、功能和细胞内靶点位置的蛋白质后，研究人员观察到几种治疗性神经蛋白的高水平细胞内递送，随后运用肌动蛋白结合蛋白(TGME49 _ 214080)和GRA16 (TGME49_208830)分别作为弓形虫内两种能够递送效应蛋白的分泌系统——棒状体和致密颗粒的靶向蛋白，并选择已知功能的蛋白质药物进行融合。

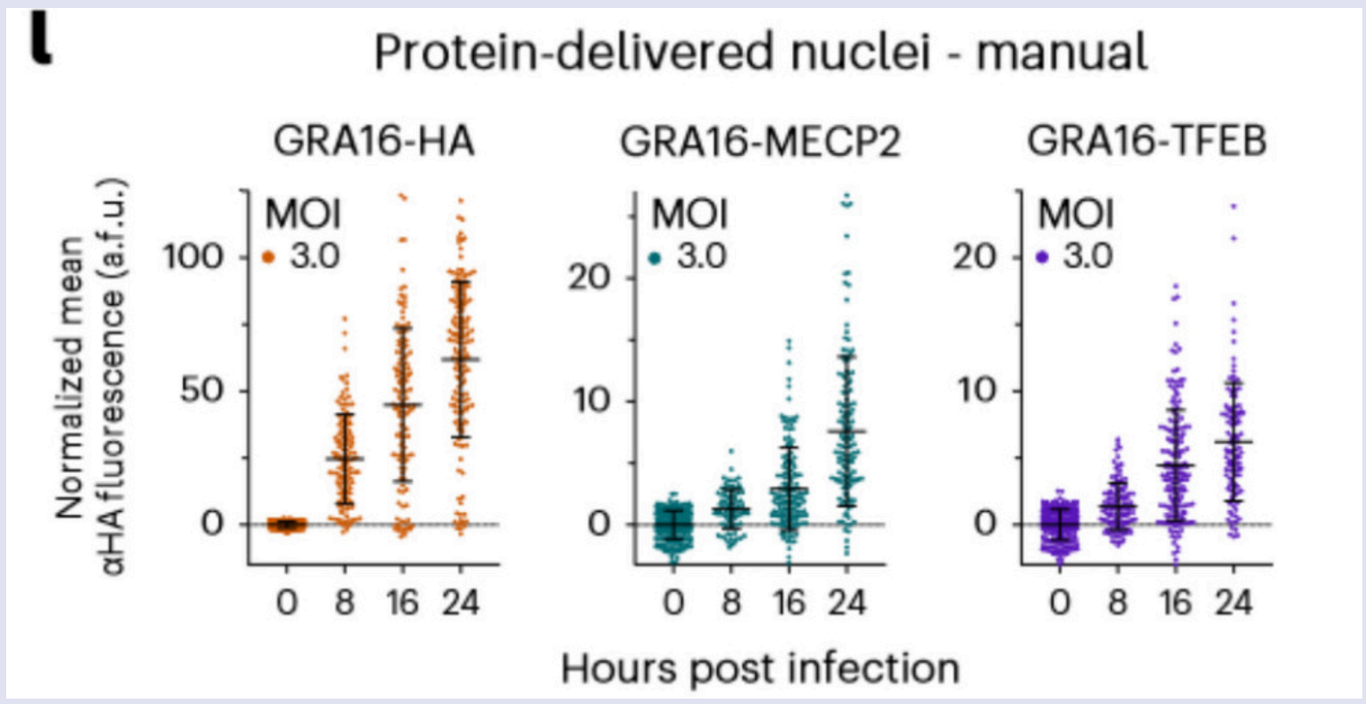
由于很难通过免疫染色探测靶向蛋白，研究人员选择使用易于检测的基因组编辑蛋白如锌指蛋白和Cas9进行测试。尽管他们均成功表达到棒状体，但是细胞中检测不到活性。这可能是分泌水平低、核酸酶活性低或基因诱导时间不足引起的，后续依然需要增加宿主细胞中融合蛋白的分泌或活性水平。



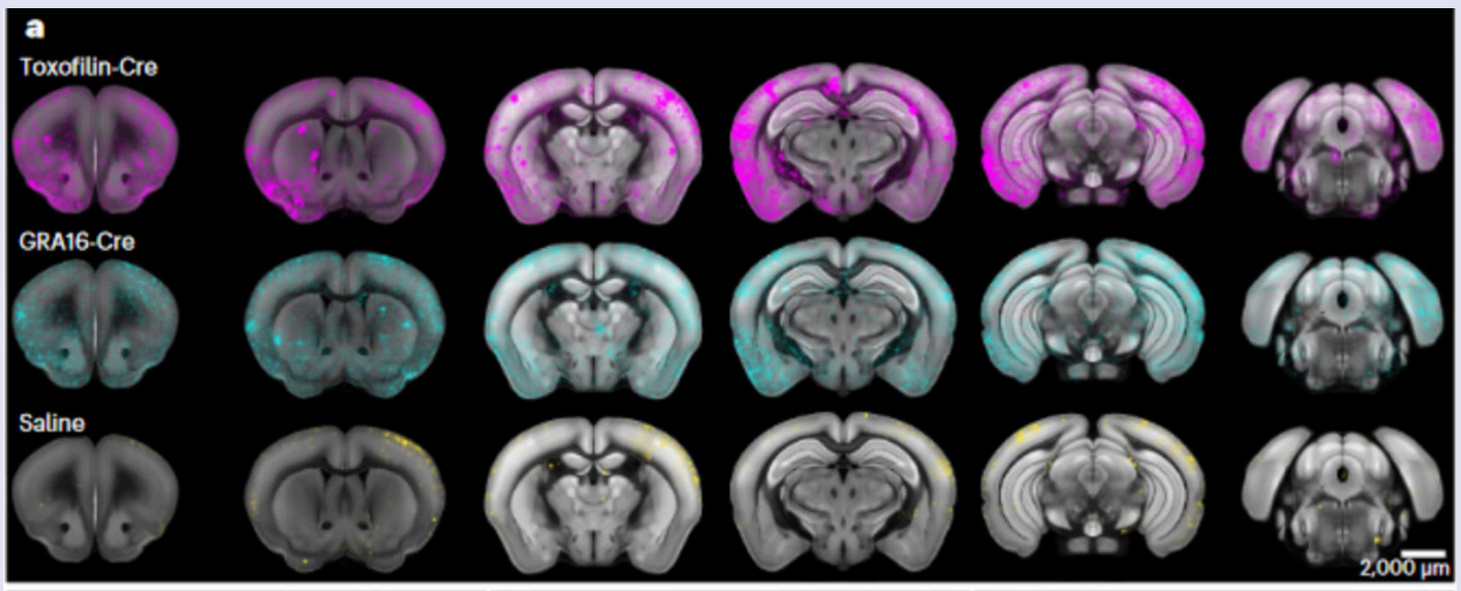
融合蛋白定位到寄生性液泡和宿主细胞核(MECP2opt、SMN1、TFEBopt)

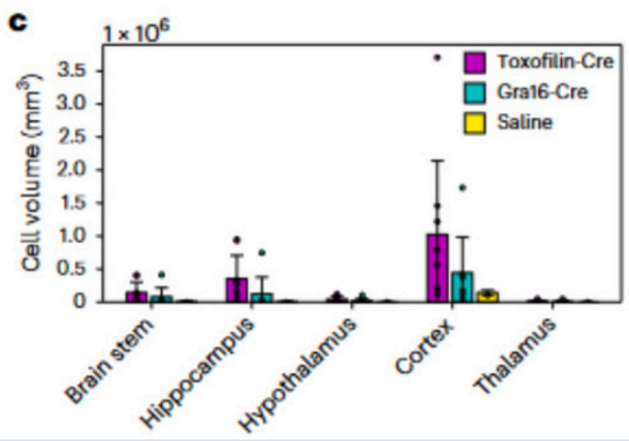
不同株系的弓形虫侵入、复制以及向宿主细胞核传递蛋白质的能力无显著差异

实验证明，弓形虫可以通过致密颗粒进行细胞内蛋白质的递送。为了将感兴趣的治疗性蛋白定向运输至致密颗粒，研究人员构建了GRA16与不同融合蛋白的融合表达载体，其中GRA16融合的核蛋白TFEB和Me CP2表现出最强大的递送和靶向能力。值得注意的是，它们是大小达到109kDa和110kDa的哺乳动物全长蛋白。小鼠大脑切片染色显示，弓形虫可以将MeCP2蛋白递送到脑中的神经元且弓形虫的分布和存活不受影响。 此外，研究还对比了表达不同蛋白质的弓形虫株系，发现这些不同株系的弓形虫在侵入、复制以及向宿主细胞核传递蛋白质的能力上并无显著差异。 尽管融合蛋白的传递效率与GRA16相似，但进入细胞后，这些融合蛋白的累积量却显著减少。



融合蛋白与单独**GRA16**蛋白在宿主细胞核内表达水平比较





研究人员通过三维成像发现**toxofilin-Cre**在传递效率上具有更显著的优势。对此，一种解释是**toxofilin-Cre**可能通过某种机制，能够更有效地穿透或进入神经元，而不需要像**GRA16-Cre**那样依赖于细胞内寄生液泡的形成。

结论：

这项研究表明，在培养的成纤维细胞、体外分化神经元、人脑类器官和小鼠体内，弓形虫都可以作为蛋白质递送系统，并受到不同条件下影响递送方式的因素的影响。棒状体系统通过瞬时开放质膜将蛋白质直接排出到宿主细胞中，避免细胞入侵或在这些细胞中持续存在。相反，致密颗粒分泌需要弓形虫与细胞共存，但可以提供更高水平的蛋白质分泌和更持久的递送。在样本中没有观察到递送效率与蛋白质大小的相关性，即蛋白质大小不是递送效率的限制因素。观察到，无论是颗粒细胞分泌的棒状蛋白还是致密颗粒分泌的蛋白，在皮层中的蛋白递送水平最高。

尽管弓形虫感染在大多数情况下都是无症状的，但是依然有可能引起一系列副作用，因此描述和提高基于弓形虫载体的安全性和有效性的进一步研究将是必要的。

引用

Bracha, S., Johnson, H. J., Pranckevicius, N. A., Catto, F., Economides, A. E., Litvinov, S., Hassi, K., Rigoli, M. T., Cheroni, C., Bonfanti, M., Valenti, A., Stucchi, S., Attreya, S., Ross, P. D., Walsh, D., Malachi, N., Livne, H., Eshel, R., Krupalnik, V., Levin, D., … Rechavi, O. (2024). Engineering Toxoplasma gondii secretion systems for intracellular delivery of multiple large therapeutic proteins to neurons. Nature microbiology, 9(8), 2051–2072. https://doi.org/10.1038/s41564-024-01750-6IF: 20.5 Q1

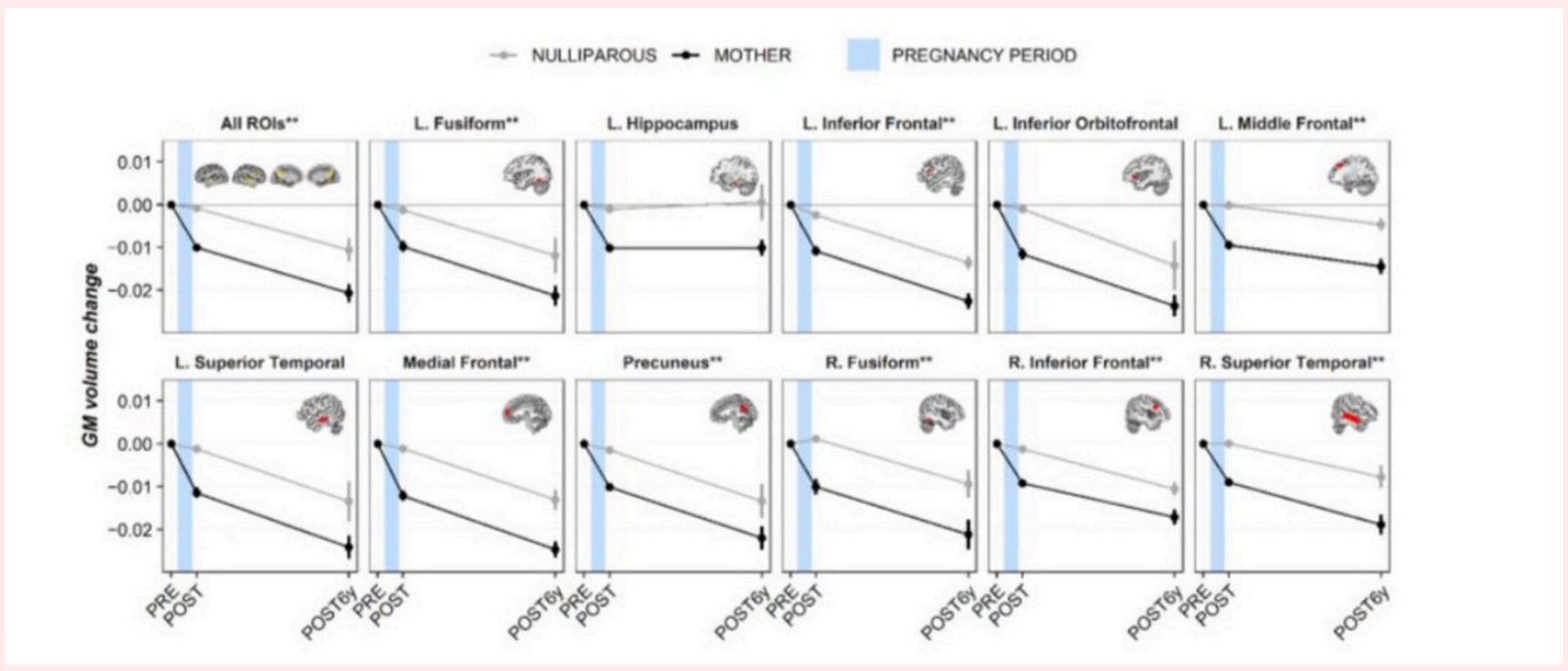
怀孕对大脑的重塑

关键词：妊娠；母体大脑；认知缺陷；灰质；生殖激素

简介:

由于生殖荷尔蒙的急剧增加和大脑的微妙重塑，怀孕常常意味着女性身体和心理状 态的巨大转变。比如，“孕期大脑”这一广泛的现象，通常用来形容怀孕期间的认知变化，如 健忘、注意力不集中和思维迟钝，这也恰好反映了怀孕对神经系统的潜在影响。此外，许多 女性还报告称，她们在怀孕和产后阶段的同理心和情感敏感度有所提升。这种变化被认为 是一种进化上的适应性机制，通过使大脑对关键刺激更为敏感，为人父母的角色做好准 备。然而，关于孕期和产后的神经科学研究仍然相对不足。直到最近十年，科学界才逐渐认 识到怀孕对大脑带来的改变。新的研究不仅观察到怀孕期间和产后大脑结构的长期变化， 还揭示了荷尔蒙波动对这些变化的深远影响。

1.对认知的影响

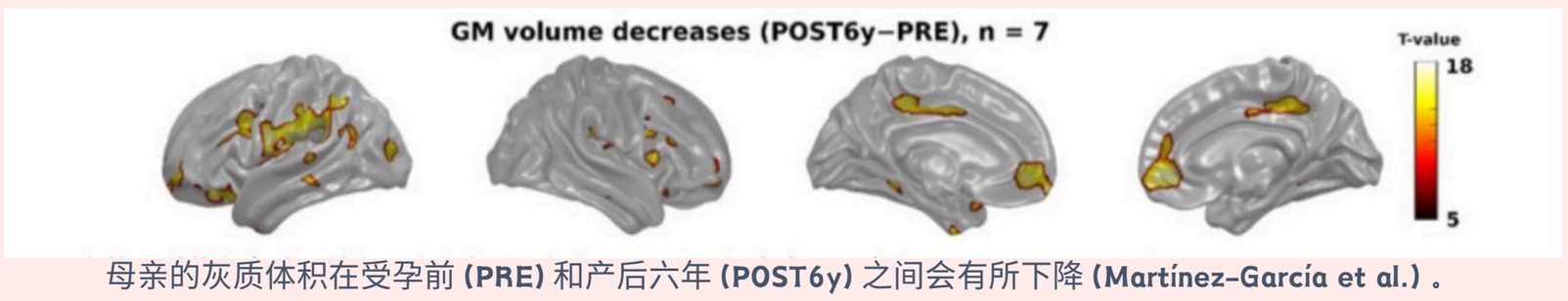


怀孕往往会催化记忆力、注意力和集中力、执行功能、情感和社会认知等方面的一系 列变化，其中最显著的表现之一是“孕期大脑”或“健忘症”。

尽管关于孕期是否会导致认知 能力下降的争论一直存在，但越来越多的研究证据表明这种现象是真实存在的。例如，在一 项涉及40名孕妇和40名非孕妇的前瞻性队列研究中，研究人员发现，非孕妇在多项认知任 务中的表现优于孕妇。这些任务包括口头配对联想(要求参与者聆听并记忆成对的单 词)、命名物体和手指(要求参与者命名日常物品和手指)，以及数字跨度测试(参与者需 要按照顺序或倒序复述一系列数字)。结果显示，孕妇在学习、记忆、语言能力和注意力方 面存在一定程度的缺陷，这与大脑中的特定区域相关，如外侧、内侧-前顶叶、枕叶区、前额 叶和左顶叶下部等脑区(Barda等人)。此外，研究还指出，这种认知功能的减退可能与怀孕 后期的荷尔蒙变化密切相关。

2. 灰质丢失

怀孕引发的其他认知变化，尤其是母性关爱和情感联系的增强，可以通过大脑结构 的变化得到解释。研究表明，怀孕会导致与社会认知、移情、奖赏处理和情绪调节相关的脑 区灰质体积显著减少。在2021年进行的一项纵向研究中，研究人员对25名初次怀孕的母亲 和20名从未怀孕的女性进行了长期跟踪调查，发现大多数怀孕引起的灰质萎缩在产后至少 六年依然存在。通过磁共振成像(MRI)扫描，研究人员能够以91.67%的准确率区分女性是 否怀孕。全脑分析进一步显示，研究中所有感兴趣区域的灰质体积均发生了变化，尤其是在 以下脑区：内侧前额叶皮层(负责社会认知、决策和移情)、楔前区(参与自我意识、社会处 理和视角转换)、海马区(与记忆和学习相关)、下眶额叶皮层(负责情绪调节、奖赏处理 和决策)以及上颞叶皮层(负责听觉处理和语言理解)(Martínez-García等人)。



每个相关区域的灰质体积变化(Martínez-García 等人)

母亲的灰质体积在受孕前(PRE)和产后六年(POST6y)之间会有所下降(Martínez-García et al.)。

值得注意的是，这些大脑变化与母性行为的强化密切相关。例如，灰质体积的显著减 少与更高的“互动中的愉悦”评分呈正相关，表明大脑的结构性变化有助于母亲在产后表现 出更强的情感连接和照顾行为。这些变化被认为是适应性的一部分，有助于促进母子关系 和提高母性功能。

3.突触修剪

然而，脑容量的减少并不是有害的，而是一种类似于青春期时发生的脑组织体积下 降现象，实际上代表了大脑回路的修剪和精简过程。在这一过程中，薄弱或多余的神经连接 会被消除，以优化神经功能，使大脑网络能够更有效地发挥其专业功能。具体来说，在怀孕 期间，这种突触修剪的过程起到了适应性功能，帮助优先整合和增强基本的认知能力，从而 使母亲能够在怀孕及产后更好地进行照顾、建立社会联系、提升养育技能和做出有效的决 策 (安德森与卢瑟福，2021) 。这种神经适应不仅是对母亲新角色的必要调整，也有助于建立母子之间的深厚情感纽带。

4.荷尔蒙的影响

荷尔蒙与人体的神经网络紧密相连，在妊娠期和分娩后的认知、情感和行为变化中 发挥着至关重要的作用。雌激素、孕酮、催产素、皮质醇和催乳素等荷尔蒙共同协调着大脑 结构和功能的重组，同时也是认知转变和情绪波动的基础，在怀孕期间，性类固醇激素，尤其是雌激素和孕酮，会急剧增加，并在怀孕的第三个 月达到高峰。雌激素是与妊娠相关的结构性神经可塑性的主要触发因素之一，并与大脑的 默认模式网络 (DMN) 相互作用。DMN 是指在进行自我参照思考、自传体记忆和社会认知 时活跃的大脑区域。例如，一项针对无子宫女性的长期跟踪研究表明，怀孕三个月时的雌二 醇 (雌激素的一种) 水平与神经可塑性密切相关，这种激素可以提高树突棘和突触的密度， 从而增强 DMN 的功能连通性和一致性。这种增强的连通性可能会导致母亲的身份和认知 重心从自身转移到孩子身上，进而提高母亲对婴儿提示的反应能力和理解力 (Hoekzema 等 人) 。

此外，压力荷尔蒙皮质醇在孕期的增加不仅支持胎儿发育，还调节免疫反应和新陈 代谢。然而，研究发现高皮质醇水平与健忘症状和认知缺陷有关，这可以解释孕期常见的 “脑雾”或“妊娠脑”现象。尽管皮质醇对胎儿发育至关重要，但它也可能增加孕妇对压力和 焦虑的敏感性，从而导致产前抑郁等情绪问题。因此，荷尔蒙的变化不仅影响母亲的认知 功能，也对她的情感健康产生深远影响。

结论:

妊娠在科学研究中长期以来常常被忽视，尤其是在关注妊娠引起的神经变化方面。 尽管技术进步使我们能够更精确地研究神经系统的动态，但对妊娠期间发生的神经变化的 认识仍然存在显著差距。许多研究主要集中在分娩后观察到的大脑变化，而较少探讨妊娠 期间的变化。此外，这些变化的长期影响也未得到充分研究。这种研究上的疏忽不仅限制了 我们对孕产妇大脑健康的理解，还可能对孕产妇保健实践的质量产生负面影响。因此，填补 这些知识空白不仅仅对学术界意义重大，更是提升产妇保健实践、改善孕产妇的身心健康 和为准妈妈创造更有利环境的关键。

引用

Anderson, M. V., & Rutherford, M. D. (2012). Cognitive reorganization during pregnancy and the postpartum period: an evolutionary perspective. Evolutionary psychology : an international journal of evolutionary approaches to psychology and behavior, 10(4), 659–687. https://doi.org/10.1177/147470491201000402 Barda, G., Mizrachi, Y., Borokchovich, I., Yair, L., Kertesz, D. P., & Dabby, R. (2021). The effect of pregnancy on maternal cognition. Scientific reports, 11(1), 12187. https://doi.org/10.1038/s41598-021-91504-9 Hoekzema, E., van Steenbergen, H., Straathof, M., et al. (2022). Mapping the effects of pregnancy on resting state brain activity, white matter microstructure, neural metabolite

喹喔啉衍生物及其生物医用

喹喔啉是一类缺电子芳环，且有多个取代位点，可用于荧光材料的设计。可通过引入一些电子给体，对喹喔啉母核进行修饰，来调控衍生物的光物理性质。近年来，喹喔啉在压致发光材料、供体-受体理论及荧光探针等领域展现了广泛的应用前景，尤其在生物医学和化学传感等高灵敏度检测技术中表现突出。然而，尽管喹喔啉类发光材料取得了一定进展，其在材料结构设计和响应机制上的研究仍不够深入，未来的研究需进一步探索其潜在应用及性能优化方向。

1.1 压致发光

压致变色(MCL)材料指的是一种灵敏的荧光材料，它的荧光颜色在外界刺激下比如机械应力(例如研磨、压制、粉碎、划痕和剪切)、热处理和溶剂蒸气，会呈现出可逆变化[1-2]。研究发现，用作检测等用途的材料发射光谱比吸收光谱受干扰更少时，灵敏度更高。由于MCL材料对外界刺激的响应特性，其在发光器件、荧光开关、机械力传感、数据存储、安全油墨等多方面具有潜在的应用价值[2]。大多数报道认为，在外界刺激下分子构象、堆积和分子间相互作用发生了变化是影响MCL性能的关键因素。

1.2 供-受体（D-A）理论

在MCL材料的设计中，供-受体（D-A）理论也常被用于调控材料的光学性质。D-A 理论是基于供体和受体单元之间的相互作用提出的，为进行分子结构的设计和能带的调控奠定了基础。喹喔啉作为一种典型的电子受体分子，具有高度共轭的π电子体系和优异的电子受容性，因此常被用作D-A系统中的受体单元。根据D-A理论，通过改变电子给体和受体，可以调控材料的能隙、结构特征，在有机光电材料领域有着广泛的应用[3-6]。

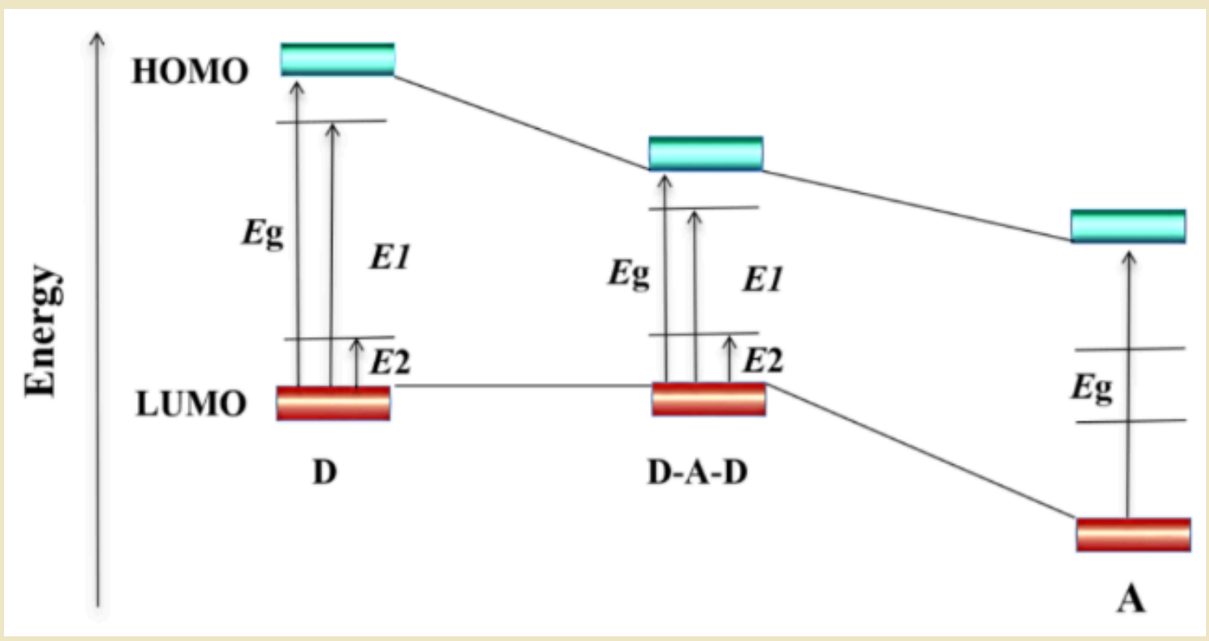


图 1.1 供体-受体（D-A）理论

1.3 荧光探针

荧光探针技术是利用特定物质的光物理和光化学特性，在分子量级上对研究对象进行定性及定量研究的一种方法[7]。该方法具有高度的灵敏性和较宽的动态响应范围，在一些检测和标记中应用广泛。比如，生物体内存在的各种离子、氨基酸和生物酶，对保持生物有机体的生理平衡和协调生物体生理活动的过程中具有不可替代的作用。目前，科研人员已经开发了不同类型的荧光探针用于研究生物体内的生理过程[8]。荧光化学传感器在分子生物学和临床诊断等领域具有重要的应用价值，近些年发展迅速[9]。

1.4 喹喔啉类发光材料的研究进展

喹喔啉别名苯并吡嗪，具有缺电子以及刚性平面结构，可用于荧光材料的设计[10-18]。喹喔啉有多个取代位置，可被引入一些电子给体基团修饰母核，得到性能良好的荧光材料[4-6]。近年来，也有科研工作者发现其对于特定的金属离子有强响应效果，可用来制作荧光探针或者化学传感器[19]。

2016年，Chen等人[19]设计并合成了一系列具有不同取代基的对称交叉共轭有机发光材料。系统地研究了它们的分子内电荷转移(ICT)、压电变色(PFC)和传感特性。结果表明，具有相同共轭主链的发光材料表现出不同的ICT相互作用。Lippert Mataga分析表明，无取代基的材料1（如图1.2所示）基态和激发态之间的偶极矩差最大。此外，由于晶态和非晶态之间的相变，目标材料具有可逆的PFC特性。以吡啶为取代基的材料2（如图1.2所示）具有最显著的压电荧光色。在研磨原始样品时，可以观察到40 nm的变色位移。此外，材料1和2对Fe3+具有选择性和敏感性。此外，材料2还可以作为银离子的比色和荧光化学传感器。2018年， Yu等人[4]为了解决对于基于热激活延迟荧光(TADF)发射体的有机发光器件(OLED)来说，同时实现高效率和低效率滚降的难题，通过在喹喔啉骨架中引入9，9-二甲基-9，10-二氢吖啶(DMAC)或10H-吩噁嗪(PXZ)作为供体单元，精心设计并合成了一系列具有TADF和聚集诱导发射(AIE)特性的新型发射体（3、4、5和6，如图1.2所示）。他们发现，通过调节供体的给电子能力和供体单元的数量，可以系统地调节TADF-AIE发射体的光物理性质，使发射范围从绿色到红色。

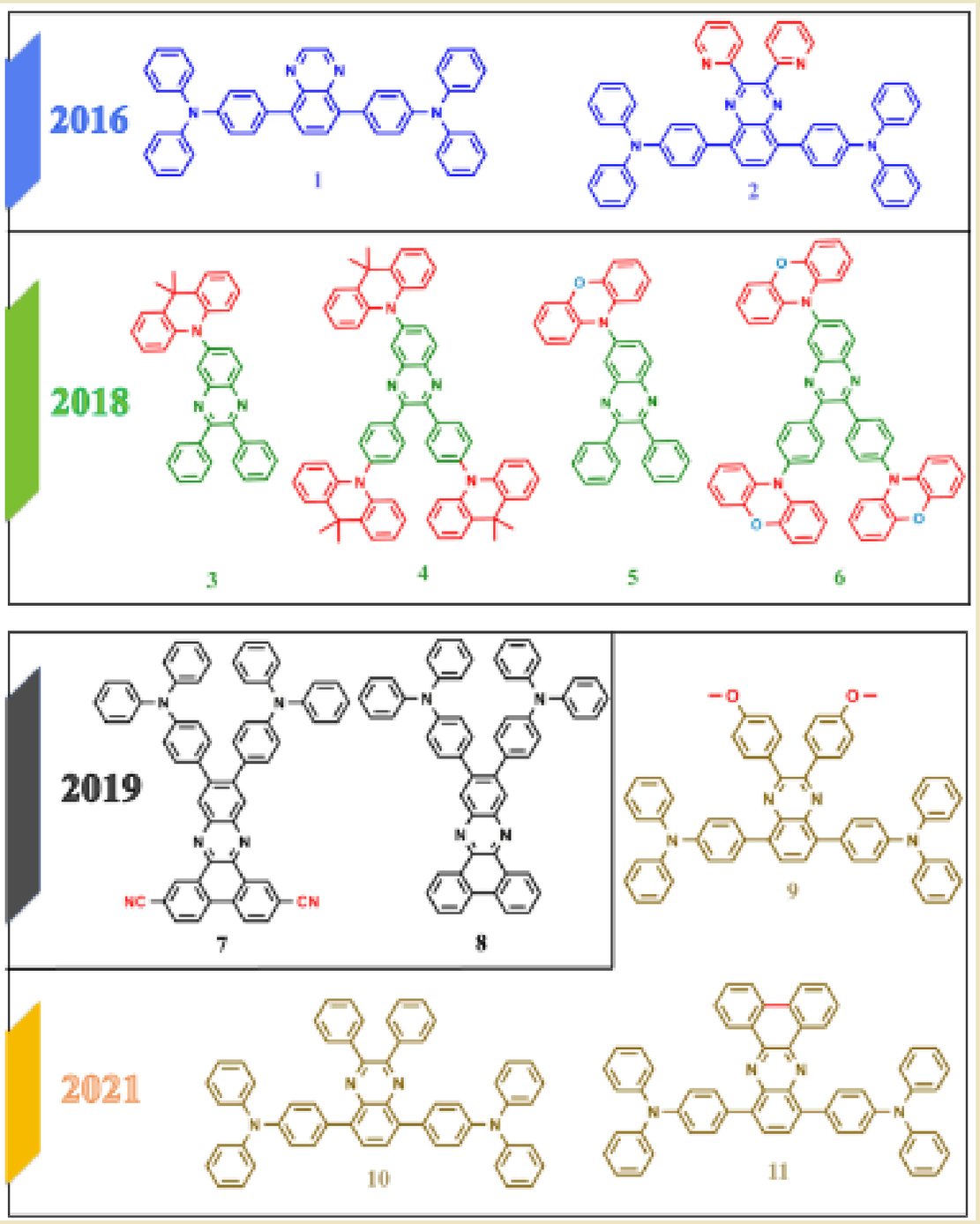


图 1.2 近几年喹喔啉衍生物

2019年，Wang等人[5]设计并合成了两种荧光发射很强的材料（7和8，如图1.2所示），其中两个相邻的三苯胺（TPA）基团用作给电子单元，一个二苯并[a，c]吩嗪基团用作吸电子基团。在7中，通过引入两个氰基连接到二苯并[a，c]吩嗪单元以增强吸电子能力。结果表明，在7的UV-vis吸收和光致发光光谱中观察到相对于8明显红移。此外，将氰基引入7导致前沿分子轨道（FMOs）的显着分离，导致小的单重态-三重态分裂能（ΔEST）和强的分子内电荷转移（ICT）状态。值得注意的是，7具有比8更高的光致发光量子产率（PLQYs）和更好的器件性能。基于7的掺杂比为10 wt%的有机发光二极管（OLED）实现了24.97 %的最大外部量子（EQE）效率。

2021年，Fu等人[6]合成了三种由三苯胺（TPA）和取代的喹喔啉部分组成的新型供体-受体-供体（D-A-D）型分子（9，10和11，如图1.2所示），并进一步用于电致变色器件。在π-共轭主链上具有两个扭曲取代基的衍生物9和10表现出有效的电致变色性质，包括高达70 %的高光学对比度，短响应时间小于3 s，高着色效率超过200 cm2 C-1，并具有良好的循环稳定性。然而，采用具有高共面性的熔融电子受体单元的衍生物11则表现出差的电致变色性能和低稳定性。

1.5 喹喔啉类发光材料在生物医药中的应用

喹喔啉类发光材料凭借其独特的结构和光电特性，在生物医药领域展现出了广泛的应用潜力。这类材料中的某些化合物具有聚集诱导发光（AIE）特性，能够在聚集状态下显著增强荧光，从而避免传统荧光染料因聚集导致的荧光猝灭问题。这一特性使得喹喔啉类发光材料在生物医学成像中表现出色，能够实现对细胞、组织和活体的高效检测与诊断，如基于喹喔啉酮骨架的荧光分子已成功应用于体内外细胞铁死亡过程的特异性检测。

此外，喹喔啉类化合物还被广泛研究并应用于抗癌、抗微生物和抗病毒药物的开发中，通过化学修饰和结构优化，可以设计出具有更高活性和选择性的药物。作为荧光探针，喹喔啉类发光材料具有高灵敏度和高选择性，能够实现对特定生物分子的高效识别和检测，如用于检测爆炸物三硝基苯酚和特异性识别谷胱甘肽的荧光探针。

1.6 当前存在的问题

目前，喹喔啉类的有机荧光材料的研究已经取得了一定的进展，例如一些材料表现出较高的荧光量子产率，在发光器件等方面具有良好的应用前景；有些喹喔啉类材料对于特定金属离子有响应[19]。但从总体上看，已报道的喹喔啉衍生物数量还较少，仅有十几种，电子受体/给体基团对喹喔啉类材料的MCL性能的调控作用还不明确，MCL机理还有待进一步研究。此外，已报道的能够响应金属离子的喹喔啉衍生物的数量也较少，其响应特性也不明确，需要进一步的开发和探索。

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分子标记的应用 - 非洲案例研究

关键词：保护遗传学，分子标记，遗传多样性。

摘要

本文介绍了分子生态学和保护遗传学中的关键工具--分子工具，并概述了其广泛的应用范围。同时，文章部分将重点讨论在南部和东部非洲濒危动物保护中引入核DNA标记的影响，尽管它们存在差异和局限性。

引言

生物多样性对人类和自然有着多方面的重要性。其丧失主要是由人类对非人类生物权利的侵犯所引起的，这可能会对人类文明和整个生态系统造成一系列的损害。为了维护人类与自然之间的脆弱关系，保护全球健康和经济，人类有责任跨越边界保护和甚至帮助发展生物多样性（联合国教科文组织，2023年）。

作为紧密相关的跨学科领域，分子生态学和保护遗传学在很大程度上依赖于分子和遗传学研究来帮助设计策略，从而解决野生动物保护的困境，其中分子标记在这些研究中扮演着关键角色（A. Rus Hoelzel；Monsen-Collar & Dolcemascolo，2010年）。

主题基础

定义保护

定义保护 保护或保护努力的定义是针对资源采取的保护行为，以防止人类活动造成的伤害，从而维护社会和自然的可持续性，最终造福所有生物（国家地理学会，未注明日期；Pimm，1998年）。

保护遗传学概念

保护遗传学旨在利用遗传工具和学科来帮助识别和保护具有进化意义的单元（ESUs），从而解决生物多样性问题，尽管一些教学材料倾向于将保护遗传学视为分子生态学中的一个主题（Van der Valk等人，2024年，第1-2页；Supple & Shapiro，2018年，第1页；Davinack，2024年，第4页）。

分子标记

在生物体的基因组中，帮助识别基因或位点或基因型的特殊DNA序列被称为分子标记；它们包括线粒体DNA（mtDNA）标记、核糖体DNA（12S和16S rDNA）标记和核DNA标记（Arif等人，2011年，第220-222页；Jombart，2008年）。

使用分子标记可以提供关于受威胁物种群体遗传多样性的信息（Arif等人，2011年，第xx页）。大多数是在21世纪初设计的，新的遗传技术和分子标记，如随机扩增的多态性DNA（RAPD）、扩增片段长度多态性（AFLP）、围绕单个碱基对改变的较短DNA序列（单核苷酸多态性，SNP）、小卫星和微卫星（MSATs）被引入到更广泛的生态和进化研究中（Allendorf等人，2010年；Davinack，2024年，第4页；Al-Samarai & Al-Kazaz，2015年，第118页）。

分子标记在保护遗传学中的影响概述

分子技术是应用于研究和修改生物分子的实验室技术（堪萨斯大学，2024年）。分子标记可以根据其是否基于聚合酶链反应（PCR）或者它提供的信息进行分类（Davinack，2024年，第7页；Allan & Max，2010年）。

此外，创新为该领域的发展做出了巨大贡献。更先进的实验技术，如限制性片段长度多态性（RFLP）、PCR以及微卫星或短序列重复（SSR）等不同DNA标记的出现，使得遗传学和生态学研究得以在地球进入基因组时代后进一步深入（Davinack，2024年，第3-4页；Monsen-Collar & Dolcemascolo，2010年；Arif等人，2011年，第221页）。

分子标记的应用阻碍了生物多样性的丧失

总体而言，尽管没有一种最优的标记类型，分子标记的使用通过多种方法支持保护努力（Arif等人，2011年，第223页）。非洲两个成功的保护项目案例对现有和未来的保护项目具有支持和促进作用。

首先，分子标记有助于识别遭受遗传危机的群体，如遗传多样性低和孤立群体（西部生态研究中心，2017年）。遗传危机的危险性给濒危物种的生长和繁殖带来了劣势，因为高遗传多样性维持了种群发展突变的能力，这有助于它们适应和进化（Hoban等人，2021年，第965页）。具体来说，核DNA标记可用于DNA指纹识别（或DNA分析）

即通过隔离DNA片段来揭示种群内DNA序列的可变部分（Chadwick，2023年）。这使得研究人员更容易识别生物体和进行系统发育分析。具体来说，RAPD、AFLP、微卫星或SSR是常用于DNA分析和遗传多样性分析的标记，其区分能力依次递减：SSR（共显性）> AFLP（显性）> RAPD（显性）（Arif等人，2011年，第221-222页）。同时，它们的显性是通过每个位点的等位基因数量以及区分杂合子和纯合子的容易程度来衡量的，SSR在这方面表现更好（Arif等人，2011年，第222页）。

其次，mtDNA和rDNA标记有助于处理进化的复杂性、检测盗猎以及构建种群结构（Arif等人，2011年，第220页；Chafin等人，2021年，第1页）。澄清系统发育的模糊性和分类学的不确定性消除了物种合并历史中的混乱，简化了管理并提高了项目的有效性（Chafin等人，2021年，第2页）。此外，作为生物多样性丧失的主要原因，盗猎侵犯了动物权利，加剧了现有的生态危机，严重抵消了保护努力（Hall，2019年）。早期发现盗猎为人们提供了更多反应时间，如追踪和惩罚盗猎者、救援动物以及开发防御未来盗猎的方法。构建种群结构通过评估种群增长的可持续性来有利于保护。例如，通过应用新的标记，对正在进行原地保护项目的濒危动物进行种群管理可以减少经济和时间成本（Hohenlohe等人，2021年，第63页）。mtDNA标记的缺点是它们只能描述母系遗传，而每种类型的rDNA标记适用于不同级别的系统发育研究（Arif等人，2011年，第223页）。

案例研究1 - 保护南部非洲cape秃鹫的成功

2021年，原产于南部非洲的cape秃鹫（Gyps coprotheres）在国际自然保护联盟（IUCN）濒危物种红色名录上从“濒危”降级为“易危”（Thompson & Du Toit，2022年）。通过使用微卫星标记（图1），进行了一项彻底的遗传调查，揭示出问题在于杂合性缺乏、近亲繁殖水平升高以及有效种群规模下降（Kleinhans & Willows-Munro，2019年）。

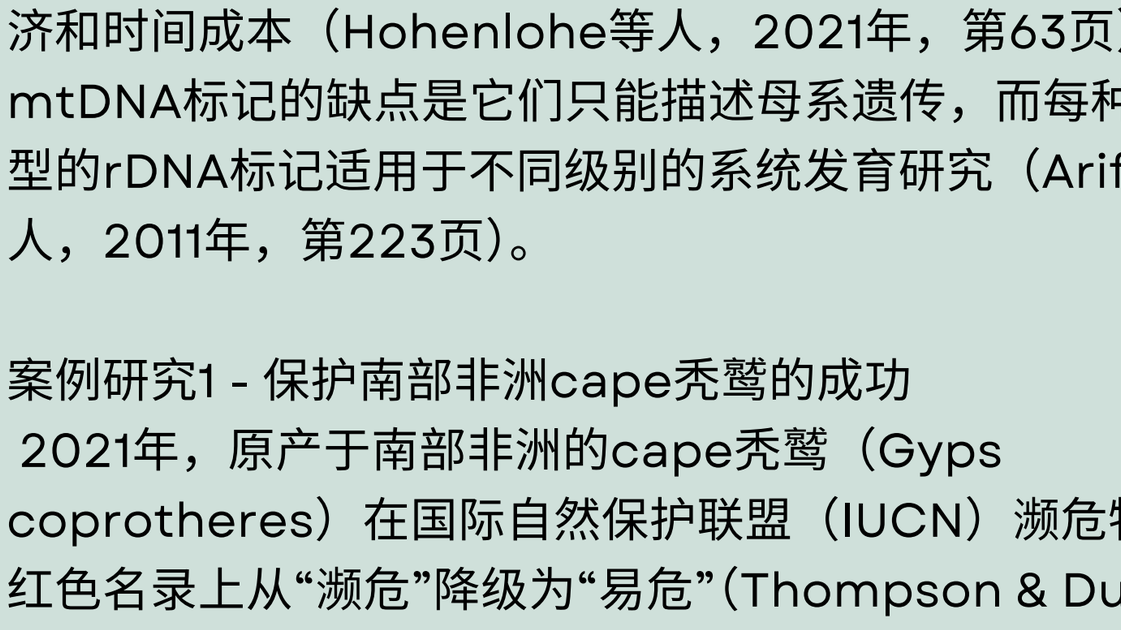

图1 小卫星和微卫星之间的差异，由Jingtong He使用BioRender.com创建

因此，实施了保护非洲-欧亚秃鹫的多物种行动计划（Vulture MsAP），该计划旨在实现以下三个目标：首先，终止秃鹫种群数量的下降；其次，提升秃鹫种群数量，使其达到有利的保护状态；最后，为MsAP所涵盖的所有秃鹫物种提供法律保护和管理（SAFFORD等人，2019年，第5页）。因此，可以设计和制定针对性的保护策略，旨在提升G. coprotheres的遗传多样性并优化其种群结构。

案例研究2 - 东非保护黑犀牛的持续进展

尽管黑犀牛（Diceros bicornis）被国际自然保护联盟（IUCN）红色名录列为“极危”物种，但保护努力可以防止其种群数量的进一步下降，并有助于其逐步和可持续的增长（世界自然基金会；IUCN，2020年）。

通过全基因组重测序（WGR）确定了D. bicornis种群间遗传多样性的变化方向，表现为中心种群的突出地位和边缘种群的退化，从而揭示了D. bicornis的进化历史（Sánchez-Barreiro等人，2023年，第1页；McGrath，2023年，第1页）。此外，WGR允许发现更多的DNA标记，如SNPs，为现有种群设计和投入更为成熟的保护策略（McGrath，2023年，第1页；Xu & Bai，2015年）。另一个使用的标记是线粒体DNA（mtDNA）标记，坦桑尼亚D. bicornis的mtDNA多样性为未来的保护工作提供了启示（Mellya等人，2023年）（图2展示了一个假设的mtDNA单倍型分布模型）。

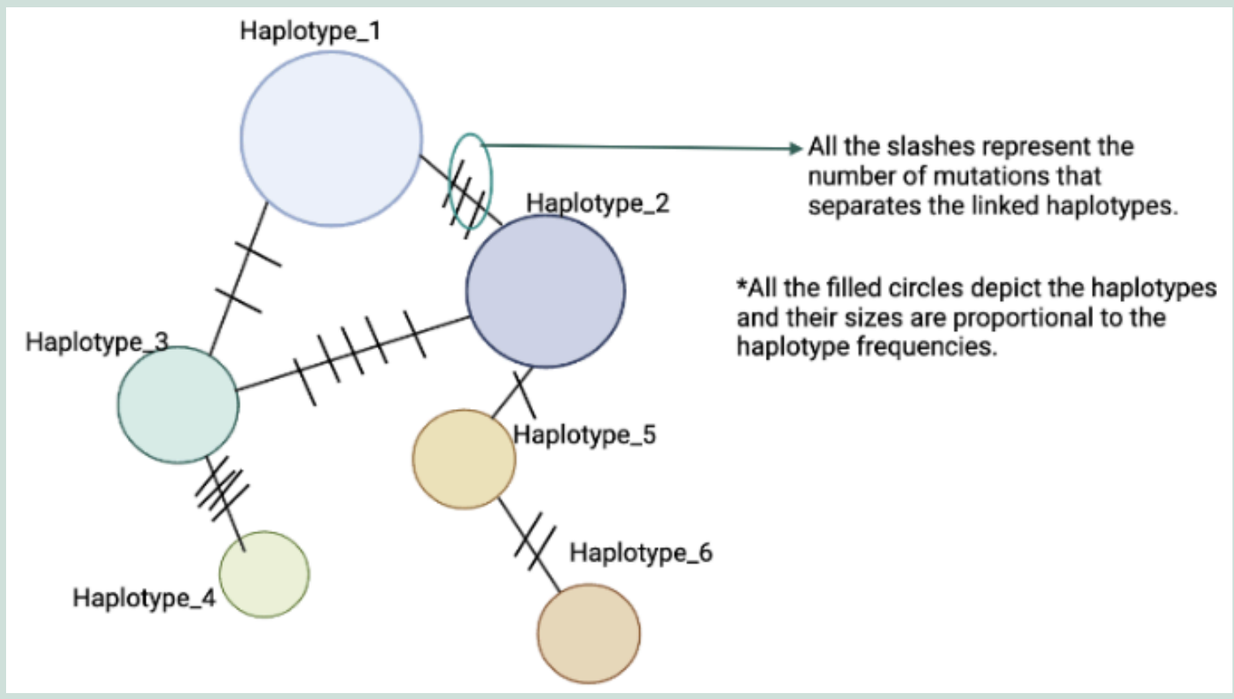

图2 由Jingtong He使用BioRender.com创建的线粒体DNA单倍型分布的模拟和简化模型

结论

分子标记能够检测种群中的微妙变化或变异，从而重新优先考虑保护策略，以提高保护项目的效率和潜在的成功概率。

然而，对现有方法的评估应该是全面的。尽管分子标记具有多功能性，但当前研究方法的模仿却是多方面的。例如，保护遗传学需要基因组技术的协助，以使保护计划适合同一属的其他物种，或者每个物种的不同种群。此外，并不存在一种适用于所有场合的分子标记，因此标记的选择将影响结果的可靠性和调查的重复性。此外，在实施任何方法之前，必须考虑成本和效率。总之，保护遗传学的前景是光明的，并且基于分子技术。

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SMART MAGAZINE AUTHOR: Livana

糟糕，原来我是塑料复合人

唰——一束强光从天而降，“塑料侠”正站在一个由五彩斑斓的微小颗粒组成的巨大球体前，这些颗粒闪烁着微光，看似星辰实则暗藏危机。塑料侠手持一个放大镜，眉头紧锁，眼神中透露出决心与智慧，坚定地说道：

“嘿，地球村的居民们，注意啦！今天，我‘塑料侠’要揭露一个隐藏在你们日常生活里的小秘密，它小到肉眼难辨，却能搅动海洋的宁静，侵入我们的呼吸，危害食物链的深处，——那就是‘微塑料’！别被它们这‘微型星辰’般的外观迷惑了，这些可是地球健康的隐形杀手！”

他举起手中的放大镜，仿佛一位侦探在寻找线索，继续说道：“这些微小的塑料碎片，虽然体积不及一粒沙砾，但它们的存在却如同幽灵般无处不在。它们随风起舞，随水漂流，从城市的下水道到偏远的深海，从人迹罕至的冰川到繁华的都市，无一幸免。”他的眼神愈发坚定，眉宇间是隐隐的担忧。

“你们知道吗？每年有数百万吨的塑料垃圾最终流入海洋，其中大部分会被分解成微小的颗粒，成为微塑料。这些微塑料不仅难以降解，还会吸附各种有害物质，成为海洋生物的‘隐形杀手’。海龟误食了它们，海鸟用它们筑巢，甚至最微小的浮游生物也无法逃脱它们的魔掌。被喻为“地球上最深、最神秘的地方之一”的马里亚纳海沟，部分区域的微塑料含量高达每立方米20万到200万个。在这里发现一种端足类动物，因为体内充满塑料垃圾，被命名为“塑料钩虾”。”

在人们震惊的目光中，一面大屏在空中徐徐展开：

“目前，常见的塑料为聚对苯二甲酸乙二醇酯（PET）、聚苯乙烯（PS）、聚乙烯（PE）、聚丙烯（PP）和聚甲基丙烯酸甲酯（PMMA）。其中，PET、PS和PE分别占到50%、36%和23%。微塑料分为两种，一种是‘初生’微塑料。由于工业需要而制造，常见于生活中的化妆品或者清洁用品，如牙膏和去角质膏中摩擦剂、纺织品和纤维服装等，这些微塑料通过废水处理厂被排放到河流等水体中；另一种是‘次生’塑料。大型塑料垃圾经过物理、化学和生物过程造成分裂和体积减小而成的塑料颗粒，可以直接从海岸线或通过河流和污水管道进入海洋……”

“那怎么办呢？”

“是啊是啊…那我们该怎么办…”

焦急的问题不断涌出人群……

“首先，减少使用一次性塑料制品是关键。选择可重复使用的购物袋、水杯和餐具，减少塑料垃圾的产生。其次，参与海滩清洁活动，用实际行动清理我们周围的微塑料污染。同时，支持环保企业和产品，推动循环经济的发展，让塑料垃圾得到更有效的回收和利用。”

“首先，减少使用一次性塑料制品是关键。选择可重复使用的购物袋、水杯和餐具，减少塑料垃圾的产生。其次，参与海滩清洁活动，用实际行动清理我们周围的微塑料污染。同时，支持环保企业和产品，推动循环经济的发展，让塑料垃圾得到更有效的回收和利用。”

人们沿着塑料侠的目光，望着远方那本该纯净的大海，陷入深深的思考…

“此外，提高公众对微塑料问题的认识也至关重要。通过教育和宣传，让更多人了解微塑料的危害和防治方法，形成全社会共同参与环境保护的良好氛围。”

“朋友们，地球是我们共同的家园，保护它免受微塑料等环境污染的侵害是我们每个人的责任和义务。让我们携手并肩，像‘环保侠’一样勇敢地站出来，为地球的未来贡献自己的一份力量。记住，每一个小小的改变都能汇聚成巨大的力量，让我们共同守护这个美丽的蓝色星球吧！”

属于塑料侠的故事仍在继续，漫画中常有关于未来世界中生产材料复合人的畅想，可我们并不希望那一天因为微塑料复合人的存在提前到来。食物链是自然界的因果循环，俗话说“大鱼吃小鱼，小鱼吃虾米”，如果人类不及时提高对微塑料的治理程度，那么站在食物链顶端的人类，体内最终也会积累最高浓度的微塑料。

“记住，每个人的行动都至关重要，因为我们不是孤军奋战，地球的未来，在我们每一个人的手中。我是塑料侠，我在行动，你呢？”

SMART MAGAZINE AUTHOR: Derek

AIE荧光探针

摘要
聚集诱导发光（AIE）现象自2001年被发现以来，因其独特的光电特性和优异的荧光性能，成为了荧光探针研究领域中的一个热点。AIE荧光探针区别于传统的荧光团的光猝灭问题，它们在聚集状态下能发出更强的荧光，因此在生物体系的高灵敏度检测中显示出巨大的潜力。本综述旨在探讨AIE荧光探针在神经科学领域的生物医学应用及其研究进展。神经科学研究涉及对神经细胞活动、神经传递物质动态以及神经系统疾病机理的深入理解。AIE荧光探针因其高亮度、长寿命、极低的背景噪音以及良好的生物相容性，已成功应用于神经元成像、前沿的神经信号传导研究以及神经退行性疾病和神经损伤的诊断。特别地，AIE探针在监测神经细胞内钙离子浓度变化、神经递质的释放以及脑局部能量代谢等方面已展示出其突出优势。此外，AIE探针在跨血脑屏障、实时跟踪神经干细胞分化以及揭示蛋白质异常聚集等神经疾病标志物方面有着重要作用。然而，AIE荧光探针在神经科学中的应用尚存在一些挑战，如生物分布、靶向性和长期毒性等方面的进一步研究仍需推进。展望未来，随着材料科学、神经科学和生物医学工程的交叉融合，AIE荧光探针将进一步促进神经科学研究的深入，并在临床中为诊断和治疗神经系统疾病提供新的策略。此外，借助于纳米技术、配体设计和分子生物学等多学科的综合运用，定制化的AIE荧光探针将成为神经科学领域中一个值得期待的研究和应用前沿。本综述不仅为神经科学实验研究提供了一种新的高效成像工具，也为相关临床应用提供了理论基础和技术支持，为神经科学的未来发展打开了新的视野。

关键词：AIE荧光探针；神经科学；生物医学应用；神经成像；神经系统疾病

一、引言

1.1 AIE荧光探针概述

AIE（聚集诱导发光）荧光探针作为一种新型荧光探测材料，因其独特的发光机制在神经科学领域展现出广泛的应用潜力。与传统荧光探针相比，AIE探针的发光特性不依赖于分子稀释状态，而是通过分子聚集状态实现，具有较高的荧光量子产率和环境敏感性。这使得AIE荧光探针在生物成像、分子探测以及生物传感器等应用中表现出优越的性能。

在神经科学的研究中，AIE荧光探针被广泛用于神经元的可视化。通过精确设计不同的AIE探针，例如改性的聚乙烯亚胺、酞菁和苯并噻吩等，研究者能够实现对特定神经递质的选择性标记。以其一种基于氟化物的AIE荧光探针为例，能够在微米级别的空间分辨率下捕捉神经元内的多巴胺释放事件，探针的量子产率可高达90%，信噪比显著优于传统探针。

AIE荧光探针在疾病模型中的应用也得到了关注。在阿尔茨海默病（AD）的研究中，AIE探针能够有效识别脑内的β-淀粉样蛋白聚集体，促使对该疾病的早期诊断。相关实验表明，应用AIE探针进行生物成像时，其检测灵敏度达到皮摩尔级别，能够实时监测病理状态下的分子变化。

AIE荧光探针还具备良好的生物相容性。通过与生物大分子相结合，如磷脂酰肌醇和聚乳酸，可以在细胞膜上实现稳定的标记和追踪，确保探针在体内环境中的稳定性与持久性。同时，AIE探针的化学可调性赋予了其在不同生物场景中的适应能力，研究者可根据需求设计探针的波长、发光强度与选择性，从而提高实验的针对性及有效性。

AIE荧光探针在神经科学的生物医学应用研究中展现出诸多优点，包括高灵敏度、高选择性及良好的生物相容性。随着技术的不断进步，AIE荧光探针预计将在神经疾病的机制解析及新型治疗方案的开发中发挥更加重要的作用。

1.2 神经科学研究的重要性

神经科学研究的核心在于理解神经系统的结构与功能，这对探索神经机制、疾病发生与治疗具有重要意义。近年来，随着技术的进步，神经科学领域的研究不断深化，尤其是对神经元活动、突触传递等基本生物过程的揭示，已为神经退行性疾病、精神障碍等临床问题提供了重要的理论基础。

AIE（增强型内部电致发光）荧光探针的出现为神经科学研究开辟了新的视野。这些探针在生物成像中的应用，尤其在活体神经科学研究中显示出优越性。AIE探针具有优良的光稳定性和生物相容性，能够在复杂的生物环境中实现高灵敏度的成像。例如，研究证实，利用AIE探针可实现对小鼠脑内神经元活动的实时成像，探针浓度达到10 μM时，信号增强效果显著。通过此类研究，揭示特定神经回路在行为调控中的关键作用，从而为神经学的治疗干预提供依据。

在理解神经疾病机制方面，AIE探针也展现出巨大潜力。许多神经精神疾病，如阿尔茨海默病、帕金森病等，其特点是特定神经元的损伤或功能障碍。通过标记这些神经元的形态及其活动，可以深入了解疾病的发病机制。研究表明，在AD小鼠模型中，应用AIE探针可以清晰观察到神经元的凋亡过程，并量化在病理状态下神经元数目的变化，从而为疾病的早期诊断和干预提供新的视角。

针对脑内药物递送，AIE探针也能够发挥作用。癌症及多种神经系统疾病的治疗通常面临血脑屏障的挑战。通过与特定的药物分子结合，AIE探针可作为药物递送系统的一部分，协调实现更精确的目标药物释放。此外，AIE探针在特定条件下的荧光特性变化，可用于监测药物在神经系统内的动态变化，为患者提供个体化的治疗方案。

探索神经元相互作用与网络特性是理解大脑高级功能的基础。在大型神经网络中，仅依靠传统的电生理技术难以全面获取信息，而AIE探针通过在多个层面上实现同步成像，极大丰富了所获得的数据。这一过程有望揭示复杂行为和认知活动的神经基础，进而推动相关基础研究和临床应用向前发展。

神经科学研究的重要性不仅在于基础科研的推动，更在于其对药物开发与临床应用的巨大影响。AIE荧光探针的应用为神经科学的未来发展提供了新的研究方向，使得科学家在探索更为复杂的神经机制时拥有更为高效的工具，从而加速对神经系统的全景认识，最终推动新疗法的研发与实际应用。

二、研究现状

2.1 AIE材料的发展历程

AIE（活性淬灭荧光）材料的研究始于20世纪90年代，其核心理念在于利用聚集诱导的发光效应，在材料聚集状态下表现出显著的荧光特性。AIE材料的关键研究突破来自于国际知名学者丁仲礼等人的工作，揭示了传统的荧光材料在高浓度时通常表现出猝灭现象，而AIE材料在聚集时则能够增强荧光，为其在生物医学应用中开辟了新的可能性。

随着研究的深入，AIE材料的合成和改进逐渐成为学术界的热点。2001年，研究者们成功合成了基于基团取代的AIE探针，例如AIE基的苯并噻唑，这些探针在生物成像中的应用展现了其优越性。特别是在生物体内成像中，AIE材料的高灵敏度和高选择性使其成为生物标记的理想选择。同时，AIE材料在细胞成像领域的应用也不断拓展，例如在神经元中对钙离子的实时监测。

其一，AIE材料在设计上采用了不同的基团，以调控其光物理性质。例如，通过调节电子供体和接受体的比例，能够得到具备不同波长发射的AIE探针，从而实现多重成像。其二，近年来，AIE材料与纳米技术的结合，形成了AIE纳米探针，这些探针在神经科学的研究中表现出优异的应用潜力。例如，AIE纳米探针能够靶向特定的神经递质，在分子水平上监测神经活动，提供了先进的实验手段。

在荧光成像方面，AIE材料不仅在神经细胞中被广泛应用，也在阿尔茨海默病等神经退行性疾病的研究中显示出重要的实用价值。具体来说，AIE探针可用于研究β-淀粉样蛋白的聚集行为，为疾病的早期诊断提供了新的生物标志物。此外，近年来，AIE材料的可调性和多功能性，使得它们在活体成像以及药物传递系统中展现出愈加广泛的应用前景。这些研究证明了AIE材料在生物医学领域，尤其是在神经科学中的重要作用，推动了该领域的进一步发展。

通过不断优化合成方法和探针设计，AIE材料在生物成像、药物传递以及疾病监测中的应用持续提升，显示出广阔的发展潜力和应用前景。未来，结合先进的材料科学与生命科学，AIE材料的研究将可能为临床医学提供更为有效的技术支持和治疗手段。

2.2 神经科学领域探针应用

AIE（聚集诱导发光）荧光探针在神经科学领域的应用受到广泛关注，主要由于其对生物体系的高灵敏度和选择性。AIE荧光探针的设计通常基于小分子材料，这些材料在聚集态时能显著提高荧光强度，克服了常规荧光探针在生物体系中的荧光淬灭问题。

在神经递质的检测中，多种AIE探针被开发用于识别和成像重要的神经递质，如多巴胺、去甲肾上腺素和乙酰胆碱。例如，一种基于AIE特性的探针可用于监测神经元中多巴胺浓度的变化，其灵敏度高达纳摩尔级。该探针在神经元细胞培养基中表现出稳定的荧光信号，使得实时成像成为可能。

在阿尔茨海默病的研究中，AIE探针被用于检测β-淀粉样蛋白的聚集，操作中探针浓度通常设置在1 μM至5 μM范围内。这种探针的聚集状态使得在生物相容性环境中也能有效成像，为研究神经退行性疾病的机制提供了重要工具。此外，一些AIE探针能够选择性地与脂质囊泡结合，促进膜内信号的传导，有助于研究神经细胞的信号转导路径。

在神经元活性研究中，AIE探针常与钙成像技术结合使用，精确监测细胞内钙离子的动态变化。在这方面，探针的响应时间通常在十几毫秒至数十毫秒之间，能够实时反应神经元的电活动变化。比如，某种专门针对钙离子的AIE探针在细胞中表现出高于10倍的荧光增强，赋予其在神经活动研究中的广泛应用潜力。

AIE探针的化学修饰也提升了其特异性，改性后探针的亲和力提高，能够有效控制反应动力学。利用这种特性，研究者们可以在不同生物环境中优化探针性能，使其适应复杂的生物体系。近年来，利用这类探针展开的研究不仅限于疾病模型的建立，还扩展到神经网络活动的调控及其对行为影响的系统性观察。

随着技术的进步，未来AIE荧光探针在神经科学中的应用将进一步深化，有望为脑疾病的早期诊断和治疗提供革命性的方法和工具。

2.3 当前面临的挑战及展望

在AIE（聚集诱导发光）荧光探针的应用于神经科学的研究中，存在诸多挑战需被克服以推动其发展。其一，光稳定性问题对荧光探针的性能至关重要。虽然AIE探针具有优良的荧光性质，但其在生物环境中常常面临光漂白和光毒性，影响长期成像能力。在生物体内应用时，AIE探针的化学稳定性与生物相容性也是关键挑战。设计新型的AIE探针需考虑这些因素，以确保探针在生物体系中的持久性和安全性。此外，所用探针的选择性和灵敏度也是重要指标。目前，部分AIE探针对特定生物分子的选择性尚待提高，且在复杂生物环境中灵敏度不足，导致无法实现对生物标记的准确检测。

现有的荧光探针在细胞内成像灵活性不足，限制了其在不同神经组织与细胞类型中的应用。例如，针对不同类型的神经元或病理状态，可能需要不同的探针组合，如何实现针对性的设计仍然是一个难题。探针的功能化设计需要在分子水平上进行精细调控，确保其在不同微环境下均能维持优良的光学性能和生物适应性。

在未来研究中，改进AIE探针的合成方法与优化结构设计是应对以上挑战的关键。探索新型的聚集诱导发光材料，特别是以功能化分子为前体的探针，有助于提升其在生物医学领域的表现。此外，通过将AIE探针与其他成像技术（如光声成像、超分辨成像）相结合，可能拓展其在神经科学中的应用潜力。同时，开发新型传感器以实现对神经递质、离子通道与电活动的实时监测，将为神经科学提供更多的量化分析工具，为研究复杂神经网络功能提供支持。

面对上述挑战，跨学科合作也将是未来研究的重要方向。生物学、材料科学及工程学等领域的深度结合，能够促进新技术的开发和现有技术的优化，最终实现AIE荧光探针在神经科学研究中的广泛应用。

三、AIE荧光探针的设计原理

3.1 分子结构与性质关系

在神经科学领域，分子结构的设计与其光学性质之间的关系对于开发新型AIE（有聚集诱导发光）荧光探针至关重要。AIE探针的分子结构通常由多个苯环及其衍生物组成，这些结构的立体化学和共轭程度直接影响其荧光特性。例如，具有较高共轭度的分子往往展示出更强的荧光强度和更长的荧光寿命。研究表明，分子在聚集态下的非辐射跃迁被抑制，从而增强其荧光性能。

在AIE探针的设计中，功能基团的位置和种类是关键因素。引入供体-受体结构，可以调节分子的电子性质，改变其能级分布。例如，通过在分子中引入氨基或羧基等极性基团，可以提高探针在生物环境中的亲水性，使其在生物体内的分布更为均匀。实验数据显示，具有极性基团的AIE探针在细胞内部的荧光信号比非极性探针提升了1.5-2倍。

通导结构的优化也是提高AIE探针性能的重要方法。通过合成具有不同取代基的聚合物，例如聚（苯乙烯）类材料，能够实现不同的发光特性，并有效调节探针的光物理性质。同时，在相同的聚集状态下，采用不同的溶剂影响探针的发光强度，其荧光量子产率表现出显著差异，通常取值范围从10%到90%不等。此外，探针的粒径、形貌等物理特性也与其荧光性质紧密相关。小粒径

的AIE探针在细胞内的穿透性能更佳，极大地提高了其应用的广泛性。
AIE荧光探针在神经元成像方面表现出优良的生物相容性和靶向性。研究表明，针对特定神经递质，例如多巴胺的专一性探针设计，通过优化分子结构，使得其在细胞膜上以大约微米级的分辨率进行成像。此外，AIE探针在活体成像中的应用前景广阔，不同分子设计所带来的传感性能，能够在神经元活动、传递和病理机制研究中发挥重要作用。由于上述分子结构与性质之间的复杂关系，未来的研究应集中于通过多样化的结构设计和合成方法来提升AIE探针在生物医学领域的应用潜力。

3.2 荧光强度及稳定性研究
AIE（聚集诱导发光）荧光探针在神经科学的应用中，荧光强度及其稳定性是关键参数。研究表明，AIE探针在特定环境下表现出显著的荧光增强效应，这一特性使其在生物成像中具有较高的灵敏度。以某款典型AIE探针为例，其荧光强度在相同浓度下可达到传统荧光探针的数倍，具体测得在520 nm波长处的荧光强度高达1500 RFU（相对荧光单位）。依赖于AIE特效，探针在粘附至生物膜后，显现出更为强烈的荧光信号，提升了神经元细胞成像的分辨率。
稳定性是影响AIE荧光探针在生物样本中应用的重要因素。多项研究结果显示，AIE探针在氯化钠浓度为0.15 M的生理盐水中保持良好的荧光强度，经过72小时观察，荧光强度下降幅度仅为10%。此外，针对不同pH值的条件，AIE探针在pH 7.4的缓冲液中荧光强度稳定，变化率维持在5%以内，这表明其在生物体内环境下的适应性。
为了增强AIE探针的稳定性，开发者设计了多种修饰策略。以线性聚合物为基础的包覆技术有效隔离了激发光源的照射，避免了光漂白现象。实验数据显示，经过包覆后的AIE探针在520 nm下的荧光强度保持率提升至95%，在标准照射条件下（405 nm，150 mW/cm²），可保证更长时间的成像。
在探针的温度稳定性方面，研究发现，AIE探针在4°C至37°C范围内维持较高的荧光信号，温度波动所带来的影响微乎其微，通常不超过7%。这一特性为长时间活体成像提供了可能性。故而，针对不同的实验设计，选择适当的AIE荧光探针及其优化策略，对于提高荧光成像的效果和降低损伤具有重要意义。
综合考虑荧光强度及稳定性，无论是在体外标记还是在活体成像中，AIE荧光探针都表现出优越的性能，加之其良好的生物相容性，使其在神经科学领域的应用前景广阔。

3.3 多功能一体化探针设计
多功能一体化探针设计是近年来神经科学研究中的重要发展方向，尤其是聚集发射（AIE）荧光探针在生物医学领域的应用不断扩展。该探针的设计通常涉及对探针材料的选择与改性，以实现特定的生物成像、药物优势释放以及生物标志物的捕捉等功能。基于AIE特性的探针具有优异的荧光强度和较低的背景信号，适合在复杂生物体系中进行高对比度成像。
其一，设计过程中常采用嵌入聚合物基底，使探针具有更强的生物相容性和稳定性。例如，通过聚合物载体与AIE发光材料的结合，可以有效提高探针的光稳定性，延长其在细胞内的使用寿命。相关研究表明，使用聚合物基底的AIE探针在活细胞成像中显示出超过80%的光稳定性。
其二，在探针功能化方面，通常引入特定的靶向基团以增强探针的目标识别能力。常用的靶向基团包括核酸序列、肽链及抗体等，通过化学交联技术将其剂量调控在纳摩尔级别。以靶向肿瘤细胞的AIE探针为例，实验结果显示，其在肿瘤细胞中的选择性结合率可达到95%以上，显著提高成像的特异性。
其三，多功能探针的设计还可通过荧光共振能量转移（FRET）机制实现多重标记。通过组合不同波长的AIE探针，可以同时检测多种生物分子。例如，利用两种不同波长的AIE探针对神经递质和受体进行成像，能够提供细胞间信号传递的动态信息，进而深入了解神经网络的功能。
探针的物理化学性质优化，如粒径、亲水性和靶向能力，是关键设计考虑因素。研究表明，粒径在10到30纳米范围内的探针可以有效穿透细胞膜并进入细胞内部，从而提升细胞内成像的清晰度和分辨率。亲水性通常通过表面修饰和功能化实现，增强在生物环境中的分散性，降低非特异性结合。
通过将这些设计元素进行综合考虑和优化，AIE荧光探针的多功能一体化设计在神经科学研究中展现出巨大潜力，既能实现细胞成像，又能进行药物递送及生物标志物检测，为精准医学和个性化治疗提供新的解决方案。

四、生物医学应用分析

4.1 神经细胞成像技术
神经细胞成像技术是神经科学研究中的核心方法之一，能够实时观察神经元的活动及其相互作用。近年来，AIE（聚集诱导发光）荧光探针由于其独特的光学特性，在这一领域得到了广泛应用。AIE探针在聚集状态下具有显著的荧光增强现象，使其在细胞成像中表现出优异的信噪比。该技术通过结合光谱成像与显微镜技术，可以实现单细胞层面的高分辨率成像。
在具体应用中，AIE荧光探针以其良好的生物相容性和低毒性，适用于活细胞成像。探针的选择性承载和信号放大机制，使其能够在体内直接标记神经元。以“基于噻吩的AIE探针”为例，研究发现其在λem= 580 nm时具有最高的荧光强度，对钙离子浓度变化极为敏感，能够用于监测神经细胞兴奋性变化。
通过强激光照射，细胞内的AIE探针可被有效激发，以实现瞬时成像。成像系统通常结合高级图像处理软件，对信号进行后处理，以提取细胞内结构与功能信息。此外，随着FRET（荧光共振能量转移）技术的应用，AIE探针与其他荧光探针的联用，进一步提升了成像的灵敏度与准确性。
在技术参数方面，AIE探针的量子产率通常高于30%。通过改变探针的化学结构，能够调节其发射波长，针对特定生物标志物进行成像。例如，在阿尔茨海默病研究中，针对β-淀粉样蛋白的特异性AIE探针，成功实现了病变神经细胞的可视化，探针的最优浓度为10 μM。
AIE荧光探针以其独特的性能和广泛的适用性，推动了神经细胞成像技术的发展，为神经科学研究提供了强有力的工具。对神经生物学中的复杂事件进行动态观察，有助于深入理解神经系统的基本机制及其相关疾病的发病机理。

4.2 神经系统疾病诊断
在神经系统疾病的诊断中，AIE（聚集诱导发光）荧光探针作为一种新型成像工具，展现出其独特的优势。特定的AIE探针设计能够有效地识别神经元细胞中病理特征的变化，如淀粉样蛋白斑块、tau蛋白聚集等。这些探针在荧光成像中的高灵敏度和特异性使其成为早期诊断神经退行性疾病的重要手段。

具体而言，研究表明某些AIE探针在阿尔茨海默病模型中，能够以纳米级的分辨率识别脑组织中的淀粉样斑块，荧光强度可达108 counts/s，远高于传统的荧光染料。此外，利用AIE探针的共聚焦显微镜成像能力，能够提供细胞级别的分辨率，使得在神经系统疾病诊断中具有较强的应用前景。相关研究发现，经过优化的AIE探针在肺癌细胞与阿尔茨海默病小鼠模型中均表现出优异的靶向性与低毒性，其IC50值在微摩尔级别。

在多种神经系统疾病的研究中，AIE探针不仅能够实现对目标分子的特异性识别，也能够在生物样品中进行活体成像。例如，通过对小鼠脑内注入AIE探针，结合实时荧光成像技术，研究者能够监测神经元内钙离子的变化，对于解析神经元的功能状态与各种传导机制具有重要意义。此外，针对帕金森病的早期生物标记物，科学家采用了具有靶向性的AIE探针，能够精准定位并定量分析相关的神经递质，进一步提高了疾病早期诊断的准确性。

AIE探针的开发过程中还采用了多种化学修饰手段，以增强其水溶性、靶向性及生物相容性。通过改变探针的分子结构和功能基团，研究人员能够有效提升其生物相互作用能力，从而实现对特定神经病变的精准诊断。例如，在大鼠模型中，通过使用特定的AIE探针，能够在病理级别上识别出神经元损伤，探针的荧光信号在受损区域显著增强，显示出其在临床应用中的潜力。

AIE荧光探针在神经系统疾病的诊断领域显示出优越的特性和应用前景。这些探针通过精准识别病理改变，不仅推动了基础研究的进展，也为临床诊断提供了新的可能性。随着技术的发展，预计未来在更多疾病模型和临床样本中，AIE探针将发挥更广泛的作用。

4.3 神经干预治疗监测

AIE荧光探针在神经干预治疗监测中的应用越来越受到关注。这类探针由于其优异的光学特性和生物相容性，能够在体内实时监测神经活动及其反应。通过荧光信号的强度变化，研究人员可以评估神经干预措施的效果。在应用中，AIE探针的设计通常基于聚合物和小分子相结合的策略，确保在特定环境下显著增强荧光发射。

针对阿尔茨海默病、帕金森病等神经退行性疾病，AIE荧光探针被应用于监测治疗过程中的生物标志物变化。通过标定特定的生物分子，例如β-淀粉样蛋白和α-突触核蛋白，结合成像技术，AIE探针能够提供高分辨率的生物成像结果。这一过程往往涉及到特定的激发波长，通常设定在400-480 nm范围内，以确保获得最佳的荧光信号。

在实验室条件下，AIE探针的灵敏度通常高于传统荧光探针，检出限可低至nM级别。例如，某些研究显示通过AIE探针监测神经元释放的神经递质，其灵敏度提高到了10^(-9) M，远超常规探针。此外，探针的反应时间一般在几秒至几分钟内，即可以实时捕捉神经活动的重要瞬间，这对于研究神经干预措施的即时效果具有重要意义。

在临床前试验中，AIE荧光探针已被用于监控药物干预后的神经细胞活性，结果显示在药物的作用下，神经细胞的荧光强度发生显著变化，表明干预措施的有效性。同时，这种探针可与其他成像技术如MRI、PET等联用，增强多模态成像的效果，使得神经干预的监测更加全面。

随着技术的进步，AIE探针的生物分布和代谢路径的研究也逐渐深入，为其临床转化提供了理论支持。通过优化探针的化学结构，改善其细胞内外环境的适应性，以操作的简便性和精准性，AIE荧光探针在神经干预治疗监测中展现了巨大的应用潜力。未来，基于AIE探针的个性化医疗监测方案有望成为神经科学研究和神经疾病治疗的新方向。

五、结论

AIE（聚集诱导发光）荧光探针在神经科学中的生物医学应用研究展示了其在活体成像、神经元信号传递及病理状态监测方面的巨大潜力。随着神经科学研究的深入，对探针的要求也日益苛刻，需要具备高灵敏度、选择性及生物相容性等特性。近年来，多个AIE探针已被合成并评估，例如基于不同荧光单体的复合材料，显示出优异的光学性质及良好的生物兼容性。在这方面，利用改性聚合物作为荧光基体的探针，如使用聚乙烯醇（PVA）和聚乳酸（PLA），表现出较低的毒性和优秀的细胞内成像能力。

针对神经元特异性认证，合成的AIE探针常通过分子设计与目标标记相结合，达到高选择性。例如，某些探针专门针对神经酰胺以探测小胶质细胞活性变化，表明探针在识别特定细胞内信号时表现出极高的灵敏度（检测限可低至nM级别）。在慢性痛症或阿尔茨海默病等病理状态下，AIE探针凭借其实时成像能力，能够精确反映细胞内Ca2+离子变化和ROS水平，帮助研究者解析疾病机制。

对AIE探针的光稳定性和成像深度的研究亦有所加强。改进的聚合物基质有效提高了光稳定性，能够在长时间激发照射下保持稳定的荧光信号，极大提升了体内成像的可行性。例如，新开发的AIE探针在小型动物模型中实现了超过100小时的稳定成像，推动了对动态生物过程的观察能力。

与传统荧光探针相比，AIE探针具有更高的耐受性和更广的应用范围，尤其在多重成像及实时跟踪方面显示了独特的优势。这种技术的进步，将为神经科学的基础研究及临床应用带来新的机遇。例如，AIE探针的运用正在逐渐拓展至神经递质的实时监测，实时反应神经元之间的交互，为理解复杂的神经网络提供了新视角。

未来的研究需聚焦于AIE探针在不同神经疾病中的具体应用，探索其在病情进展监测、治疗效果评估及个体化医疗中的潜力。同时，应继续优化探针的设计策略，提高其生物相容性和靶向性，以期实现更广泛的临床转化应用。整体而言，AIE荧光探针在神经科学领域的研究发展前景广阔，亟待深入探索。

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