2024年第1期总2期

饲料用酶工程

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前沿资讯

1．中国农业大学胡永飞团队揭示酶解制备新琼寡糖调控肠道菌群改善鸡肠道健康的新机制

简介：中国农业大学动物科学技术学院胡永飞团队在期刊《总环境科学》（Science of The Total Environment）上在线发表研究论文《酶解制备新琼寡糖通过促进粪杆菌属产生亚精胺改善鸡肠道功能和健康》（Enzymatically prepared neoagarooligosaccharides improve gut health and function through promoting the production of spermidine by Faecalibacterium in chickens）。该研究通过克隆表达β-琼胶酶来制备新琼寡糖（NAOS），发现日粮添加NAOS能够促进肠道粪杆菌属的生长，粪杆菌通过产生亚精胺调控宿主自噬通路，改善鸡肠道健康，提高动物生产性能。

来源：中国农业大学

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2．Diverse gut bacteria communities protect against harmful pathogens by nutrient blocking(不同的肠道细菌群落通过营养阻断来抵御有害病原体)

简介：The human gut is home to hundreds of different bacterial species collectively known as the gut microbiome. A major health benefit these provide is to protect the gut against invading pathogens (disease-causing microorganisms) that could cause harmful infections. But up to now, how this protective effect comes about has been unclear, and whether certain bacterial species have a more important role than others.To investigate this, researchers at the University of Oxford tested 100 different gut bacteria strains individually and in combination for their ability to limit the growth of two harmful bacterial pathogens: Klebsiella pneumoniae and Salmonella enterica. Individual gut bacteria showed a very poor ability to restrict the spread of either pathogen. But when communities of up to 50 species were cultured together, the pathogens grew up to 1000 times less effectively than when cultured with any individual species. This ‘community protection effect’ was seen regardless of whether the bacteria were cultured together in vials, or in ‘germ-free’ mice (which had no resident gut bacteria at the start of the experiments).

来源：EurekAlert

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3．Researchers at TU Graz Decipher Enzyme Scissors of Intestinal Microbes(格拉茨工业大学的研究人员破译了肠道微生物的酶剪刀)

简介：Fruit and vegetables contain a variety of plant natural products such as flavonoids, which give fruits their colour and are said to have health-promoting properties. Most plant natural products occur in nature as glycosides, i.e. chemical compounds with sugars. In order for humans to absorb the healthy plant natural products, the sugar must be split off in the intestine. Microorganisms in the intestinal flora help to speed up the process. So-called C-glycosides, i.e. plant natural products with a carbon-based bond to a sugar, would even be practically indigestible without the intestinal microbes (e.g. nothofagin in rooibos tea). A research team led by Johannes Bitter, Martin Pfeiffer and Bernd Nidetzky from the Institute of Biotechnology and Biochemical Engineering at Graz University of Technology (TU Graz) has now been able to determine

which tool the intestinal bacteria use to cleave glycosides and how it works.The microbes use “enzymatic scissors” whose catalytic effect is based on so-called beta-elimination: a special type of reaction for the flexible cleavage of chemical bonds, including those of C-glycosides. The researchers succeeded in deciphering the enzyme’s mode of action at an atomic level and demonstrating the highly efficient cleavage of various glycosides. A manganese metal centre in the enzyme turned out to be essential for the cleavage process and its catalysis. “These enzymatic scissors are a universal catalytic principle that allows the natural product glycosides to be broken down regardless of the type of sugar linkage,” explains Bernd Nidetzky.The investigation of the enzymatic reaction mechanisms and the catalytic steps required not only high-resolution experimental methods such as protein crystallography but also computer-aided methods by which the dynamics of the biochemical processes could be mapped.

来源： TU Graz

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学术文献

1．Mechanisms by which microbial enzymes degrade four mycotoxins and application in animal production: A review(微生物酶降解四种真菌毒素的机制及其在动物生产中的应用综述)

简介：Mycotoxins are toxic compounds that pose a serious threat to animal health and food safety. Therefore, there is an urgent need for safe and efficient methods of detoxifying mycotoxins. As biotechnology has continued to develop, methods involving biological enzymes have shown great promise. Biological enzymatic methods, which can fundamentally destroy the structures of mycotoxins and produce degradation products whose toxicity is greatly reduced, are generally more specific, efficient, and environmentally friendly. Mycotoxin-degrading enzymes can thus facilitate the safe and effective detoxification of mycotoxins which gives them a huge advantage over other methods. This article summarizes the newly discovered degrading enzymes that can degrade four common mycotoxins (aflatoxins, zearalenone, deoxynivalenol, and ochratoxin A) in the past five years, and reveals the degradation mechanism of degrading enzymes on four mycotoxins, as well as their positive effects on animal production. This review will provide a theoretical basis for the safe treatment of mycotoxins by using biological enzyme technology.

来源： Animal Nutrition

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2．Genetic hypogonadal mouse model reveals niche-specific influence of reproductive axis and sex on intestinal microbial communities(性腺功能低下小鼠遗传模型揭示了生殖轴和性别对肠道微生物群落的生态位特异性影响)

简介：Background: The gut microbiome has been linked to many diseases with sex bias including autoimmune, metabolic, neurological, and reproductive disorders. While numerous studies report sex differences in fecal microbial communities, the role of the reproductive axis in this differentiation is

unclear and it is unknown how sex differentiation affects microbial diversity in specific regions of the small and large intestine.Methods: We used a genetic hypogonadal mouse model that does not produce sex steroids or go through puberty to investigate how sex and the reproductive axis impact bacterial diversity within the intestine. Using 16S rRNA gene sequencing, we analyzed alpha and beta diversity and taxonomic composition of fecal and intestinal communities from the lumen and mucosa of the duodenum, ileum, and cecum from adult female (n = 20) and male (n = 20) wild-type mice and female (n = 17) and male (n = 20) hypogonadal mice.Results: Both sex and reproductive axis inactivation altered bacterial composition in an intestinal section and niche-specific manner. Hypogonadism was significantly associated with bacteria from the Bacteroidaceae, Eggerthellaceae, Muribaculaceae, and Rikenellaceae families, which have genes for bile acid metabolism and mucin degradation. Microbial balances between males and females and between hypogonadal and wild-type mice were also intestinal section-specific. In addition, we identified 3 bacterial genera (Escherichia Shigella, Lachnoclostridium, and Eggerthellaceae genus) with higher abundance in wild-type female mice throughout the intestinal tract compared to both wild-type male and hypogonadal female mice, indicating that activation of the reproductive axis leads to female-specific differentiation of the gut microbiome. Our results also implicated factors independent of the reproductive axis (i.e., sex chromosomes) in shaping sex differences in intestinal communities. Additionally, our detailed profile of intestinal communities showed that fecal samples do not reflect bacterial diversity in the small intestine.Conclusions: Our results indicate that sex differences in the gut microbiome are intestinal niche-specific and that sampling feces or the large intestine may miss significant sex effects in the small intestine. These results strongly support the need to consider both sex and reproductive status when studying the gut microbiome and while developing microbial-based therapies.

来源： Biology of Sex Differences

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3．Prediction of Cytochrome P450 Inhibition Using a Deep Learning Approach and Substructure Pattern Recognition（利用深度学习方法和子结构模式识别预测细胞色素P450抑制）

简介： Cytochrome P450 (CYP) is a family of enzymes that are responsible for about 75% of all metabolic reactions. Among them, CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4 participate in the metabolism of most drugs and mediate many adverse drug reactions. Therefore, it is necessary to estimate the chemical inhibition of Cytochrome P450 enzymes in drug discovery and the food industry. In the past few decades, many computational models have been reported, and some provided good performance. However, there are still several issues that should be resolved for these models, such as single isoform, models with unbalanced performance, lack of structural characteristics analysis, and poor availability. In the present study, the deep learning models based on python using the Keras framework and TensorFlow were developed for the chemical inhibition of each CYP isoform. These models were established based on a large data set containing 85715 compounds extracted from the PubChem bioassay database. On external validation, the models provided good AUC values with 0.97, 0.94, 0.94, 0.96, and 0.94 for CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4, respectively. The models can be freely accessed on the Web server named CYPi-DNNpredictor (cypi.sapredictor.cn), and the codes for the model were made open source in the Supporting Information. In addition, we also analyzed the structural characteristics of

chemicals with CYP450 inhibition and detected the structural alerts (SAs), which should be responsible for the inhibition. The SAs were also made available online, named CYPi-SAdetector (cypisa.sapredictor.cn). The models can be used as a powerful tool for the prediction of CYP450 inhibitors, and the SAs should provide useful information for the mechanisms of Cytochrome P450 inhibition.

来源： J Chem Inf Model

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4. Deep flanking sequence engineering for efficient promoter design using DeepSEED（使用DeepSEED进行侧翼序列深度改造实现高效启动子设计）

简介： Designing promoters with desirable properties is essential in synthetic biology. Human experts are skilled at identifying strong explicit patterns in small samples, while deep learning models excel at detecting implicit weak patterns in large datasets. Biologists have described the sequence patterns of promoters via transcription factor binding sites (TFBSs). However, the flanking sequences of cis-regulatory elements, have long been overlooked and often arbitrarily decided in promoter design. To address this limitation, we introduce DeepSEED, an AI-aided framework that efficiently designs synthetic promoters by combining expert knowledge with deep learning techniques. DeepSEED has demonstrated success in improving the properties of Escherichia coli constitutive, IPTG-inducible, and mammalian cell doxycycline (Dox)-inducible promoters. Furthermore, our results show that DeepSEED captures the implicit features in flanking sequences, such as k-mer frequencies and DNA shape features, which are crucial for determining promoter properties.

来源： Nature Communications

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5. Prediction and design of protease enzyme specificity using a structure-aware graph convolutional network（基于结构感知图卷积网络的蛋白酶特异性预测与设计）

简介： Site-specific proteolysis by the enzymatic cleavage of small linear sequence motifs is a key posttranslational modification involved in physiology and disease. The ability to robustly and rapidly predict proteasesubstrate specificity would also enable targeted proteolytic cleavage by designed proteases. Current methods for predicting protease specificity are limited to sequence pattern recognition in experimentally derived cleavage data obtained for libraries of potential substrates and generated separately for each protease variant. We reasoned that a more semantically rich and robust model of protease specificity could be developed by incorporating the energetics of molecular interactions between protease and substrates into machine learning workflows. We present Protein Graph Convolutional Network (PGCN), which develops a physically grounded, structure-based molecular interaction graph representation that describes molecular topology and interaction energetics to predict enzyme specificity. We show that PGCN accurately predicts the specificity landscapes of several variants of two model proteases. Node and edge ablation tests identified key graph elements for specificity prediction, some of which are consistent with known biochemical constraints for protease:substrate recognition. We used a pretrained PGCN model to guide the design of protease libraries for cleaving two noncanonical substrates, and found good

agreement with experimental cleavage results. Importantly, the model can accurately assess designs featuring diversity at positions not present in the training data. The described methodology should enable the structure-based prediction of specificity landscapes of a wide variety of proteases and the construction of tailor-made protease editors for site-selectively and irreversibly modifying chosen target proteins.

来源：PNAS

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6. Protein engineering and iterative multimodule optimization for vitamin B6 production in Escherichia coli（大肠杆菌生产维生素B6的蛋白质工程及迭代多模块优化）

简介：Vitamin B6 is an essential nutrient with extensive applications in the medicine, food, animal feed, and cosmetics industries. Pyridoxine (PN), the most common commercial form of vitamin B6, is currently chemically synthesized using expensive and toxic chemicals. However, the low catalytic efficiencies of natural enzymes and the tight regulation of the metabolic pathway have hindered PN production by the microbial fermentation process. Here, we report an engineered Escherichia coli strain for PN production. Parallel pathway engineering is performed to decouple PN production and cell growth. Further, protein engineering is rationally designed including the inefficient enzymes PdxA, PdxJ, and the initial enzymes Epd and Dxs. By the iterative multimodule optimization strategy, the final strain produces 1.4 g/L of PN with productivity of 29.16 mg/L/h by fed-batch fermentation. The strategies reported here will be useful for developing microbial strains for the production of vitamins and other bioproducts having inherently low metabolic fluxes.

来源：Nature Communications

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7. Saccharomyces cerevisiae as probiotic, prebiotic, synbiotic, postbiotics and parabiotics in aquaculture: An overview（酿酒酵母在水产养殖中的益生菌、益生元、合成菌、后生菌和共生菌研究综述）

简介：Aquaculture is the fastest-growing food production area in the world and this productive activity requires nutrients that fit the needs of cultured species, as well as additives or supplements that help keep organisms healthy. The use of probiotics, prebiotics, synbiotics and parabiotics as an alternative to regular feed has been proved to stimulate good health, safeguard the gut against pathogenic microorganisms, and reduce inflammation. In turn, these compounds have improved the growth, immunity, and gut health of cultured species. Yeasts are a noble product to use in aquaculture (as a whole or as components/pieces) as supplements in animal feed because they are an emerging alternative ingredient because of their nutritional value and some of the bioactive compounds that they contain. Saccharomyces cerevisiae has been the most commonly used yeast in aquaculture, particularly for its health stimulating effects in various cultured species. Most of the research carried out in fishes and crustaceans have confirmed that S. cerevisiae and its cellular components (β-glucan, mannaoligosaccharides, glucooligosaccharides, enzymes) improve growth, morphology and physiology of the host digestive system and also immune responses. However, the

different works on yeast S. cerevisiae applied to aquaculture has not been fully integrated. This scientific knowledge is needed to be subsequently transferred to aquaculture mainly to seafood industrial production. The use of S. cerevisiae allows to replace the use of antibiotics, generating an eco-friendly methodology to control pathogens. Therefore, this review aims to integrate the effects of S. cerevisiae as probiotic, prebiotic, synbiotic, and parabiotic-postbiotics on aquaculture of fishes and crustaceans, and open a new insight to future investigations.

来源： Aquaculture
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