饲料用酶工程

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中国农业科学院农业信息研究所
联系人：彭爽
联系电话：010-82109896
邮箱：agri@ckcest.cn
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➤ **前沿资讯**

1. 南京农业大学消化道微生物团队发现生命早期瘤胃微生物衍生物对反刍动物瘤胃发育影响

简介： 日粮在塑造胃肠道微生物群落方面扮演不可或缺的角色，微生物的代谢产物可作为信号或底物，影响宿主器官的发育和代谢健康。日粮、微生物和宿主之间的相互作用构建了一个复杂的共生体系，其如何共同促进人类和动物的健康已经引起了广泛关注，但它们之间的直接关联在很大程度上仍然是一个未解之谜。在瘤胃中，微生物发挥着多重作用，它们不仅能有效地将膳食纤维转化为重要的代谢前体，例如挥发性脂肪酸（VFA）、微生物蛋白质和维生素，还能显著影响瘤胃复层上皮和肌层的发育。瘤胃微生物的初始定植及其在出生后逐渐稳定的过程会受到不同日粮（如液态奶、谷物固体饲料、干草或这些日粮的组合）的显著影响。然而，目前仍然难以明确在出生后不同日粮营养条件下，瘤胃微生物群究竟如何影响瘤胃壁的发育以及动物的生长过程。研究以哺乳羔羊为研究对象，利用极端化早期营养干预策略构建了瘤胃上皮/肌层的差异化发育表型；基于天然植物成分的微生物产物标准物质质谱库和极性/非极性物质的色谱选择策略，首次鉴定出与瘤胃上皮和肌层发育密切相关的代谢物吲哚-3-甲醛（IA1d）和前列腺素D2（PGD2）；利用宏基因组技术厘清了IA1d和PGD2在瘤胃内的微生物合成路径并筛选出候选代谢微生物菌株，进一步通过单菌体外纯培养试验，发现假长双歧杆菌可代谢色氨酸生成IA1d，白色念珠球菌具有生成PGD2的能力；利用转录组技术锚定瘤胃差异化发育的信号调控通路，体内外试验揭示了IA1d通过激活Wnt/β-catenin信号通路促进瘤胃上皮发育，PGD2依赖Ca2+信号通路调控瘤胃肌层发育。研究结果加深了对生命早期日粮-微生物-宿主互作的理解，首次明确了瘤胃特定菌株及其下游代谢物与瘤胃生理的直接联系，为幼龄反刍动物开食料添加剂的开发应用提供新思路。

来源： 南京农业大学

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2. 西北农林科技大学姚军虎团队在青年奶山羊后肠道健康调控的微生物机制研究领域取得新进展

简介： 研究以青年奶山羊为模型，利用整粒和粉碎玉米构建低肠内淀粉日粮（LES）和高肠内淀粉日粮（HES）。选取40只健康、断奶的3月龄奶山羊，随机均分为两组，分别饲喂LES日粮（n="20）和HES日粮（n=20）。通过结合结肠转录组、代谢组、宏基因组和组织学形态学、免疫荧光染色等分析发现：HES会导致胆汁酸积聚，并减弱宿主黏膜MUC2生物合成及上皮紧密连接，从而使腔内大分子突破物理屏障。同时，结肠微生物群及其代谢产物通过促进抗原呈递和促进TH2介导的炎症过程，刺激了结肠炎症和组织损伤发生，抑制结肠水分吸收能力。研究还采用线性混合效应模型计算了微生物（细菌和真菌）及其代谢物对结肠功能和病理变化的组学可解释性，系统揭示了山羊模型中结肠稳态破坏的微生物机制，并鉴定了真菌在其中发挥的潜在调控作用。本研究解析幼龄反刍动物因淀粉过量而导致后肠失调的潜在机制，并针对性改变玉米加工方式来调控后肠道淀粉含量，改善微生物区系并调控后肠道健康。相关发现对于开发新的营养策略以缓解幼年反刍动物因过量淀粉引起的后肠道功能障碍和微生态失衡具有重要意义。

来源： 西北农林科技大学

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学术文献

1. Engineering Saccharomyces cerevisiae for targeted hydrolysis and fermentation of glucuronoxylan through CRISPR/Cas9 genome editing（利用CRISPR/Cas9基因组编辑技术工程酿酒酵母，实现葡萄糖醛酸木聚糖的靶向水解和发酵）

简介：BackgroundThe abundance of glucuronoxylan (GX) in agricultural and forestry residual side streams positions it as a promising feedstock for microbial conversion into valuable compounds. By engineering strains of the widely employed cell factory Saccharomyces cerevisiae with the ability to directly hydrolyze and ferment GX polymers, we can avoid the need for harsh chemical pretreatments and costly enzymatic hydrolysis steps prior to fermentation. However, for an economically viable bioproduction process, the engineered strains must efficiently express and secrete enzymes that act in synergy to hydrolyze the targeted polymers.ResultsThe aim of this study was to equip the xylose-fermenting S. cerevisiae strain CEN.PK XXX with xylanolytic enzymes targeting beechwood GX. Using a targeted enzyme approach, we matched hydrolytic enzyme activities to the chemical features of the GX substrate and determined that besides endo-1,4-β-xylanase and β-xylosidase activities, α-methyl-glucuronidase activity was of great importance for GX hydrolysis and yeast growth. We also created a library of strains expressing different combinations of enzymes, and screened for yeast strains that could express and secrete the enzymes and metabolize the GX hydrolysis products efficiently. While strains engineered with BmXyn11A xylanase and XylA β-xylosidase could grow relatively well in beechwood GX, strains further engineered with Agu115 α-methyl-glucuronidase did not display an additional growth benefit, likely due to inefficient expression and secretion of this enzyme. Co-cultures of strains expressing complementary enzymes as well as external enzyme supplementation boosted yeast growth and ethanol fermentation of GX, and ethanol titers reached a maximum of 1.33 g L− 1 after 48 h under oxygen limited condition in bioreactor fermentations.ConclusionThis work underscored the importance of identifying an optimal enzyme combination for successful engineering of S. cerevisiae strains that can hydrolyze and assimilate GX. The enzymes must exhibit high and balanced activities, be compatible with the yeast's expression and secretion system, and the nature of the hydrolysis products must be such that they can be taken up and metabolized by the yeast. The engineered strains, particularly when co-cultivated, display robust growth and fermentation of GX, and represent a significant step forward towards a sustainable and cost-effective bioprocessing of GX-rich biomass. They also provide valuable insights for future strain and process development targets.

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2. Gut microbiota-gonadal axis: the impact of gut microbiota on reproductive functions（肠道微生物-性腺轴：肠道微生物对生殖功能的影响）

简介：The influence of gut microbiota on physiological processes is rapidly gaining attention globally. Despite being under-studied, there are available data demonstrating a gut microbiota-gonadal cross-talk,

and the importance of this axis in reproduction. This study reviews the impacts of gut microbiota on reproduction. In addition, the possible mechanisms by which gut microbiota modulates male and female reproduction are presented. Databases, including Embase, Google scholar, Pubmed/Medline, Scopus, and Web of Science, were explored using relevant key words. Findings showed that gut microbiota promotes gonadal functions by modulating the circulating levels of steroid sex hormones, insulin sensitivity, immune system, and gonadal microbiota. Gut microbiota also alters ROS generation and the activation of cytokine accumulation. In conclusion, available data demonstrate the existence of a gut microbiota-gonadal axis, and role of this axis on gonadal functions. However, majority of the data were compelling evidences from animal studies with a great dearth of human data. Therefore, human studies validating the reports of experimental studies using animal models are important.

来源：Frontiers in Immunology

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3. Machine Learning Integrating Protein Structure, Sequence, and Dynamics to Predict the Enzyme Activity of Bovine Enterokinase Variants（整合蛋白质结构、序列和动力学的机器学习来预测牛肠激酶变异体的酶活性）

简介：Despite recent advances in computational protein science, the dynamic behavior of proteins, which directly governs their biological activity, cannot be gleaned from sequence information alone. To overcome this challenge, we propose a framework that integrates the peptide sequence, protein structure, and protein dynamics descriptors into machine learning algorithms to enhance their predictive capabilities and achieve improved prediction of the protein variant function. The resulting machine learning pipeline integrates traditional sequence and structure information with molecular dynamics simulation data to predict the effects of multiple point mutations on the fold improvement of the activity of bovine enterokinase variants. This study highlights how the combination of structural and dynamic data can provide predictive insights into protein functionality and address protein engineering challenges in industrial contexts.

来源：Journal of Chemical Information and Modeling

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4．Discovery of Toxin-Degrading Enzymes with Positive Unlabeled Deep Learning（利用阳性非标记深度学习发现毒素降解酶）

简介：Identifying functional enzymes for the catalysis of specific biochemical reactions is a major bottleneck in the de novo design of biosynthesis and biodegradation pathways. Conventional methods based on microbial screening and functional metagenomics require long verification periods and incur high experimental costs; recent data-driven methods apply only to a few common substrates. To enable rapid and high-throughput identification of enzymes for complex and less-studied substrates, we propose a robust enzyme's substrate promiscuity prediction model based on positive unlabeled learning. Using this model, we identified 15 new degrading enzymes specific for the mycotoxins ochratoxin A and zearalenone, of which six could degrade >90% mycotoxin content within 3 h. We anticipate that this model will serve as a useful tool for identifying new functional enzymes and understanding the nature of biocatalysis, thereby advancing the fields of synthetic biology, metabolic engineering, and pollutant biodegradation.

5．DIProT: A deep learning based interactive toolkit for efficient and effective Protein design（DIProT：一个基于深度学习的交互式工具箱，用于高效的蛋白质设计）

简介：The protein inverse folding problem, designing amino acid sequences that fold into desired protein structures, is a critical challenge in biological sciences. Despite numerous data-driven and knowledge-driven methods, there remains a need for a user-friendly toolkit that effectively integrates these approaches for in-silico protein design. In this paper, we present DIProT, an interactive protein design toolkit. DIProT leverages a non-autoregressive deep generative model to solve the inverse folding problem, combined with a protein structure prediction model. This integration allows users to incorporate prior knowledge into the design process, evaluate designs in silico, and form a virtual design loop with human feedback. Our inverse folding model demonstrates competitive performance in terms of effectiveness and efficiency on TS50 and CATH4.2 datasets, with promising sequence recovery and inference time. Case studies further illustrate how DIProT can facilitate user-guided protein design.

6．The action of endo-xylanase and endo-glucanase on cereal cell wall polysaccharides and its implications for starch digestion kinetics in an in vitro poultry model（内切木聚糖酶和内切葡聚糖酶对谷物细胞壁多糖的作用及其对体外家禽模型中淀粉消化动力学的影响）

简介：Endo-xylanase and endo-glucanase are supplemented to poultry diets in order to improve nutrient digestion and non-starch polysaccharide (NSP) fermentation. Here, the action of these enzymes on alcohol insoluble solids (AIS) from wheat and maize grains as well as its implications for starch digestion in milled grains were evaluated in vitro, under conditions mimicking the poultry digestive tract. For wheat AIS, GH11 endo-xylanase depolymerized soluble arabinoxylan (AX) during the gizzard phase, and proceeded to release insoluble AX under small intestine conditions. At the end of the in vitro digestion (480 min), the endo-xylanase, combined with a GH7 endo-β-1,4-glucanase, released 30.5 % of total AX and 18.1 % of total glucan in the form of arabinoxylo- and gluco-oligosaccharides, as detected by HPAEC-PAD and MALDI-TOF-MS. For maize AIS, the combined enzyme action released 2.2 % and 7.0 % of total AX and glucan, respectively. Analogous in vitro digestion experiments of whole grains demonstrated that the enzymatic release of oligomers coincided with altered grain microstructure, as examined by SEM. In the present study, cell wall hydrolysis did not affect in vitro starch digestion kinetics for cereal grains. This study contributes to understanding the action of feed enzymes on cereal NSP under conditions mimicking the poultry digestive tract.

7．**Harnessing generative AI to decode enzyme catalysis and evolution for enhanced engineering**(利用生成式人工智能解码酶催化与进化，促进酶工程设计)

简介：Enzymes, as paramount protein catalysts, occupy a central role in fostering remarkable progress across numerous fields. However, the intricacy of sequence-function relationships continues to obscure our grasp of enzyme behaviors and curtails our capabilities in rational enzyme engineering. Generative artificial intelligence (AI), known for its proficiency in handling intricate data distributions, holds the potential to offer novel perspectives in enzyme research. Generative models could discern elusive patterns within the vast sequence space and uncover new functional enzyme sequences. This review highlights the recent advancements in employing generative AI for enzyme sequence analysis. We delve into the impact of generative AI in predicting mutation effects on enzyme fitness, catalytic activity and stability, rationalizing the laboratory evolution of de novo enzymes, and decoding protein sequence semantics and their application in enzyme engineering. Notably, the prediction of catalytic activity and stability of enzymes using natural protein sequences serves as a vital link, indicating how enzyme catalysis shapes enzyme evolution. Overall, we foresee that the integration of generative AI into enzyme studies will remarkably enhance our knowledge of enzymes and expedite the creation of superior biocatalysts.

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8．**The relationship between vitamin A status and oxidative stress in animal production**(动物生产中维生素A状态与氧化应激的关系)（ESI热点论文）

简介：Oxidative stress is caused by an imbalance between the production of harmful oxygen molecules and the body's ability to repair their detrimental implications, leading to reduced growth rates, increased disease susceptibility, and decreased reproductive performance in animals. Vitamin A, comprising retinol, retinal, and retinoic acid, is crucial for normal growth, reproduction, and vision. Vitamin A possesses antioxidant properties by directly scavenging reactive oxygen species, boosting antioxidant enzyme activity, and promoting antioxidant defence mechanisms. Numerous studies have shown that livestock with adequate levels of vitamin A in their diet experience reduced oxidative stress compared to those with vitamin A deficiency. Moreover, vitamin A supplementation can mitigate oxidative stress in animals exposed to stressful conditions like heat stress. Adequate vitamin A status in livestock through dietary interventions and improved animal management practices can significantly benefit animal health and well-being. However, further research is still needed to optimize dosing strategies and fully understand the relationship between vitamin A and oxidative stress in different animal species and production systems. Therefore, continued research efforts are essential to fully harness the potential of vitamin A as an effective tool for mitigating oxidative stress and improving animal welfare.

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