杂粮健康功效机制及本实验室研究思路

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全谷物、杂粮、粗粮内涵与外延

按照加工程度分：精制谷物、全谷物

按照口感分：细粮、粗粮

按照产量分：主粮、杂粮

杂粮可以精制、可以细作，满足适口性，功能呢？

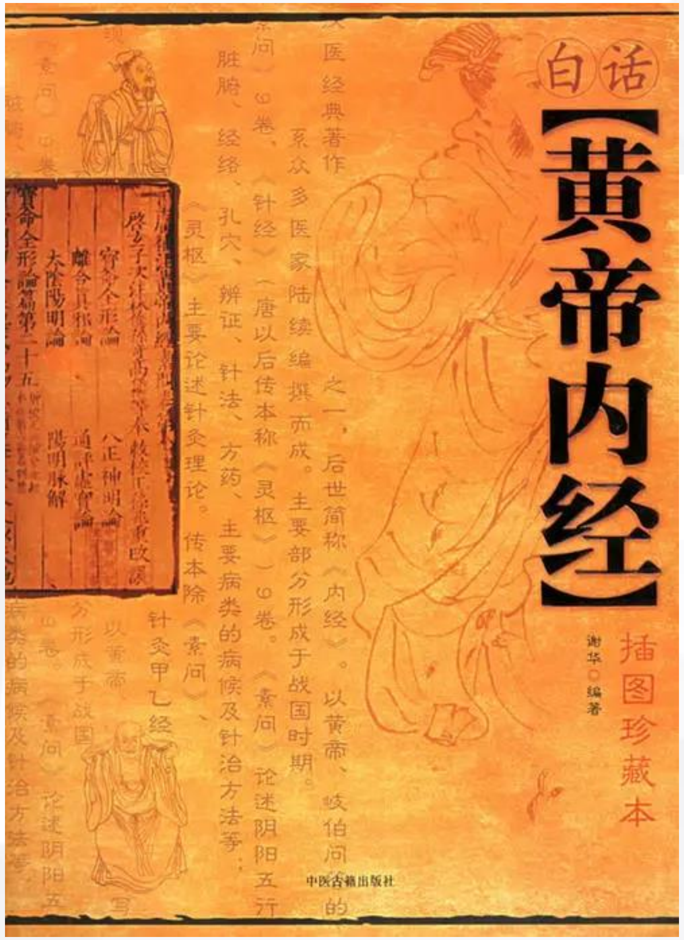
汇报提纲

- 杂粮健康功效机制
  - 大数据
  - 组分
  - 精准营养
  - 加工过程
- 本实验室青稞研究进展

中国农业大学
China Agricultural University

FSNE College
食品科学与营养工程学院
COLLEGE OF FOOD SCIENCE & NUTRITIONAL ENGINEERING

杂粮健康功效机制-大数据



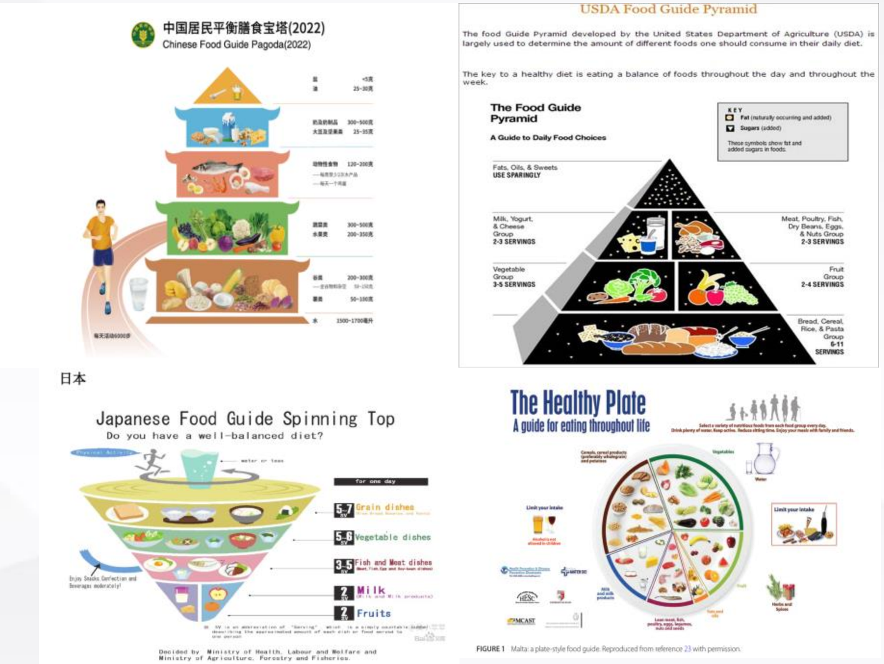
公元前 722 ~前 221 年?

五谷为养，五果为助，五畜为益，五菜为充，气味合而服之，以补精益气

⇨

养什么?

怎么合?

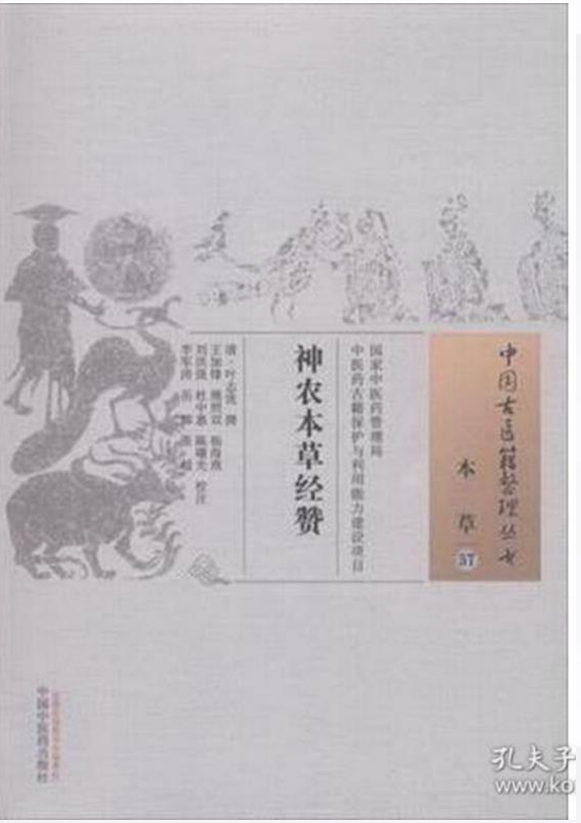


Anna Herforth, et al.，A Global Review of Food-Based Dietary Guidelines，American Society for Nutrition, 2019;10:590–605; doi: https://doi.org/10.1093/advances/nmy130.

阴阳五行：外界与人体的相关性研究

中国最早的医学典籍，基本素材源于中国古人对生命现象的长期观察、大量的临床实践以及简单的解剖学知识。包括阴阳五行、经络、养生、脉象、病因、病机、诊法等

杂粮健康功效机制-大数据



中医四大经典著作之一
东汉时期（公元25年 ~ 公元220年）

小米：主养肾气,去胃脾中热,益气；陈者,味苦,主胃热,消渴,利小便。

青稞：补中益气；主脾胃气虚；四肢无力，大便稀溏。

荞麦：开胃宽肠，下气消积；治绞肠痧，肠胃积滞，慢性泄泻，噤口痢疾，赤游丹毒，痈疽发背，蓑（gǔn）疬，汤火灼伤。

绿豆：清热解毒，消暑，利水。治暑热烦渴，水肿，泻利，丹毒，痈肿，解热药毒。

红豆：性偏凉，味甘。能促进心脏血管的活化，利尿；健胃生津、祛湿益气。

山药：味甘,性平 ,入脾、肺、肾经。

1552年- 1578年

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杂粮健康功效机制-大数据

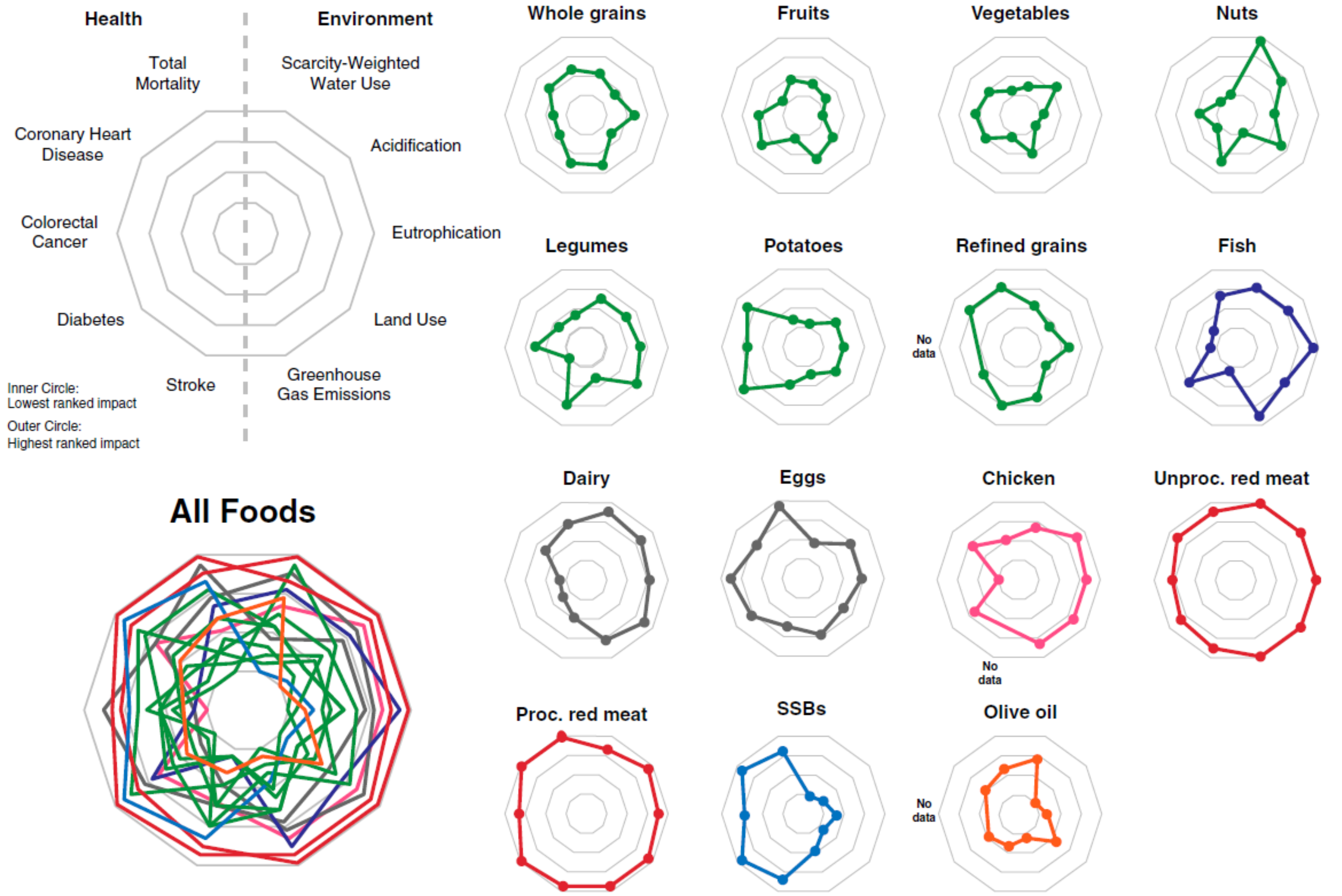

Fig. 2. Radar plots of rank-ordered health and environmental impacts per serving of food consumed per day. Data are plotted on a rank order axis such that the food group with the lowest mean impact for a given health or environmental indicator (lowest is best health or environmental outcome) has a value of 1 (innermost circle), and the food group with the highest mean impact for a given indicator has a value of 15 (outermost circle). The *Left* side of each radar plots shows health outcomes; the *Right* side shows environmental impacts. A food group with low mean impacts for the 10 outcomes would have a small circular radar plot, and one with high impact for the 10 outcomes would have a large circular radar plot. The "all foods" radar plot combines data for the 15 food groups into a single plot. Data used to create the plot are available in Dataset S1. SSBs are sugar-sweetened beverages. The association between total mortality and olive oil was estimated by weighting disease-specific contributions (e.g., CHD, stroke, and diabetes) to mortality by disease-specific relative risk (2).

Michael A Clarka, et al.,Multiple health and environmental impacts of foods, PNAS, 2019,116(46):23357-23362

杂粮健康功效机制-大数据

185项前瞻性研究和58项临床试验(4635名成年参与者)的不到1.35亿人年的数据。

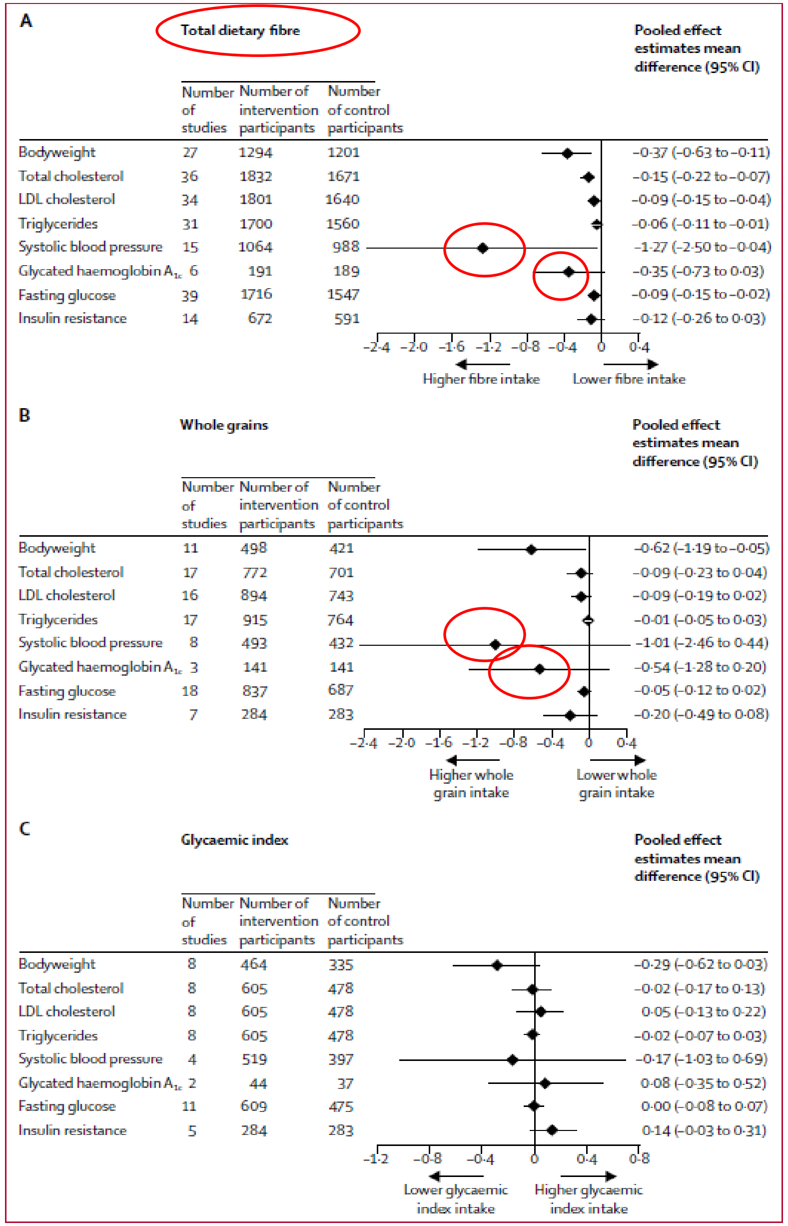

Figure 4: **Summary forest plots of key outcomes from clinical trials**
(A) Higher compared with lower total fibre intakes. (B) Higher compared with lower whole grain intakes. (C) Comparison of diets characterised by lower compared with higher glycaemic index foods.

最高膳食纤维消费者与最低膳食纤维消费者进行比较时，全因和心血管相关的死亡率、冠心病的发病率、中风的发病率和死亡率、2型糖尿病和结肠直肠癌的发病率降低了15-30%。

全谷物摄入方面也观察到了类似的结果。

在比较以低血糖指数或高血糖负荷为特征的饮食效果时，观察数据发现风险降低幅度较小或没有降低。

Andrew Reynolds，et al.，Carbohydrate quality and human health: a series of systematic reviews and meta-analyses, Lancet, 2019; 393: 434–45

汇报提纲

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  - 大数据：杂粮有健康功效
  - 组分
  - 精准营养
  - 加工过程
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杂粮健康功效机制-组分-调节血糖

1.植物多糖增强肝脏葡萄糖激酶活性及抑制 α-糖苷酶活性

2. 膳食纤维增加食物的黏滞性，限制营养物质向胃肠道黏膜表面弥散，延缓或阻碍葡萄糖在肠道的吸收

3.黄酮类物质通过抗氧化机制来降低糖尿病患者的血糖值

降低了类胰岛素生长因子结合蛋白 3、血 管 内 皮 生 长 因 子VEGF、Hb A1c，NF-κB 和 TNFα相关基因的表达

李笑蕊，等. 杂粮健康功效和作用机理的分子营养学解析，粮油食品科技，2016，24(1):46-49 DOI:10.16210/j.cnki.1007-7561.2016.01.011

杂粮健康功效机制-组分-调节血脂

调节血脂

- 减少膳食中胆固醇的吸收、影响机体中胆固醇的代谢、促进胆固醇的排泄，降低血浆中胆固醇水平
- 增加食物在肠道内的过渡时间、延缓胃排空、减缓或降低脂肪的吸收等机制降低血浆中甘油三酯水平。

上调体内脂肪连接蛋白和脂肪细胞分化过程中的关键因子 PPARγ 的表达水平，阻止细胞外调节蛋白激酶erk1/2 的激活来抑制高脂饮食所导致的脂肪积累。

下调多个脂肪酸合成基因，如FAS、ACC 和 SREBP-1 等的表达，降低体内脂肪积累；

下调胆固醇合成基因 SREBP -2的表达，降低体内胆固醇浓度。

李笑蕊，等. 杂粮健康功效和作用机理的分子营养学解析，粮油食品科技，2016，24(1):46-49 DOI:10.16210/j.cnki.1007-7561.2016.01.011

过氧化物酶体增殖物激活受体PPARγ；脂肪酸合成酶 FAS；乙酰辅酶A羧化酶ACC；固醇调节元件结合蛋白SREBP

杂粮健康功效机制-组分-调节血压

缺乏叶酸和VB12，导致同型半胱氨酸无法重新甲基化为蛋氨酸；

缺乏VB6影响胱硫醚 β-合成酶将同型半胱氨酸转硫化为半胱氨酸；

同型半胱氨酸对血管内皮有毒性作用，可增加血小板黏附性并促进凝血因子的改变，导致血压异常。

抑制脂蛋白氧化和血管细胞氧化损伤的作用，干预动脉粥样硬化和血栓形成过程，从而改善血压状况。

李笑蕊，等. 杂粮健康功效和作用机理的分子营养学解析，粮油食品科技，2016，24(1):46-49 DOI:10.16210/j.cnki.1007-7561.2016.01.011

杂粮健康功效机制-组分-防抗肿瘤

黄酮类

降低PI3K/Akt 途径的活性来抑制结肠癌细胞的增殖;

通过诱导 Wnt5a的表达，来影响结肠癌细胞Wnt信号传导途径的活性，从而影响结肠癌细胞的活性;

抑制FOXO3 蛋白表达，显著提高肿瘤抑制因子p53 的表达活性，从而抑制肿瘤细胞的增殖活性

多糖

诱导细胞产生分化因子抑制人白血病细胞 THP-1的增殖活性

B-葡聚糖

肠道发酵产生短链脂肪酸(丁酸),丁酸可以减少肿瘤细胞的生长，诱导癌细胞的分化，抑制肿瘤基因，诱导癌细胞凋亡;

降低葡萄糖苷酶、葡萄糖醛酸酶和脲酶等微生物代谢酶的活性，这些酶都是结肠癌的诱发因子

蛋白

降低人乳腺癌细胞 bcl-2 蛋白的表达水平，同时提高 Fas 蛋白的表达水平，bcl -2 蛋白被认为具有细胞凋亡抑制作用， Fas 属于肿瘤坏死因子受体蛋白家族，具有诱导细胞凋亡的作用

李笑蕊，等. 杂粮健康功效和作用机理的分子营养学解析，粮油食品科技，2016，24(1):46-49 DOI:10.16210/j.cnki.1007-7561.2016.01.011

杂粮健康功效机制-组分-抗氧化

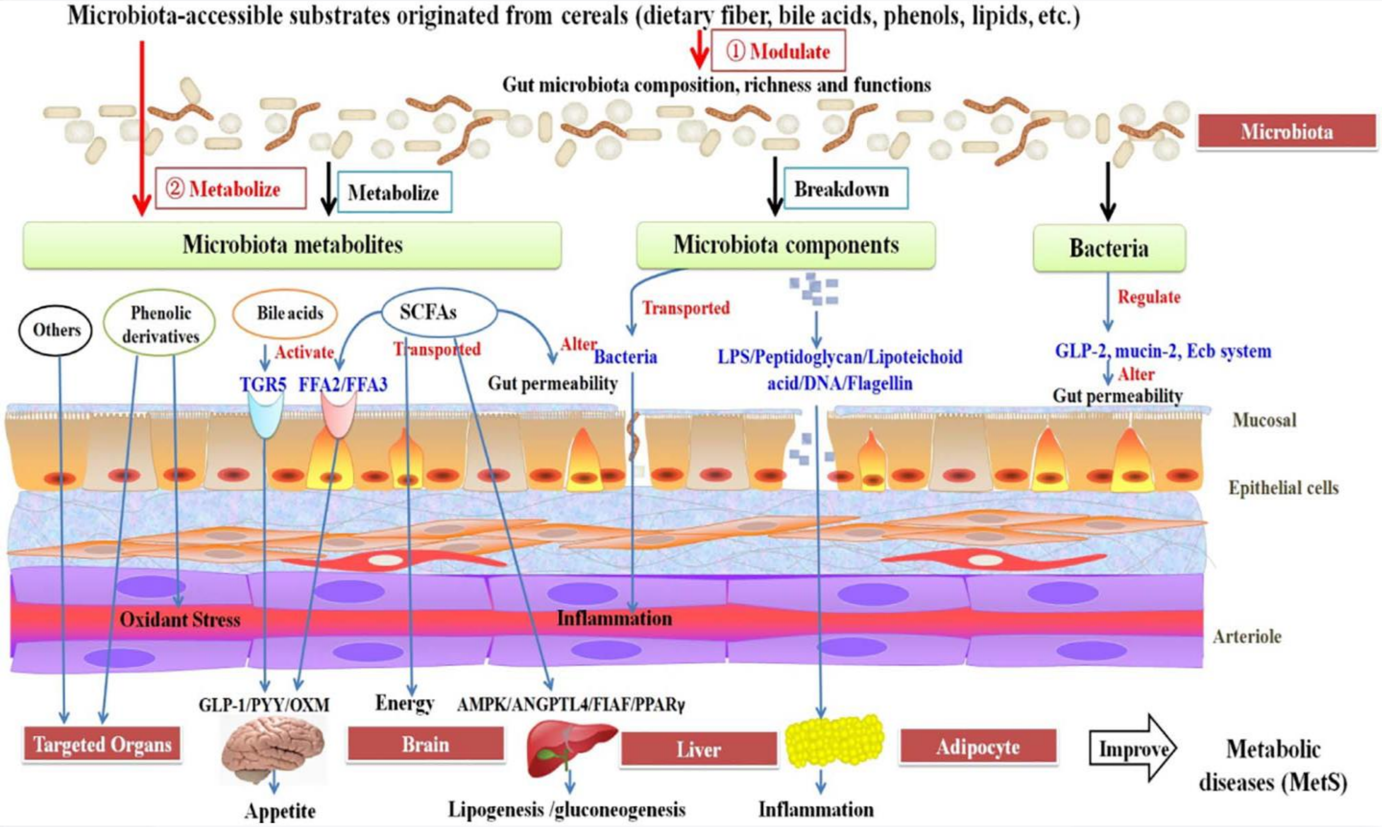
抑制卵磷脂脂质过氧化、肝自发性脂质过氧化和 $Fe^{2+}-H_2O_2$ 诱导的肝脂质过氧化；

提高肝细胞抗氧化酶如 CAT、GR、GP_X、SOD 的酶活性，从而缓解胰岛素的耐受性

超氧化物歧化酶SOD；过氧化氢酶CAT；谷胱甘肽还原酶GR、谷胱甘肽过氧化物酶GPX

李笑蕊，等. 杂粮健康功效和作用机理的分子营养学解析，粮油食品科技，2016，24(1)：46-49 DOI:10.16210/j.cnki.1007-7561.2016.01.011

杂粮健康功效机制-组分-肠道微生物



Lingxiao Gong et al.，Whole cereal grains and potential health effects: Involvement of the gut microbiota，Food Research International, 2018,103:84-102

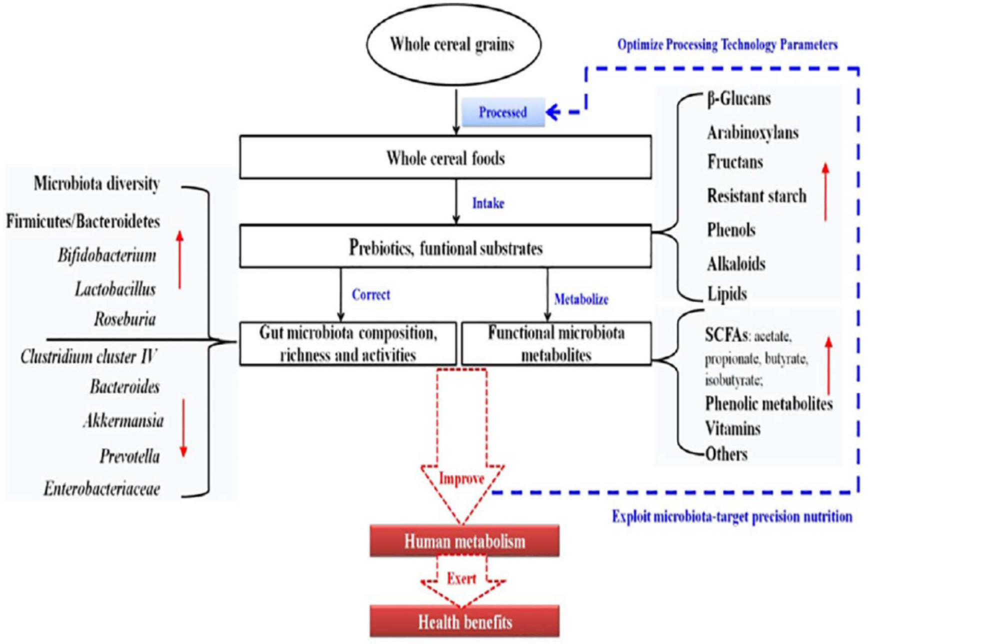


Fig. 2. Development of whole cereal grain foods for microbiota-target precision nutrition to prevent metabolic disease. The microbiota-target whole cereal grain foods may correct the ecology unbalance in the gut or increase functional microbiota metabolites to improve the human metabolism.

提供益生元调节肠道微生物群的组成、丰富度和活动；

微生物代谢产物，如短链脂肪酸等，参与控制宿主免疫、食欲、脂肪生成、糖异生、肠道屏障和氧化应激多个信号通路；

降低肠道pH值，为肠上皮细胞提供能量，增加粘蛋白的产生，从而抑制致病微生物的生存。

China Agricultural University

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汇报提纲

- 杂粮健康功效机制
  - 大数据：杂粮有健康功效
  - 组分：抗氧化、调控基因、肠道微生物
  - 精准营养
  - 加工过程
- 本实验室青稞研究进展

杂粮健康功效机制- 精准营养-适量

在全谷物、水果、坚果、乳制品和红肉与冠心病之间存在明显的非线性剂量-反应关系。

全谷物、蔬菜、水果、坚果、豆类、乳制品、鱼、红肉和加工肉类、鸡蛋和含糖饮料的最佳摄入量可显著降低冠心病、中风和心衰的风险。

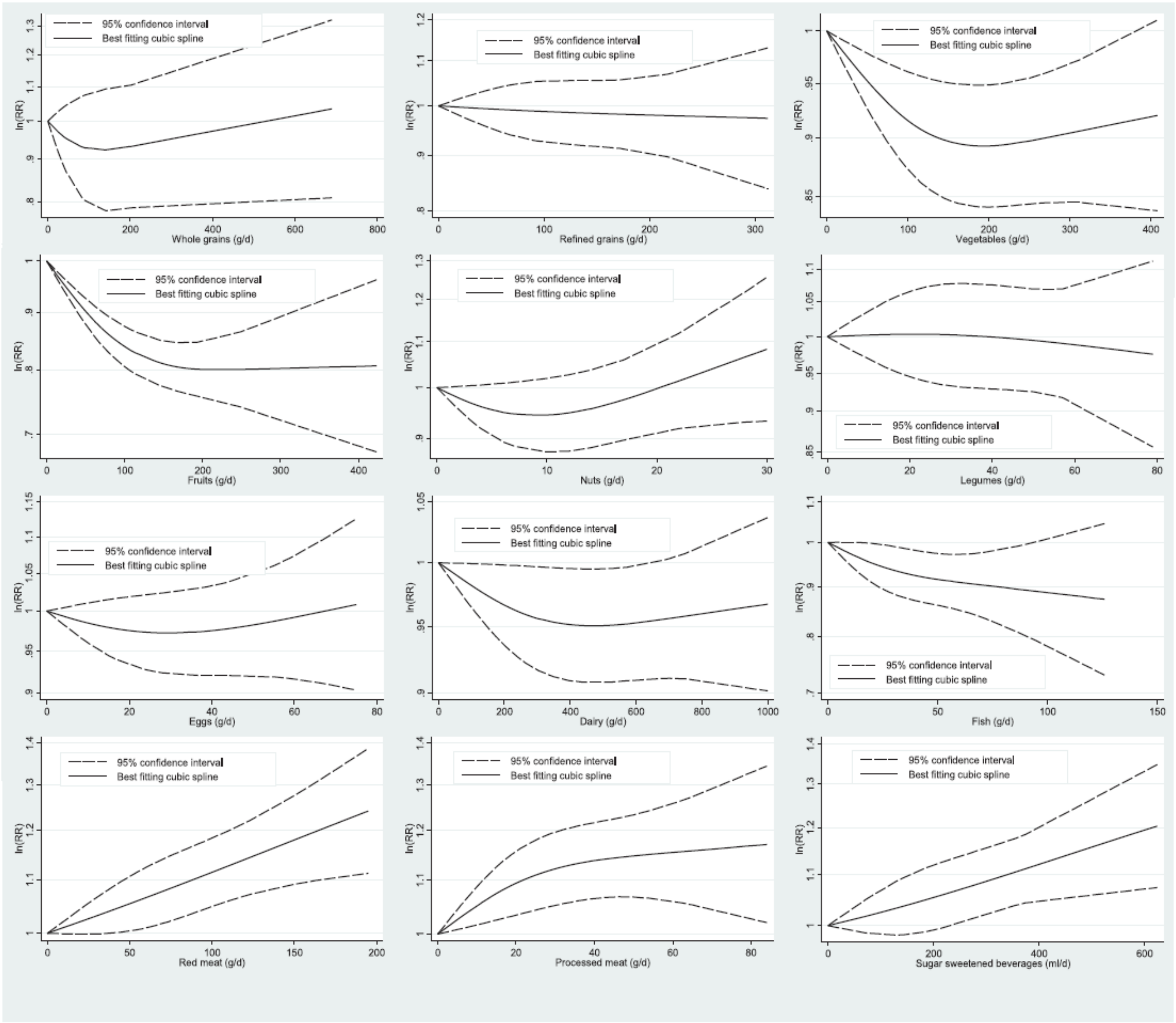
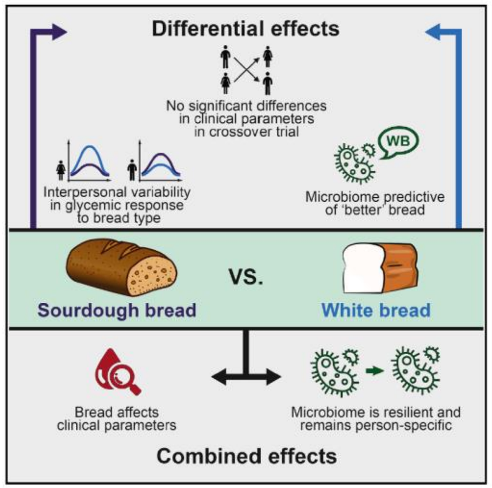
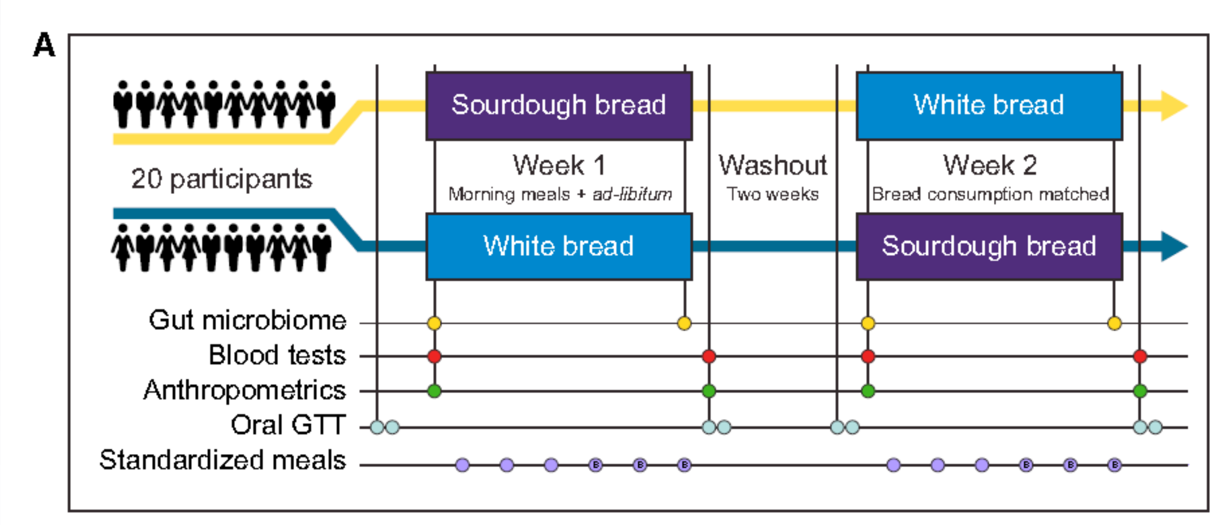


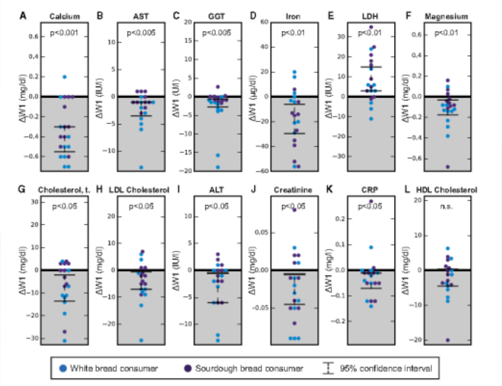
Figure 3. Non-linear dose-response relationship between daily intakes whole grains (p for non-linearity = 0.77; n = 3 studies), refined grains (p for non-linearity = 0.42; n = 4 studies), vegetables (p for non-linearity = 0.03; n = 8 studies), fruits (p for non-linearity = 0.54; n = 8 studies), nuts (p for non-linearity = 0.05; n = 5 studies), legumes (p for non-linearity = 0.08; n = 5 studies), eggs (p for non-linearity = 0.39; n = 9 studies), dairy (p for non-linearity = 0.71; n = 8 studies), fish (p for non-linearity = 0.37; n = 15 studies), red meat (p for non-linearity = 0.91; n = 6 studies), processed meat (p for non-linearity = 0.65; n = 6 studies), and sugar sweetened beverages (p for non-linearity = 0.83; n = 6 studies) and risk of stroke.

Angela Bechthold,et al., Food groups and risk of coronary heart disease, stroke and heart failure: A systematic review and dose-response meta-analysis of prospective studies, Critical Reviews in Food Science and Nutrition, 2019, 59:7, 1071-1090, DOI: 10.1080/10408398.2017.1392288

杂粮健康功效机制- 精准营养-个体







- 发现问题：只有少数临床指标有所改善，额外的大规模介入交叉试验显示对这些疾病风险标志物没有显著影响。
- 实验结论：对两种面包的血糖反应中，人与人之间存在显著且高度显著的差异。面包代谢和肠道微生物组的显著个性化，表明了解饮食的影响需要整合人的特定因素。

Tal Korem, et al., Cell Metabolism, 2017,25,1243-1253

杂粮健康功效机制- 精准营养- 谷物类型

健康人群中，不同类型的全谷物摄入量与全因死亡率和死因特异性死亡率的关系

All-cause mortality	Quartile 1 MRR*	Quartile 2 MRR*	Quartile 2 95 % CI	Quartile 3 MRR*	Quartile 3 95 % CI	Quartile 4 MRR*	Quartile 4 95 % CI	$P_{trend\ over\ quartiles}$
Women (deaths = 3658)†								
MRR in quartile 2, 3 and 4 compared to quartile 1 (reference) of whole-grain product intake								
Breakfast cereals	1	0·77	0·67, 0·89	0·79	0·71, 0·88	0·75	0·69, 0·82	< 0·0001
Non-white bread	1	0·84	0·76, 0·93	0·74	0·65, 0·84	0·72	0·65, 0·81	< 0·0001
Crisp bread	1	0·90	0·82, 0·99	0·86	0·78, 0·94	0·91	0·81, 1·01	0·012
Total whole-grain products	1	0·78	0·71, 0·86	0·77	0·71, 0·85	0·68	0·62, 0·75	< 0·0001
MRR in quartile 2, 3 and 4 compared to quartile 1 (reference) of whole-grain type intake								
Oat	1	0·85	0·78, 0·93	0·74	0·67, 0·82	0·78	0·70, 0·87	< 0·0001
Rye	1	0·92	0·84, 1·01	0·81	0·73, 0·90	0·93	0·83, 1·03	0·134
Wheat	1	0·72	0·65, 0·79	0·65	0·58, 0·72	0·63	0·53, 0·74	< 0·0001
Total whole-grain types‡	1	0·80	0·73, 0·87	0·74	0·67, 0·81	0·74	0·67, 0·81	< 0·0001
Men (deaths = 4181)†								
MRR in quartile 2, 3 and 4 compared to quartile 1 (reference) of whole-grain product intake								
Breakfast cereals	1	0·92	0·82, 1·04	0·82	0·76, 0·89	0·74	0·68, 0·81	< 0·0001
Non-white bread	1	0·92	0·83, 1·03	0·85	0·75, 0·95	0·78	0·69, 0·88	< 0·0001
Crisp bread	1	0·97	0·89, 1·06	0·94	0·86, 1·02	1·03	0·90, 1·17	0·617
Total whole-grain products	1	0·87	0·80, 0·95	0·74	0·68, 0·81	0·75	0·68, 0·81	< 0·0001
MRR in quartile 2, 3 and 4 compared to quartile 1 (reference) of whole-grain type intake								
Oat	1	0·87	0·80, 0·95	0·85	0·77, 0·94	0·76	0·69, 0·85	< 0·0001
Rye	1	0·91	0·83, 1·00	0·82	0·74, 0·91	0·86	0·78, 0·95	0·001
Wheat	1	0·87	0·80, 0·95	0·76	0·69, 0·84	0·71	0·64, 0·78	< 0·0001
Total whole-grain types‡	1	0·82	0·75, 0·90	0·72	0·66, 0·78	0·75	0·68, 0·82	< 0·0001

Johnsen NF, et al *Br J Nutr* 2015;114:608-23.

杂粮健康功效机制- 精准营养- 指标

150 g石磨全麦粉制作馕饼替代部分主食对肥胖者体重的影响。招募48名肥胖者和20名正常体重者,48名肥胖者随机分2组为干预组（27名）和对照组（21名）,正常体重者作为正常对照组（20名），为期3个月的膳食干预。

指标	体质指数（BMI）	腰臀比	体重（Kg）	腰围（cm）	C-反应蛋白（mg/L）
干预前	32.43±3.04	0.94±0.06	86.44±12.67	106.19±9.44	2.99±2.22
干预后	31.80±3.07	0.91±0.06	84.76±12.41	103.84±9.14	2.21±1.86

干预后可降低肥胖人群体重和腰围；
对腹型肥胖作用明显；
机制可能通过降低机体低度炎症反应而发挥作用。

TC、TG、LDL-C均显著升高, HDL-C降低;
干预组与肥胖对照组空腹血糖（FBG）升高;
空腹胰岛素（FINS）及HOMA-IR干预后无显著变化;
全麦粉并没有显著改善机体胰岛素抵抗状态。

木海热姆·杰力力，职业与健康，2020，2338-2342

杂粮健康功效机制- 精准营养

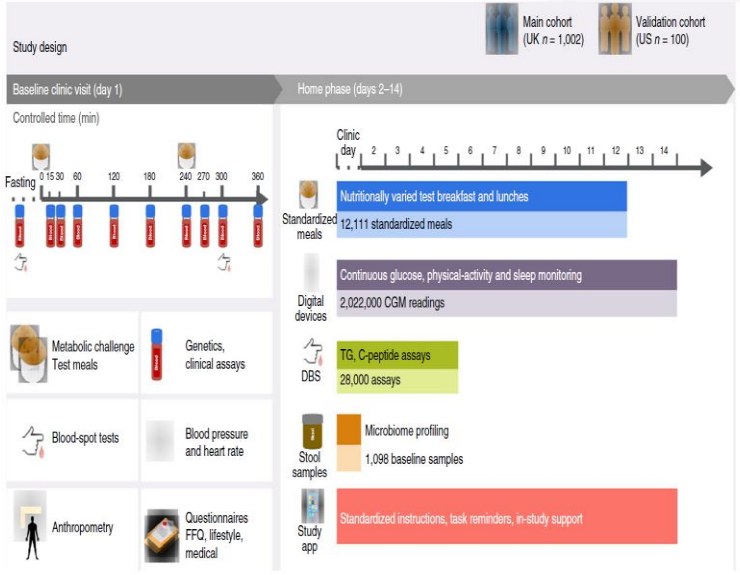


Fig. 1 | Experimental design. The PREDICT 1 study comprised a primary UK-based cohort (n_{max} = 1,002 participants) and an independent US-based validation cohort (n_{max} = 100 participants). TG, triglyceride.

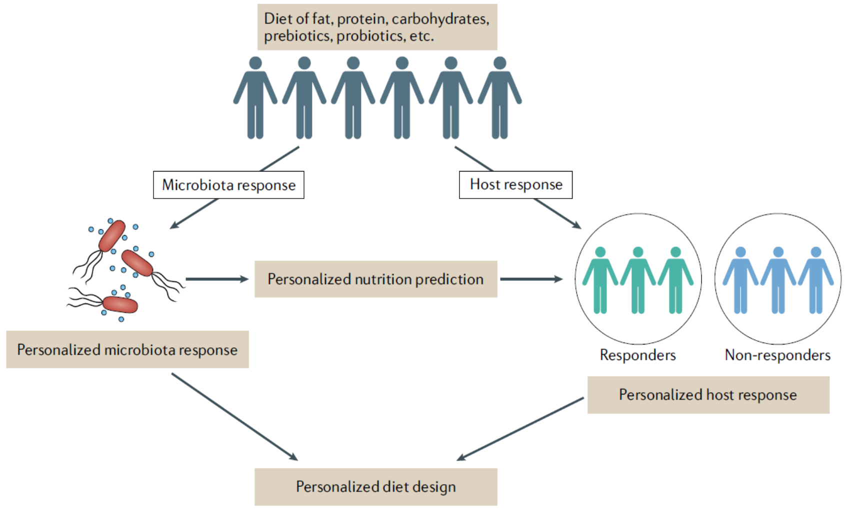


Fig. 2 | **Personalized microbiota and host responses to diet.** Diet changes the gut microbiome composition and function in a person-specific manner, which is associated with the specific pre-intervention microbiome profile. Diet also results in highly individualized variation in host responses (for example, glycaemic response), which can be accurately predicted by the host's unique microbiome signatures. By utilizing both aspects, personalized nutritional strategies can be developed in order to modify an individual's microbiome and further improve the response to a specific diet.

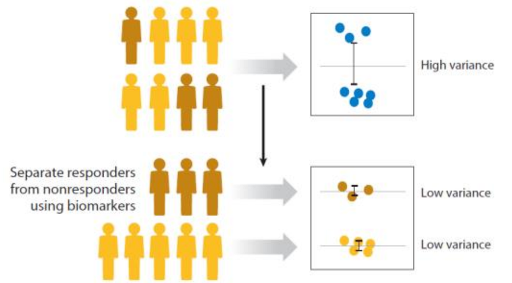


Figure 1

Precision nutrition enables scientists to better understand why there are responders and nonresponders to dietary interventions. Because of genetic, epigenetic, microbiota, and environmental differences, metabolic heterogeneity can result in differences in how people (or animals) respond to nutrients or bioactive molecules. When heterogeneous people are lumped together in studies of dietary interventions, large interindividual variance makes it difficult to detect significant effects. Large groups of people, usually of similar ancestry, share common underlying causes of metabolic heterogeneity. Using appropriate biomarkers, including genetic data, researchers can stratify people so that responders and nonresponders can be predicted for an intervention, and the resulting data analyzed separately, thereby reducing interindividual variability and enhancing the capacity to detect significant differences between groups.

个体间差异很大，肠道微生物比膳食常量营养素对餐后血脂有更大的影响，但对餐后血糖影响不大。

Sarah E. Berry, et al., Nature Medicine, 2020, 26: 964-973

不存在单一的、适用于所有人的饮食，不同人对饮食的反应可能是独特的、可量化的。可通过宿主和微生物群特征预测。

Aleksandra A. Kolodziejczyk, et al., Nature, 2019, 17: 742-753

精准营养而不是个性化营养；精准营养的商业应用（基因芯片）

Steven H. Zeisel. Annual Review of Food Science and Technology, 2020. 11:71－92

限制精确营养改进的最大挑战是：很少有数据集可以同时测量饮食摄入量、遗传学、表观遗传学、微生物组、环境暴露和代谢表型数据。

杂粮健康功效机制- 精准营养

David Zeevi, et al., Personalized Nutrition by Prediction of Glycemic Responses, Cell, 2015,163:1079-1094

中国农业大学
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FSNE College
食品科学与营养工程学院
COLLEGE OF FOOD SCIENCE & NUTRITIONAL ENGINEERING

汇报提纲

- 杂粮健康功效机制
  - 大数据：杂粮有健康功效
  - 组分：抗氧化、调控基因、肠道微生物
  - 精准营养：适量、人以群分
  - 加工过程
- 本实验室青稞研究进展

杂粮健康功效机制- 加工过程

TABLE 5 | Effects, mechanism, and process of increasing bioavailability of cereals and pseudo-cereal grains.

Crop	Effects	Mechanism	Process to increase bioavailability
Foxtail millet	Significant increase in extractability of calcium, phosphorus, iron, zinc, and copper	NA	Roasting
	Digestibility and biological values increased	NA	Fortified with lysine
	Highest concentration of thiamine, vitamin E, and stearic and linoleic acid	NA	NA
	Loss of protein, mineral, and fiber content	NA	Dehulling/soaking/ cooking
	Increase in percentage of ionizable iron and soluble zinc	By the removal of polyphenols and breaking down of polyphenols-protein-minerals	
	Two types of fatty acid patterns observed	Glutinous and non-glutinous varieties	NA
	High amount of protein (11%) and fat (4%). The protein fractions are represented by albumins and globulins (13%), prolamins (39.4%), and glutelins (9.9%). It is thus recommended as an ideal food for diabetics.	NA	NA

Juan Pablo Rodr ǵuez, et al., Healthy and Resilient Cereals and Pseudo-Cereals for Marginal Agriculture: Molecular Advances for Improving Nutrient Bioavailability, Frontiers in Genetic,2020, 11:49. doi:10.3389/fgene.2020.00049

杂粮健康功效机制- 加工过程

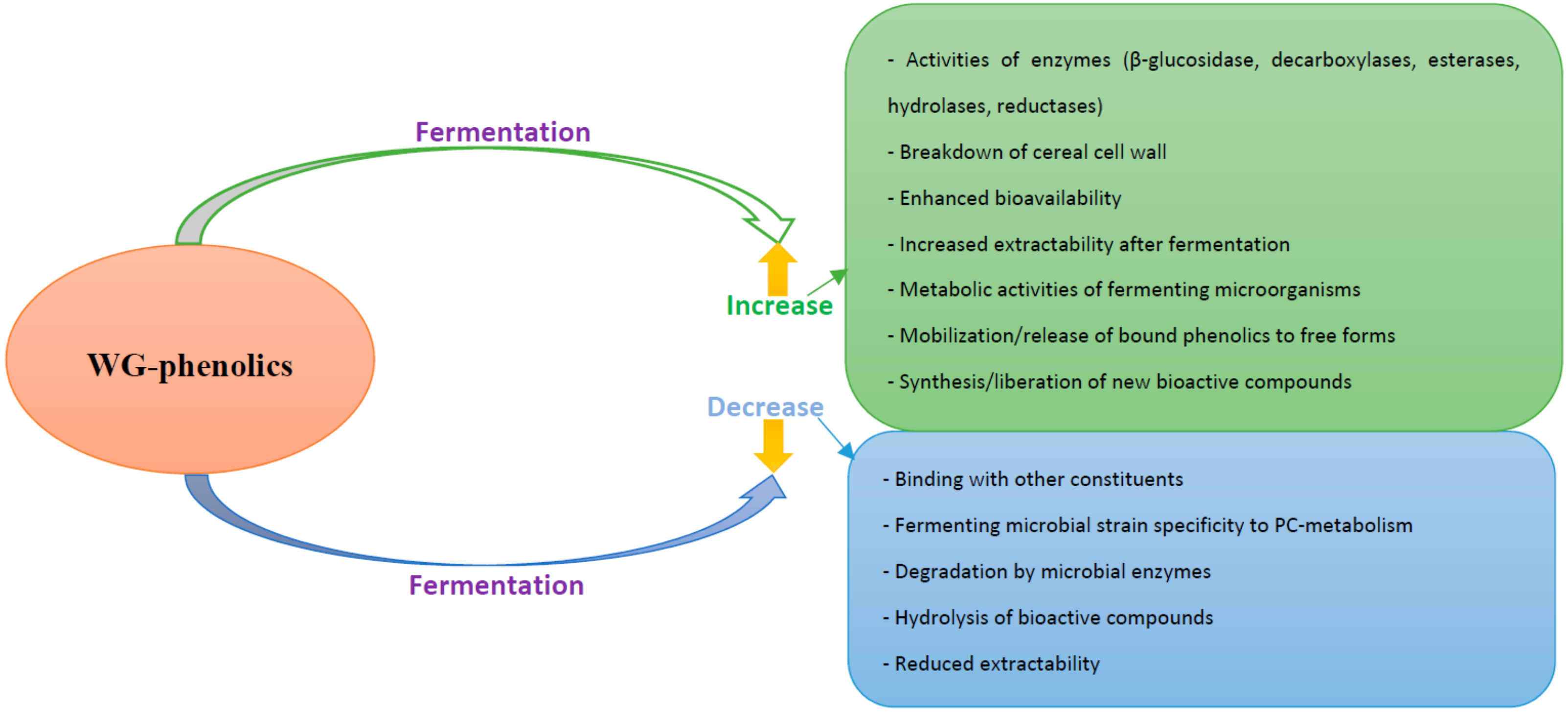

Figure 3. A summary of ways by which whole grain phenolic compounds are modified during fermentation.

Oluwafemi Ayodeji Adebo, et al., Impact of Fermentation on the Phenolic Compounds and Antioxidant Activity of Whole Cereal Grains: A Mini Review， Molecules 2020, 25, 927

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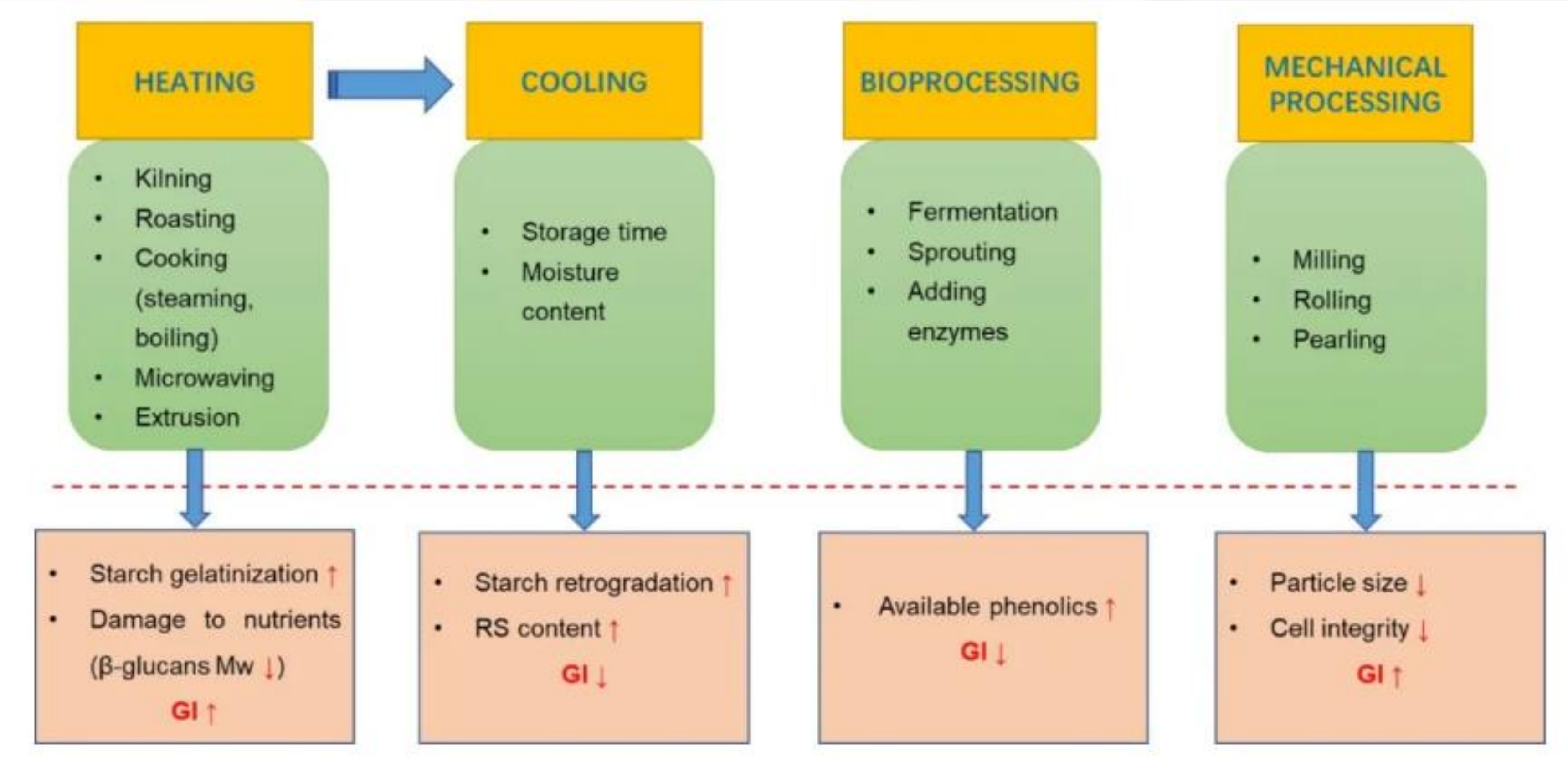

Kailong Zhang, et al., Oat-Based Foods: Chemical Constituents, Glycemic Index, and the Effect of Processing, Foods, 2021,10(6）： 1304

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杂粮健康功效机制- 加工过程-品种

白、黑、灰、红糜子。 总共有672鉴定出代谢物，其中121、116和148个代谢物存在差异积累。 主要途径差异：色氨酸代谢、类黄酮、异类黄酮、黄酮和黄酮醇生物合成。不同品种间酚酸和酚酸积累量差异较大。

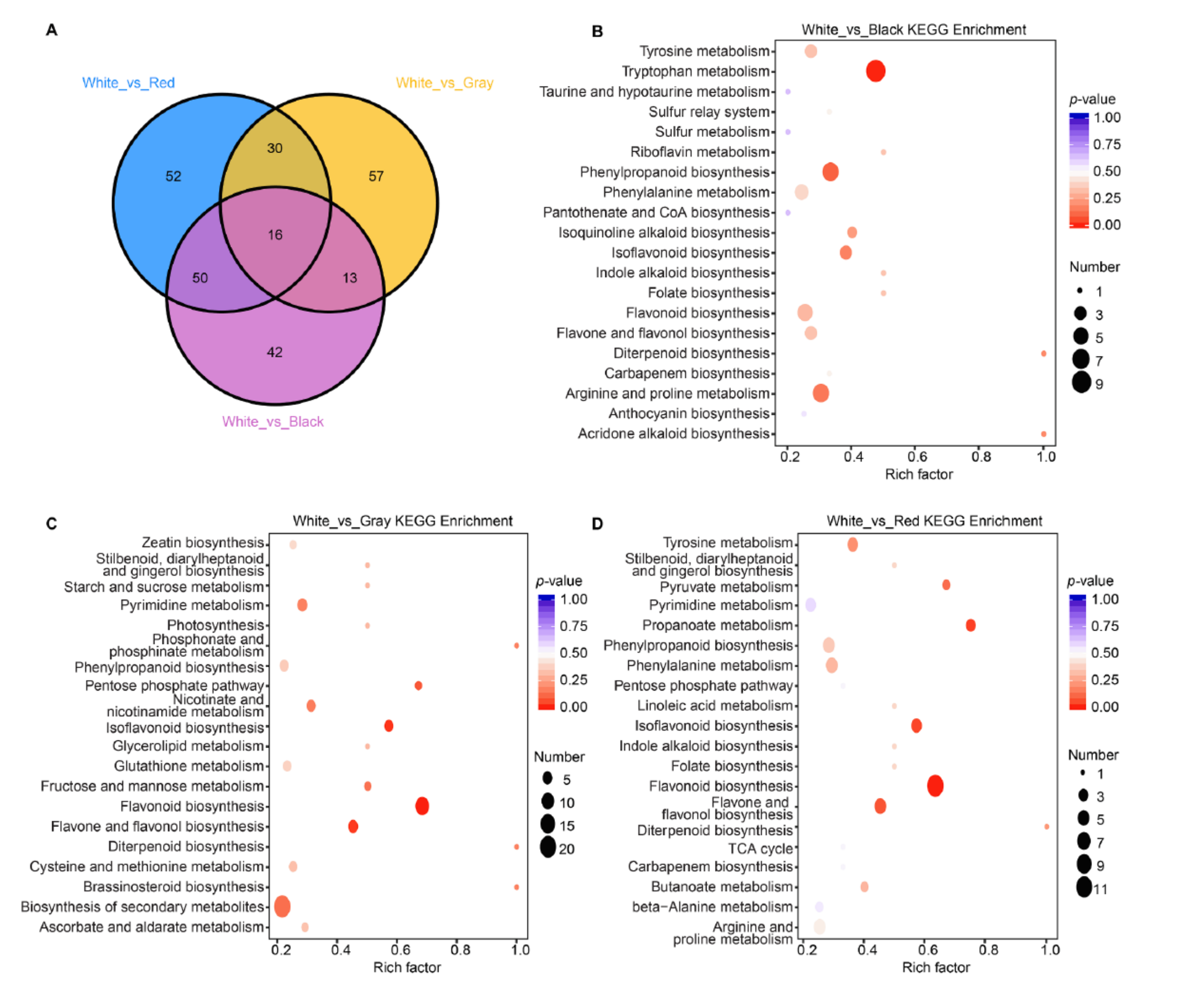

Fig. 3. Venn diagram and pathway analysis of differential metabolites for three comparison groups (White vs. Black, White vs. Gray, White vs. Red). A, Venn diagram shows the overlapping and unique metabolites amongst the comparison groups. B-D, KEGG enrichment of differential metabolites' between the comparison groups (White vs. Black/Gray/Red). Each bubble in the plot represents a metabolic pathway whose abscissa and bubble size jointly indicate the magnitude of the impact factors of the pathway. A larger bubble size indicates a larger impact factor. The bubble colors represent the *p*-values of the enrichment analysis, with darker colors showing a higher degree of enrichment. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Wei Li, et al., Study on metabolic variation in whole grains of four proso millet varieties reveals metabolites important for antioxidant properties and quality traits, Food Chemistry,2021, 357:129791

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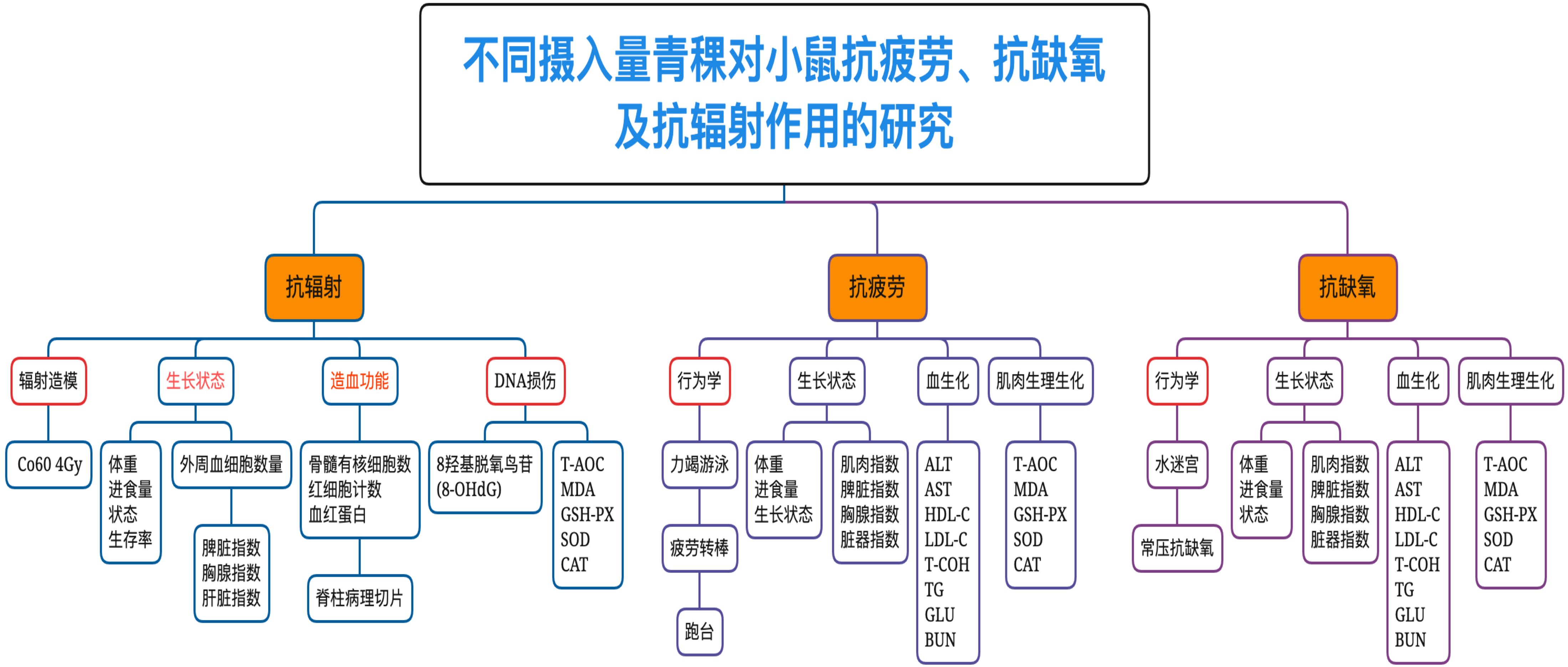
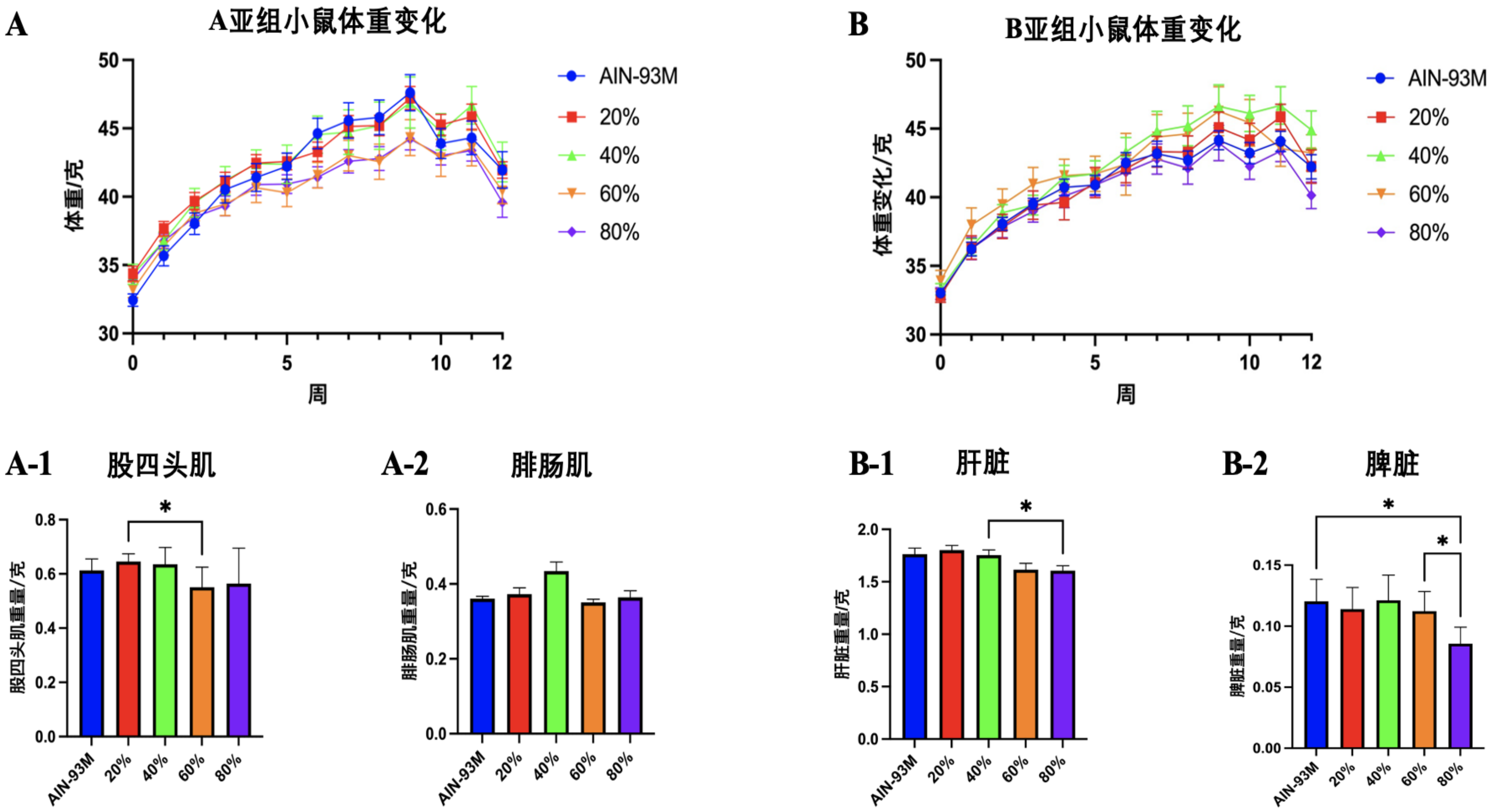
《本草纲目拾遗》青稞：补中益气；主脾胃气虚；四肢无力，大便稀溏。

唐·陈藏器《本草拾遗》青稞：下气宽中、壮精益力、除湿发汗、止泻。

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股四头肌
股四头肌重量/克
A-2
腓肠肌
腓肠肌重量/克
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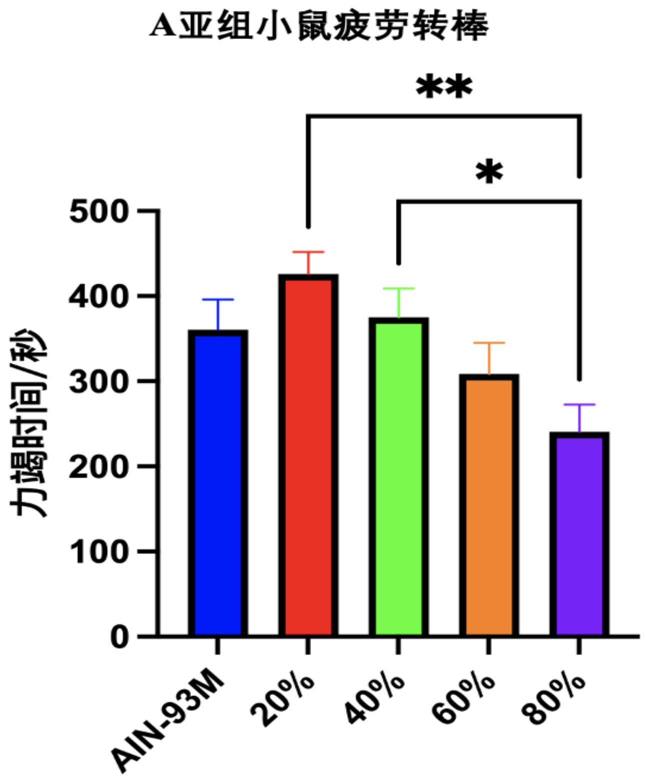
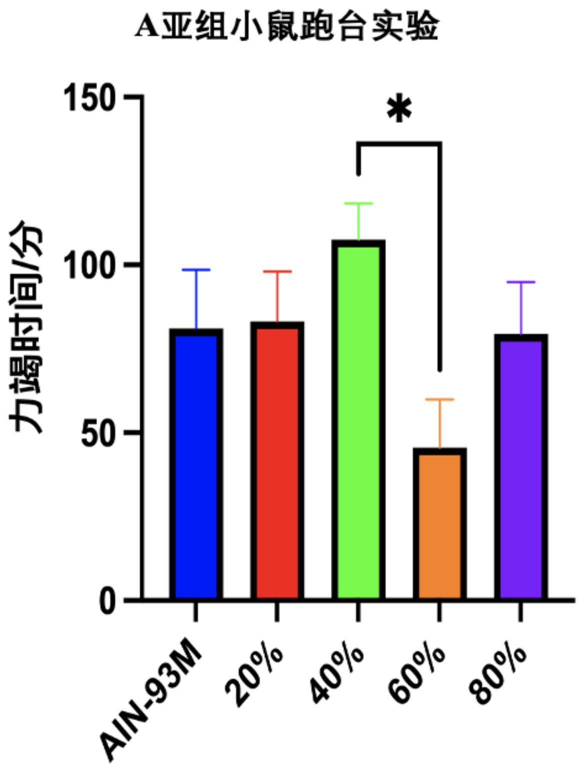
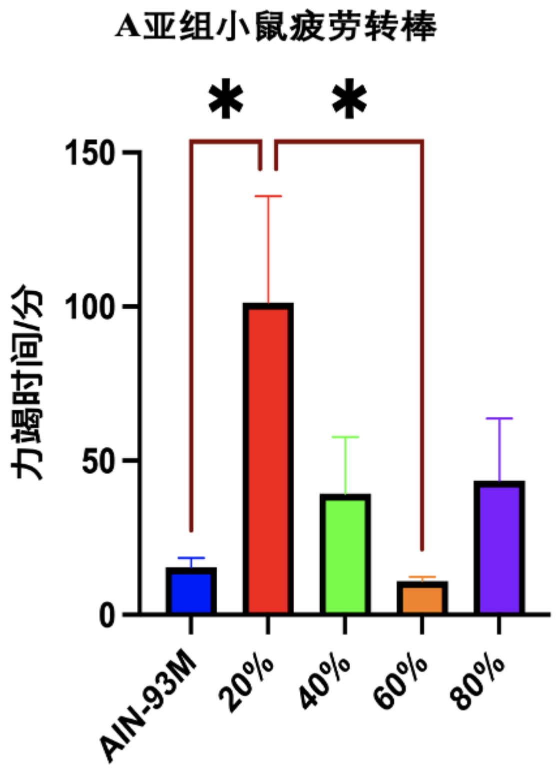
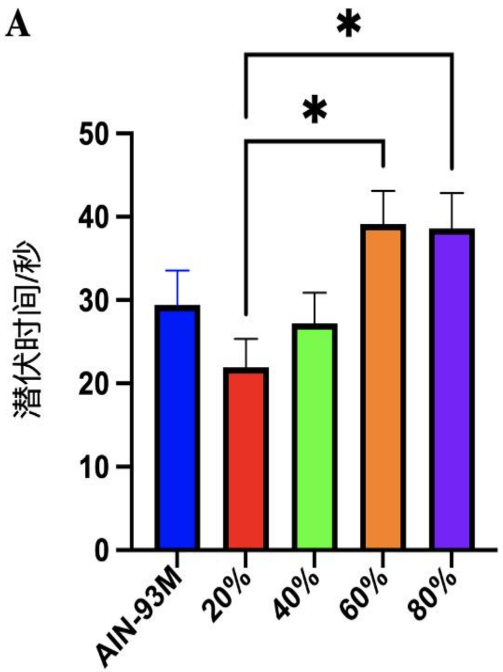


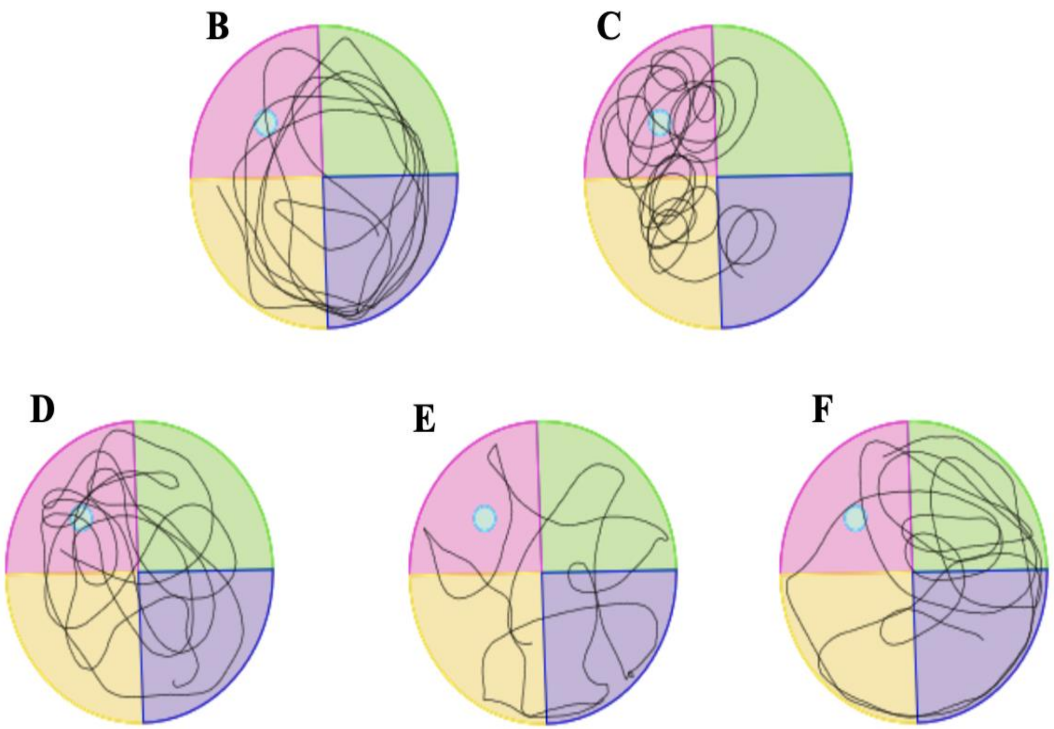




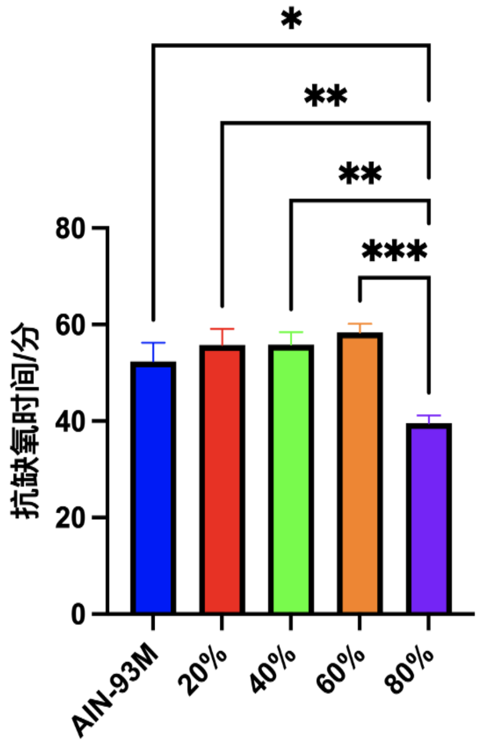
B亚组小鼠水迷宫潜伏期



水迷宫轨迹图



B亚组小鼠耐缺氧实验



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