



Novel Microbial Modifications of Bile Acids and Their Functional Implications

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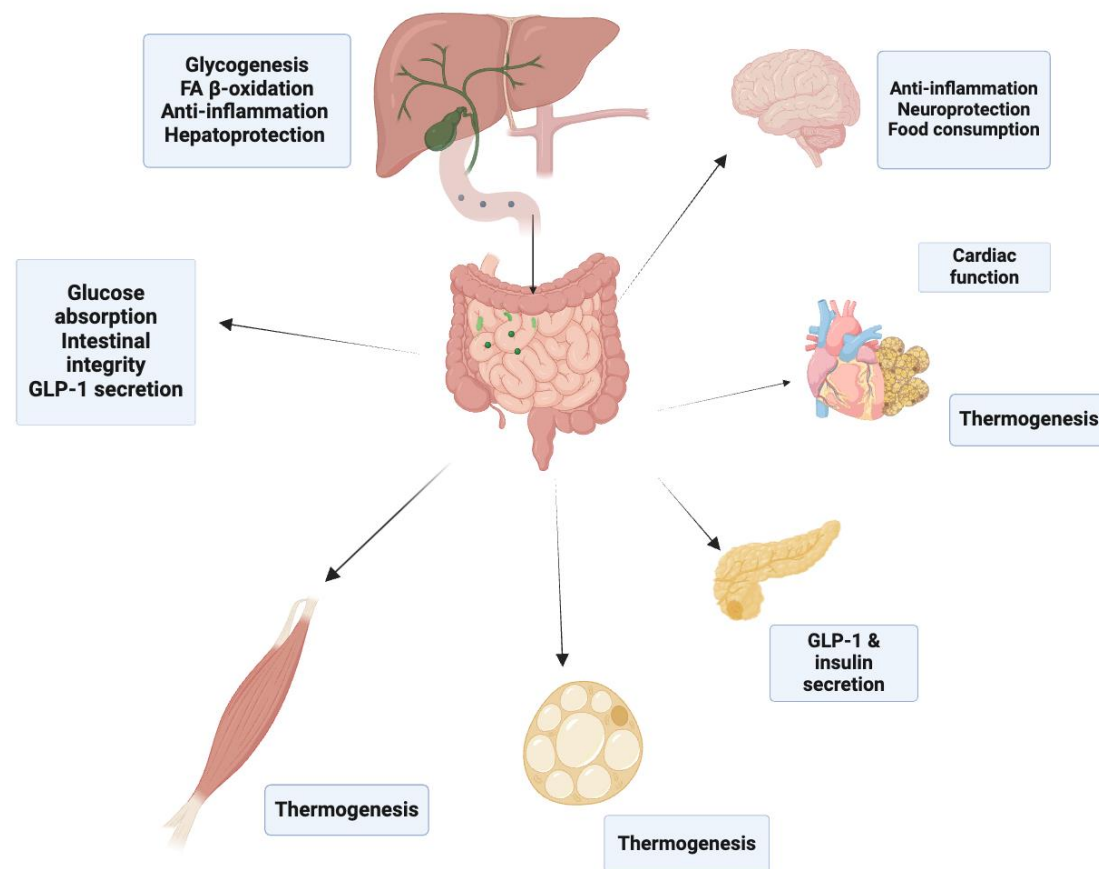
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Background

Bile acids (BAs)

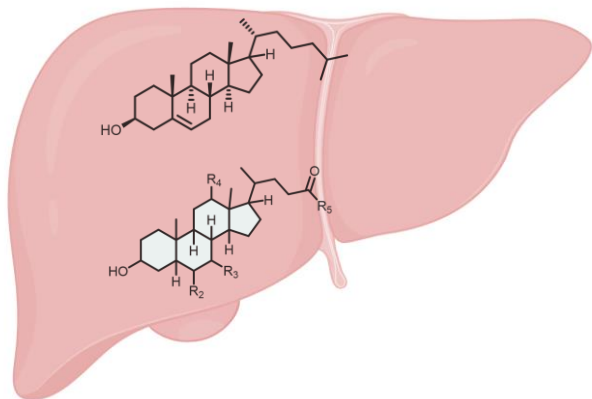
- play a crucial role in facilitating fat digestion and absorption in the small intestine.
- regulate lipid and glucose metabolism, inflammation, and energy expenditure through signaling pathways.





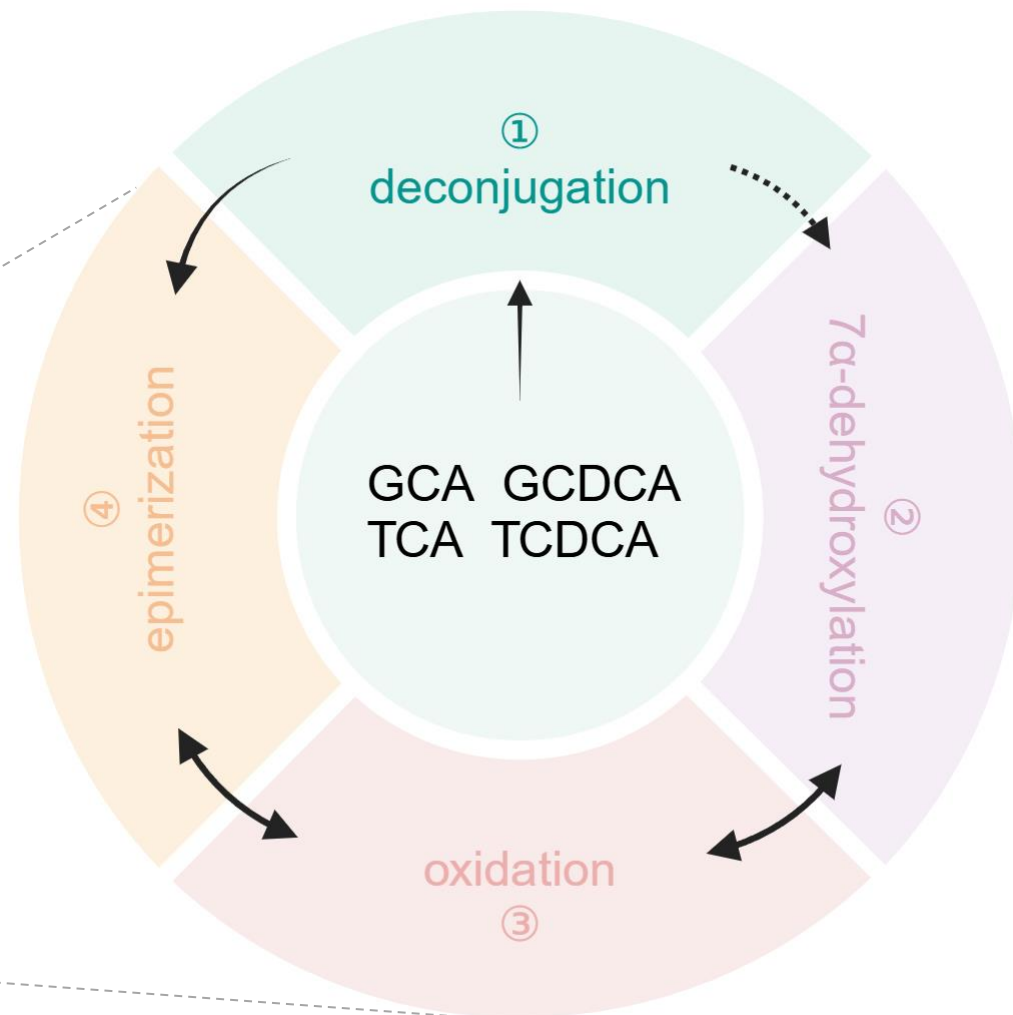
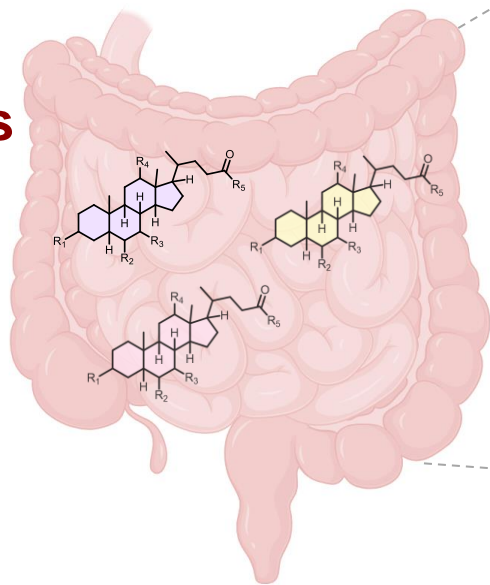
Background

cholesterol



primary BAs

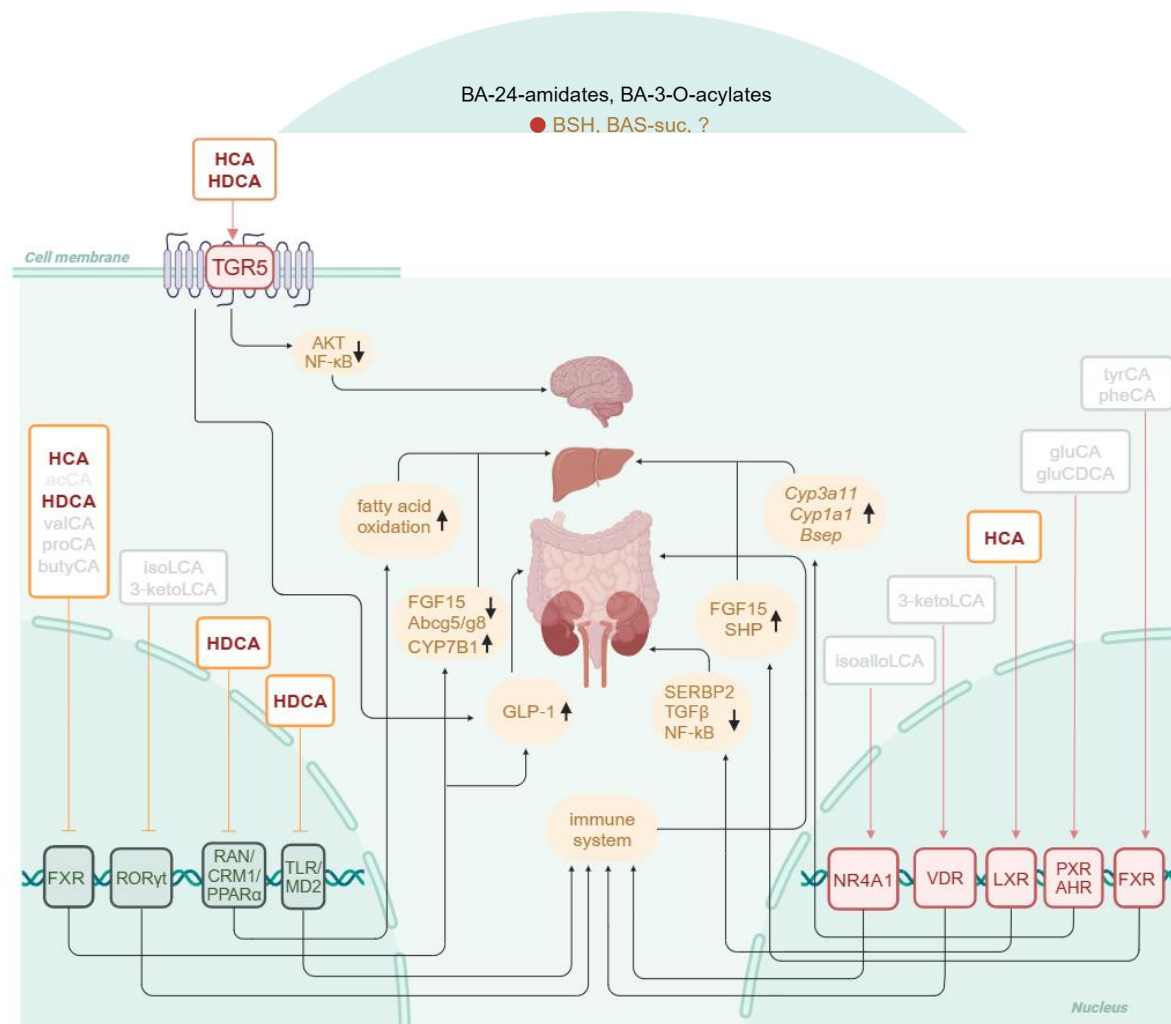
secondary BAs



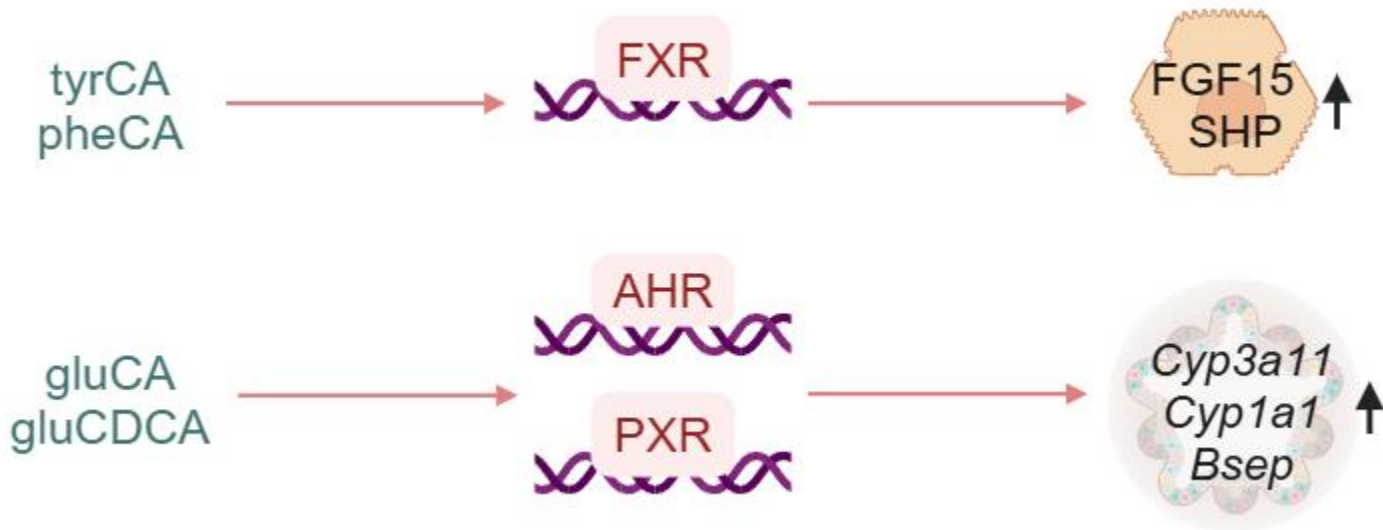
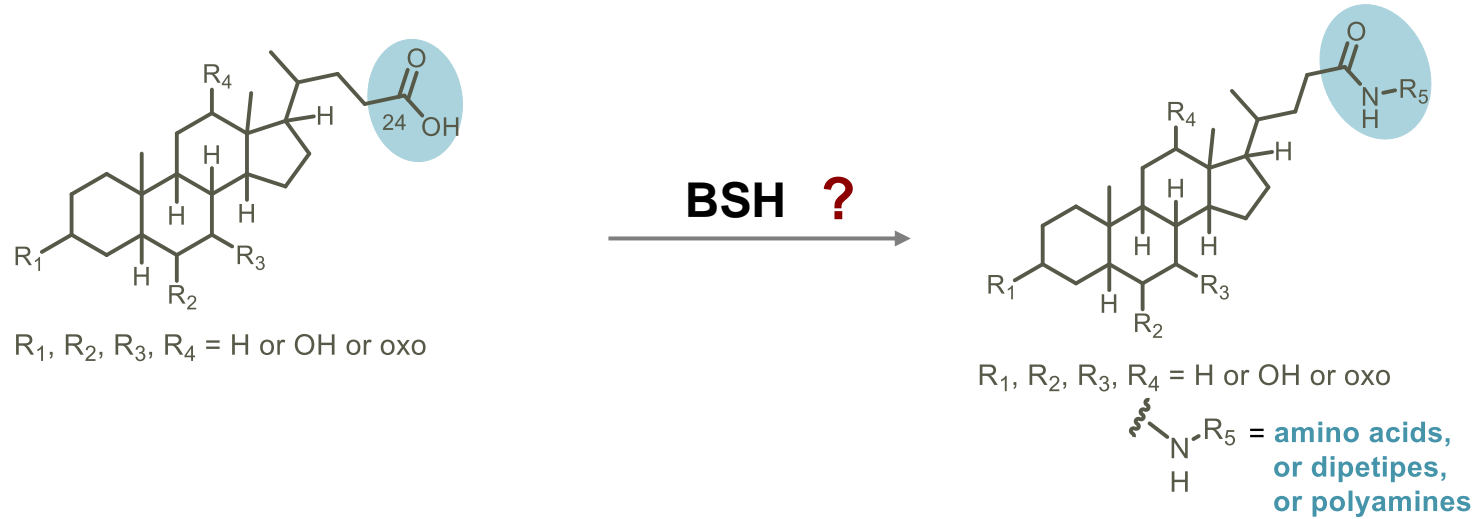


Breakthroughs in Microbial Metabolism of Bile Acids in the Last Five Years

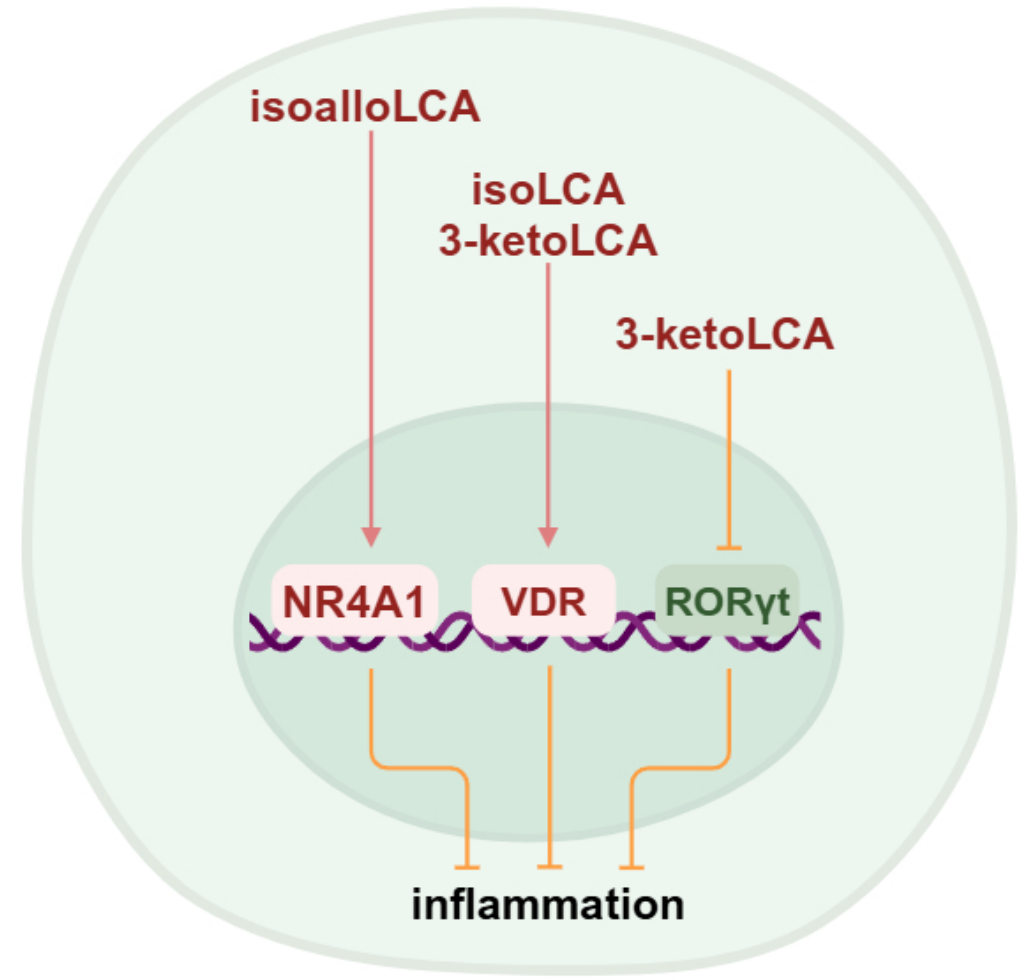
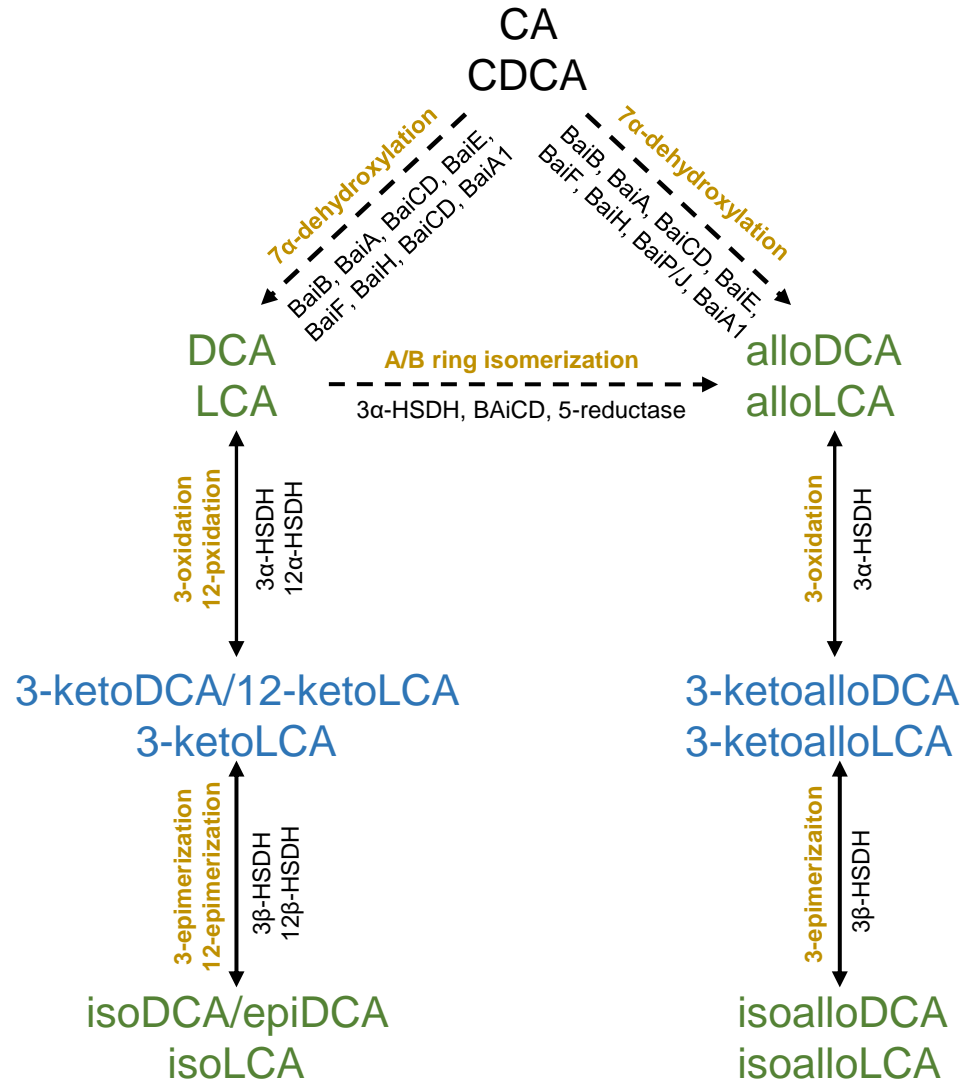
- Bile acid novel microbial modifications—reconjugation: 24-amidation and 3-O-acylation.
- The enzymes and immunobiological roles of gut microbially-driven 7α -dehydroxylation and epimerization.
- The biological roles of hyocholic acid species in metabolic diseases.



Gut Microbial-derived BA-24-amidated and Their Biological Roles



The Enzymes and Immunobiological Roles of Gut Microbial-derived 7 α -Dehydroxylation and Epimerization

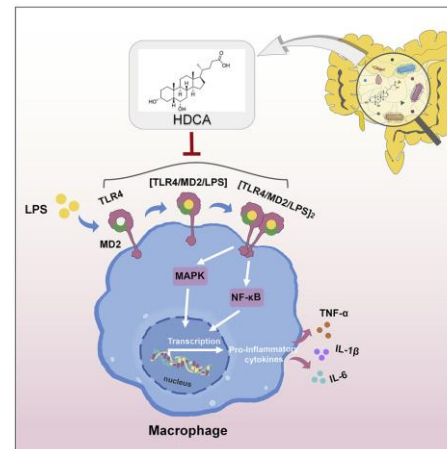
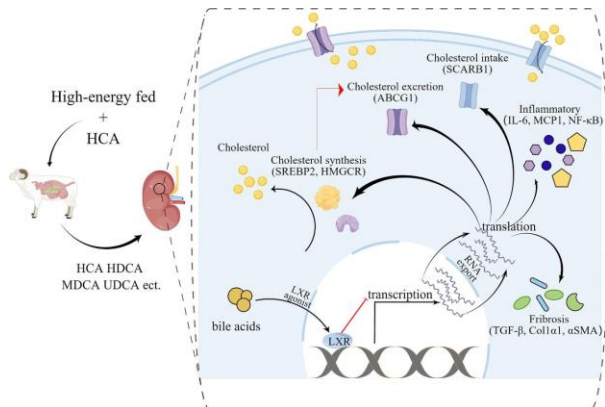
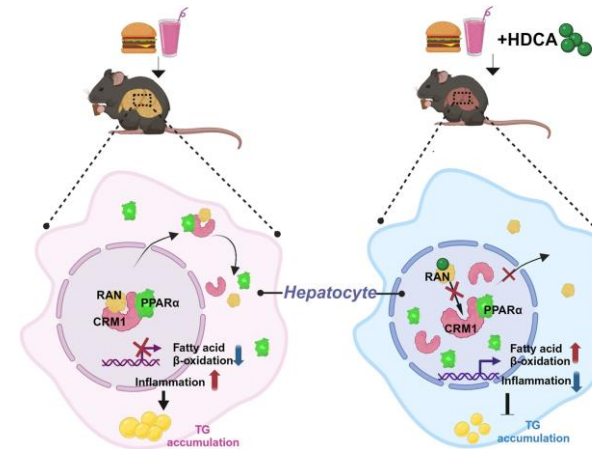
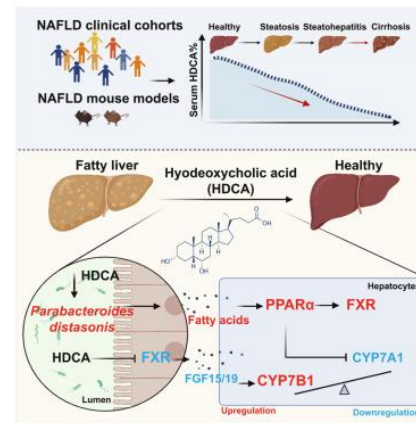
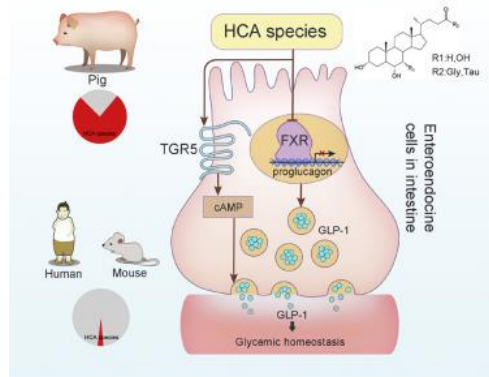




HCA's Roles in Metabolic Diseases

HCA species BAs

- HCA, HDCA, and their glyco- and tauro- conjugates
- regulating blood glucose homeostasis, improving MAFLD et al.



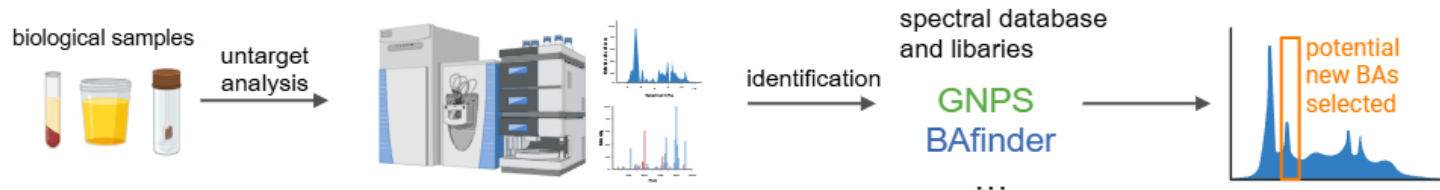
Figures sources:

- Hyocholic acid species improve glucose homeostasis through a distinct TGR5 and FXR signaling mechanism. *Cell Metabolism* 33: 791-803.
- Hyodeoxycholic acid alleviates non-alcoholic fatty liver disease through modulating the gut-liver axis. *Cell Metabolism* 35: 1752-1766.
- Hyodeoxycholic acid ameliorates nonalcoholic fatty liver disease by inhibiting RAN-mediated PPARα nucleus-cytoplasm shuttling. *Nature Communications* 14: 5451.
- Gut microbial metabolite hyodeoxycholic acid targets the TLR4/MD2 complex to attenuate inflammation and protect against sepsis. *Molecular Therapy* 31: 1017-1032.
- Hyodeoxycholic acid attenuates cholesterol gallstone formation via modulation of bile acid metabolism and gut microbiota. *European Journal of Pharmacology* 955: 175891.

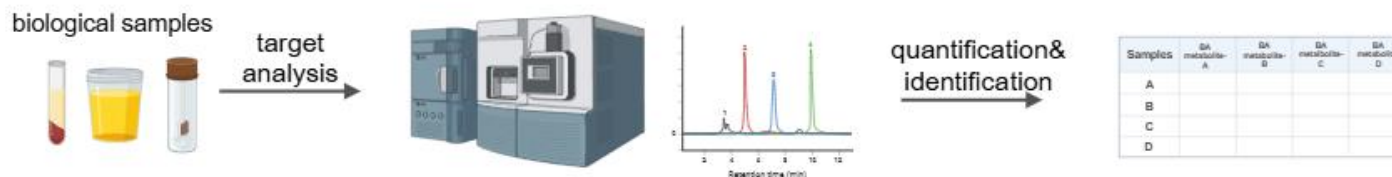


Metabolomic Techniques for Discovering Novel BAs

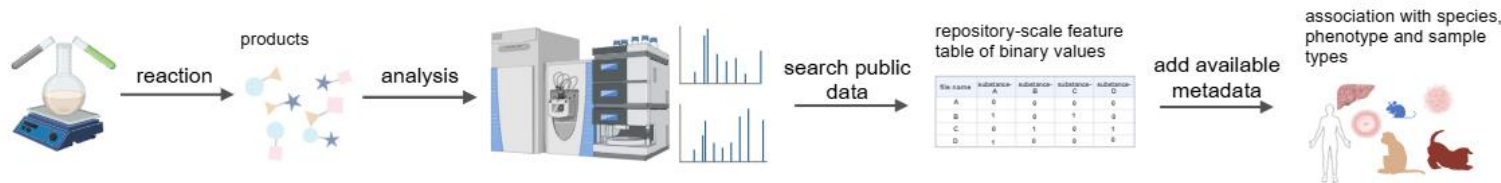
- **Untargeted metabolomics**



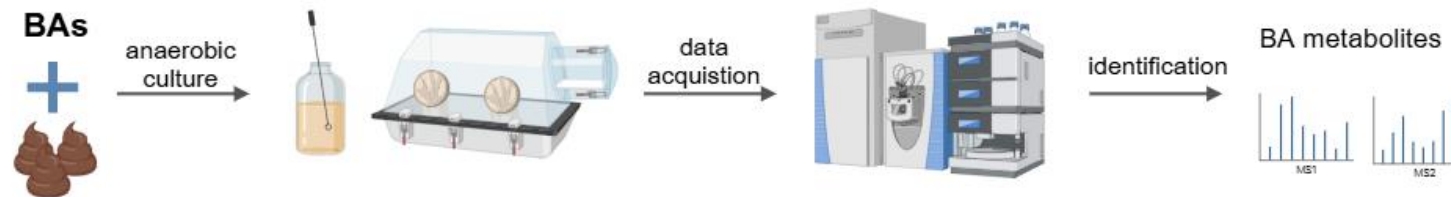
- **Targeted metabolomics**



- **Reverse metabolomics**



- **Combination culturomics with metabolomics**



Perspective for Future BA Research and New Drug Discovery

➤ Artificial Intelligence Applications

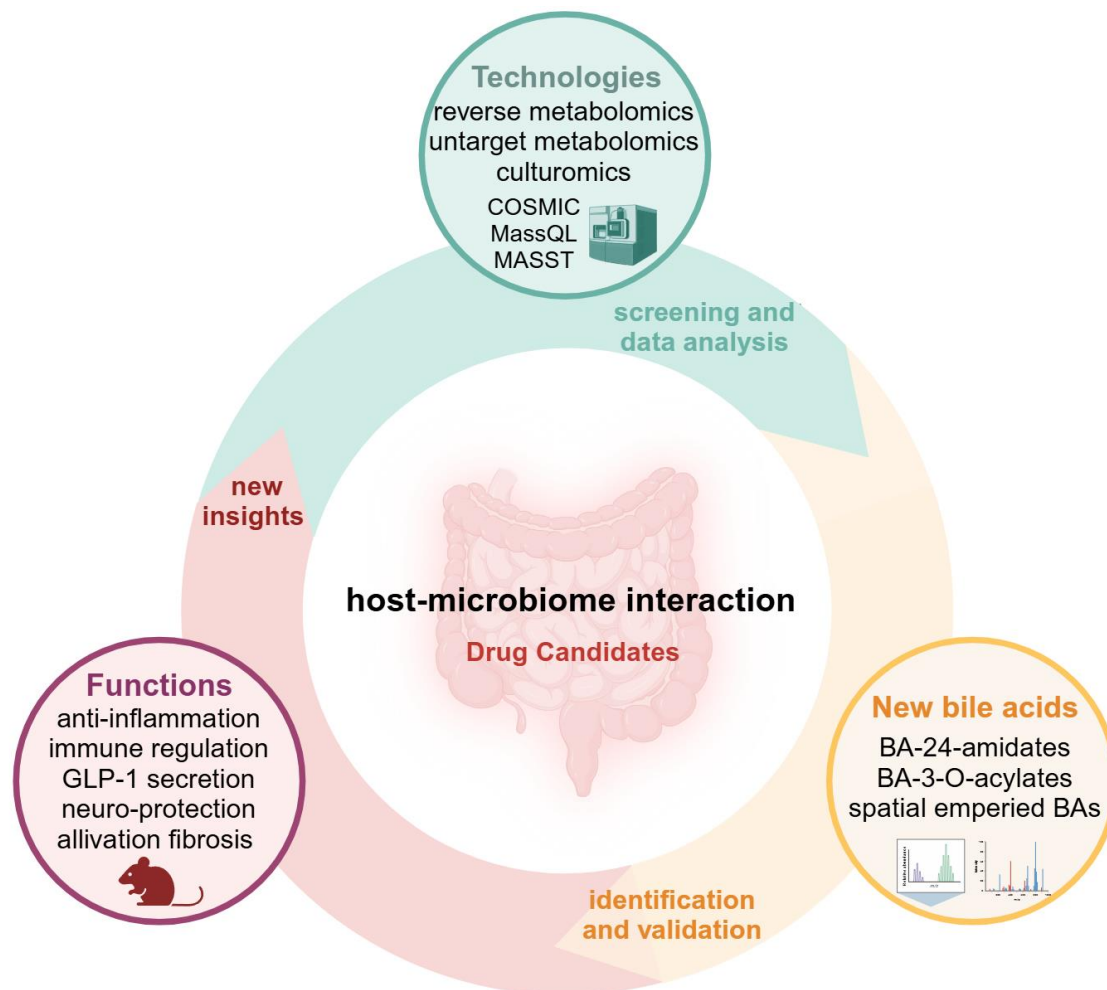
Discovery of new BAs, elucidate microbiota's modifying effects, predict enzyme functions, and uncover BA novel metabolic pathway.

➤ Fungal Modification of BAs Research

Explore fungal modification BAs, and understand the complex microbiome-host interactions.

➤ New Drug candidates

New bioactivities of microbial-derived BA derivatives and potential lead compounds of new drug candidates.




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