IAA Journal of Biological Sciences 14(1):75-81, 2026 **www.iaajournals.org**

©IAAJOURNALS **ISSN:2636-7254**

https://doi.org/10.59298/IAAJB/2026/1417581 **IAAJB1411**

Gut Microbial Bile Acid Signaling as a Shared Therapeutic Axis in Obesity and Diabetes

Winniefred Nankya

Department of Clinical Pharmacy Kampala International University Uganda
Email:winniefred.nankya@studwc.kiu.ac.ug

ABSTRACT

Bile acids (BAs) have emerged as pleiotropic signaling molecules that connect gut microbiota, liver, intestine, and peripheral metabolic tissues. Beyond their classical role in lipid absorption, BAs act as endocrine regulators via receptors such as the farnesoid X receptor (FXR) and the G-protein–coupled receptor TGR5, shaping glucose and lipid metabolism, energy expenditure, and inflammation. Gut microbes profoundly remodel the BA pool through bile salt hydrolase (BSH) and other enzymes, altering receptor affinity and signaling bias. Dysbiosis in obesity (OB) and type 2 diabetes (T2D) perturbs this "microbiota–BA axis,", contributing to insulin resistance, fatty liver, and impaired incretin responses. This review frames gut microbial BA signaling as a shared therapeutic axis in OB and T2D. We summarize BA synthesis and microbial transformations, then detail how BA receptors integrate microbial cues to control hepatic gluconeogenesis, adipose and muscle insulin sensitivity, incretin (GLP-1) secretion, and energy expenditure. We highlight human and preclinical data linking altered BA profiles and receptor activity to metabolic disease, including mechanistic insights from bariatric surgery, BA sequestrants, and FXR/TGR5-targeted drugs. We further discuss next-generation strategies that exploit microbiota-derived BA species or receptor-selective agonists, including microbial amino acid–conjugated BAs that stimulate GLP-1 via novel G-protein–coupled receptors. Finally, we outline biomarker and precision-medicine opportunities based on BA and microbiome signatures, and key knowledge gaps for safely manipulating this axis in chronic metabolic disease. Understanding and harnessing gut microbial BA signaling may allow convergent treatments that simultaneously tackle OB, T2D, and associated liver disease.

Keywords: bile acids; gut microbiota; FXR; TGR5; GLP-1

INTRODUCTION

OB and T2D share overlapping pathophysiology: excess caloric intake, adipose dysfunction, ectopic lipid deposition, chronic low-grade inflammation, and impaired incretin and insulin signaling. Traditionally, these have been framed in terms of adipose and hepatic metabolism, but over the last decade, the gut microbiota and BAs have been recognized as central upstream regulators of this network[1–3]. BAs originate in the liver, where cholesterol is converted into primary BAs (cholic acid, chenodeoxycholic acid in humans) via classical (CYP7A1) and alternative pathways. These are conjugated with glycine or taurine, secreted into bile, and released into the small intestine to emulsify dietary fats. Most are reabsorbed in the ileum and returned to the liver via enterohepatic circulation; a fraction escapes to the colon, where gut microbes extensively modify them into secondary BAs through deconjugation, dehydroxylation, dehydrogenation, and epimerization[4–6].

Microbial enzymes, particularly BSHs and 7α-dehydroxylases, thus determine the size, composition, and hydrophobicity of the BA pool. These structural changes markedly affect binding to BA receptors. FXR, a nuclear receptor highly expressed in the liver and ileum, senses BAs and regulates genes controlling BA synthesis, lipid metabolism, gluconeogenesis, and inflammation. TGR5 (GPBAR1), a membrane GPCR expressed in enteroendocrine cells, macrophages, brown adipose tissue, and muscle, responds preferentially to secondary BAs and modulates GLP-1 secretion, energy expenditure, and inflammatory tone. Additional receptors (VDR, S1PR2, newly identified GPCRs) broaden BA signaling capacity[7].

In metabolic health, this microbiota–BA–receptor triad forms a finely tuned feedback loop:

hepatic BA synthesis is constrained by FXR-FGF15/19 signaling from the ileum and direct hepatic FXR activity; intestinal FXR and TGR5 signaling coordinate lipid absorption, gut barrier function, and GLP-1 secretion; peripheral FXR/TGR5 activity influences hepatic gluconeogenesis, hepatic and adipose lipogenesis/FAO, brown fat thermogenesis, and skeletal muscle fuel selection[8]. In OB and T2D, both gut microbiota and BA pools are altered. Human studies report shifts toward Gram-negative, BSH-rich species and altered secondary BA profiles; these changes correlate with BMI, insulin resistance, and T2D risk[8]. T2D is associated with disrupted BA homeostasis, modified total BA levels, altered primary/secondary and conjugated/unconjugated ratios, and altered FXR/TGR5 activation patterns[9, 10].

Why does this matter therapeutically? Because BA signaling sits at a nexus of pathways that are already drug targets in OB/T2D:

Hepatic glucose output – FXR activation suppresses gluconeogenic genes and VLDL secretion[11].

Adiposity and energy expenditure – TGR5 in BAT and muscle promotes thermogenesis and energy expenditure; intestinal FXR/TGR5 axes influence adiposity via GLP-1 and FGF15/19[11].

Incretins – Bile acids trigger GLP-1 release from L-cells via TGR5 and possibly other receptors; GLP-1 receptor agonists are already mainstream T2D/OB drugs[12, 13].

Liver disease – BA signaling via FXR is central to MASLD/NASH pathogenesis and therapy, conditions highly prevalent in T2D[14].

Clinical interventions provide “natural experiments” that implicate this axis. Bariatric procedures (Roux-en-Y gastric bypass, sleeve gastrectomy) induce rapid increases in circulating BAs, changes in BA composition, and enhanced FXR/TGR5 signaling. These changes track with improved glucose homeostasis and often T2D remission, sometimes preceding major weight loss[15, 16]. Experimental bile diversion to the ileum or manipulation of intestinal BAs can improve glycemia via an intestinal FXR–GLP-1 axis, dependent in part on Akkermansia muciniphila[15].

Parallel pharmacologic work shows that FXR agonists (e.g., obeticholic acid and newer agents) and TGR5 agonists modulate weight, glycemia, and hepatic steatosis in preclinical models, with early-phase human data in metabolic liver disease[17]. More recently, microbial amino-acid–conjugated BAs such as tryptophan-cholic acid have been shown to improve T2D in mice by stimulating GLP-1 via the orphan receptor MRGPRE, further expanding the receptor repertoire and confirming microbial BAs as drug-like molecules[17].

Collectively, these findings justify treating gut microbial BA signaling as a *shared* therapeutic axis for OB and T2D: a single pathway that can, in principle, influence body weight, insulin sensitivity, hepatic steatosis, and incretin biology. The remaining sections: (2) outline BA synthesis and microbial transformation; (3) detail links to obesity; (4) focus on glucose homeostasis and T2D; (5) summarize current interventions that exploit this axis; (6) discuss receptor-targeted pharmacology; and (7) highlight biomarkers and future directions for precision manipulation of the microbiota–BA system.

2. Bile Acid Synthesis, Microbial Transformation, and Receptor Signaling

Primary BAs are synthesized from cholesterol via hepatic cytochrome P450 enzymes, predominantly CYP7A1 (classical pathway) and CYP27A1/CYP7B1 (alternative pathway). They are conjugated with glycine or taurine, secreted into bile, and stored in the gallbladder. After a meal, cholecystokinin triggers BA release into the duodenum, where they act as detergents to solubilize dietary fats and fat-soluble vitamins[18]. About 95% of BAs are reabsorbed in the terminal ileum via the apical sodium-dependent bile acid transporter (ASBT), enter the portal circulation, and are taken up by hepatocytes through NTCP/OATPs, completing the enterohepatic cycle. The remaining 5% reach the colon and are substrates for the microbiota[18].

Gut microbes transform BAs via **BSHs**, which deconjugate glycine/taurine, making BAs better substrates for further modification; **7α-dehydroxylases**, which convert primary BAs into secondary forms (e.g., cholic acid to deoxycholic acid; chenodeoxycholic acid to lithocholic acid); oxidoreductases and epimerases, generating a wide diversity of secondary and tertiary BAs, including microbially conjugated species[19–22].

This biotransformation reshapes the BA pool’s hydrophobicity and receptor-binding profile. FXR has high affinity for chenodeoxycholic acid and certain secondary BAs, while TGR5 is particularly sensitive to lithocholic acid and other hydrophobic species. Microbial conjugation (e.g., tryptophan-cholic acid) can redirect signaling to additional GPCRs such as MRGPRE[23].

FXR acts as a BA sensor in ileal enterocytes and hepatocytes. Intestinal FXR activation induces FGF15/19, which signals to the liver via FGFR4/β-Klotho to repress CYP7A1, limiting BA synthesis; FXR also modulates lipid absorption, barrier integrity, and inflammation. Hepatic FXR regulates BA transporters and genes controlling lipogenesis, gluconeogenesis, and VLDL secretion[24]. TGR5 is a Gs-coupled receptor whose activation increases cAMP. In L-cells, TGR5 promotes GLP-1 release; in BAT and muscle, it enhances mitochondrial respiration and thermogenesis; in immune cells, it exerts anti-inflammatory effects[24]. Other receptors—VDR, S1PR2, and emerging GPCRs add layers of context-dependent BA signaling in immune regulation and metabolism.

Crucially, because microbial composition controls BA transformations, and BAs in turn modulate microbiota via antimicrobial and signaling effects, a bidirectional microbiota–BA feedback loop emerges. Disruption of either component dysbiosis or BA dysregulation can therefore propagate systemic metabolic dysfunction[24].

3. Microbial Bile Acid Signaling in Obesity Pathophysiology

OB is consistently associated with changes in gut microbiota composition and BA profiles. Human and animal studies report: Increased BSH-active microbes and altered primary/secondary BA ratios; increased total BA concentrations in some OB cohorts; and shifts toward more hydrophobic, potentially FXR-biased BA pools[25, 26].

These alterations have mechanistic implications. In the liver, excessive or mis-patterned FXR activation can suppress BA synthesis but also influence lipogenesis and VLDL secretion. Some rodent models suggest that intestinal FXR activation promotes diet-induced obesity via induction of ceramide synthesis and suppression of energy expenditure, whereas intestinal FXR inhibition or BA sequestration can protect against weight gain and steatosis[27].). In adipose tissue and muscle, BA signaling via TGR5 supports energy expenditure and mitochondrial function. Reduced availability of TGR5-active secondary BAs or impaired TGR5 responsiveness may therefore contribute to decreased thermogenesis and weight gain in OB. Conversely, enhancing TGR5 signaling increases BAT activity, browning of WAT, and whole-body energy expenditure in mice[28].

Microbial BA transformations also feedback on the microbiota itself, selecting for specific taxa and shaping SCFA production, intestinal barrier function, and endotoxemia, all contributors to metabolic inflammation. Hydrophobic BAs can be toxic and promote mucosal damage at high levels, while specific BA species support barrier integrity and anti-inflammatory signaling[29]. Bariatric surgery offers a clinically relevant example. Post-surgical patients typically show increased circulating BAs, a higher proportion of secondary and unconjugated species, and enrichment of BA-metabolizing bacteria such as A. muciniphila. These changes correlate with reduced body weight and improved metabolic profiles independent of calorie restriction, suggesting that a remodeled microbiota–BA axis contributes causally to weight loss and metabolic benefits[29].

Taken together, data support a model where OB is both a cause and consequence of altered microbial BA signaling: high-fat diets and excess adiposity reshape the microbiota and BA pool, which then feed forward via FXR/TGR5 and related pathways to favor further weight gain, steatosis, and low-grade inflammation. Conversely, interventions that “normalize” this axis can contribute to weight reduction and metabolic recovery.

4. Gut Microbial Bile Acid Signaling in Glucose Homeostasis and T2D

Glucose regulation is influenced by BA signaling at multiple levels: intestinal incretin release, hepatic gluconeogenesis, and peripheral insulin sensitivity.

Incretins and the BA–GLP-1 axis: TGR5 expressed on L-cells mediates BA-induced GLP-1 secretion. Secondary BAs and specific BA species (e.g., ω-muricholic acid, hyocholic acid) can stimulate GLP-1 via TGR5, and microbiota-dependent BA changes modulate postprandial GLP-1 responses[13]. Recent work shows that microbiota depletion blunts ileal GLP-1 release and that restoring microbiota or supplementing specific BAs rescues GLP-1 responses via BA–TGR5 signaling[30]. Microbially conjugated BAs add another layer: tryptophan-cholic acid, produced by gut bacteria, improves glucose tolerance in T2D models by activating MRGPRE on enteroendocrine cells, stimulating GLP-1[30]. These findings underscore microbial control over BA-incretin crosstalk.

Hepatic glucose output and insulin sensitivity: FXR signaling in liver and intestine regulates genes involved in gluconeogenesis (PEPCK, G6Pase) and glycogen metabolism. Proper FXR activation suppresses gluconeogenic flux and improves glycemia; dysregulated FXR signaling in T2D is associated with increased hepatic glucose production and insulin resistance[31, 32]. Microbiota-driven BA profiles thus modulate FXR tone. Experimental manipulation of intestinal Bas via bile diversion, sequestrants, or intestinal FXR agonists can improve hepatic insulin sensitivity and gluconeogenesis, often in a microbiota-dependent manner[31, 33].

Peripheral tissues: TGR5 activation in muscle and BAT increases energy expenditure, indirectly improving insulin sensitivity. BA-TGR5 signaling in macrophages and other immune cells dampens inflammation, which is central to insulin resistance pathogenesis[34–36].

Clinical studies show that patients with T2D have altered serum and fecal BA profiles, including changes in total BA concentrations and specific primary/secondary species. These alterations correlate with glucose levels, insulin resistance, and β-cell function, supporting BA signatures as integrated markers of glycemic history and gut–liver axis status[37]. Overall, gut microbial BA signaling affects T2D via (i) GLP-1 secretion (BA–TGR5/MRGPRE), (ii) hepatic gluconeogenesis and steatosis (FXR/FGF15/19), and (iii) systemic insulin sensitivity through effects on energy expenditure and inflammation. This multifocal influence explains why interventions that rewire BA signaling—surgery, sequestrants, or receptor agonists—can produce surprisingly large improvements in glycemic control.

5. Therapeutic Manipulation of the Microbiota–Bile Acid Axis

Several existing and emerging therapies already act, intentionally or not, on the microbiota–BA axis.

Bariatric and metabolic surgery: Roux-en-Y gastric bypass and sleeve gastrectomy consistently increase circulating BA levels, shift BA composition, and change microbiota structure. Enhanced FXR and TGR5 signaling, especially in the ileum, is linked to increased GLP-1, improved insulin sensitivity, and T2D remission. Experiments with bile diversion to the ileum mimic some of these metabolic benefits, underscoring BA signaling as a key mediator[38].

Bile acid sequestrants: Colesevelam and related resins bind BAs in the gut, preventing reabsorption, increasing fecal loss, and forcing hepatic BA synthesis from cholesterol. Clinically, they reduce LDL-C and modestly improve glycemia in T2D. Mechanistically, sequestrants change BA pool composition, reduce intestinal FXR activation, and can secondarily enhance GLP-1 secretion, likely via increased BA flux to the distal gut and altered microbiota[39].

Microbiota-directed approaches: Prebiotics (e.g., fermentable fibers), probiotics, and fecal microbiota transplantation (FMT) can shift BA-metabolizing taxa and BSH activity, changing BA composition and FXR/TGR5 signaling. Some trials report improved insulin sensitivity with microbiota modulation, although results are variable and often modest. Rational design of consortia with defined BSH/7α-dehydroxylase profiles may enable more predictable BA remodeling[40].

Dietary manipulation: Diet strongly influences BA production and microbiota. High-fat diets increase BA synthesis and select for BA-resistant, BSH-active microbes, whereas fiber-rich diets favor SCFA producers and may normalize BA pools. Specific nutrients and phytochemicals modulate FXR/TGR5 activity directly or via microbiota shifts, offering opportunities for “BA-smart” dietary patterns in OB/T2D[40].

Emerging microbial BA therapeutics: The identification of microbial amino acid–conjugated BAs that robustly stimulate GLP-1 via MRGPRE hints at a new class of small-molecule therapeutics derived from or inspired by microbial metabolites. Synthetic analogs with improved potency, selectivity, and pharmacokinetics could expand incretin-based therapies beyond current GLP-1 receptor agonists[40]. Together, these interventions demonstrate that the microbiota–BA axis is modifiable in humans and that such modulation can meaningfully affect weight and glycemia. The key challenge is to move from “off-target” modulation to rational, receptor- and depot-specific targeting.

6. FXR, TGR5 and Emerging Bile Acid Receptors as Drug Targets

FXR and TGR5 are the most advanced BA receptors in drug development, but the therapeutic landscape is complex.

FXR agonists: Systemic FXR agonists such as obeticholic acid (OCA) were developed for cholestatic and fatty liver diseases. OCA is approved for primary biliary cholangitis and has shown histologic benefits in NASH; multiple FXR agonists (cilofexor, tropifexor, vonafexor, others) are under evaluation in MASLD/NASH. These agents reduce BA synthesis, improve hepatic steatosis, and modulate lipids and inflammation[41]. Metabolic readouts (weight, glycemia) are variable and often constrained by side effects (pruritus, LDL-C elevations).

Because intestinal vs hepatic FXR activation has distinct effects, intestinal FXR can shape microbiota and activate TGR5/GLP-1 axes; hepatic FXR chiefly regulates BA/lipid metabolism. There is interest in *intestinally restricted* FXR agonists to harness beneficial gut–liver signaling with fewer systemic adverse effects[42].

TGR5 agonists: TGR5 agonists improve GLP-1 secretion, energy expenditure, and inflammation in preclinical models of OB/T2D. However, systemic activation can cause adverse effects such as gallbladder filling and potential pruritus, limiting development. Tissue-selective or biased TGR5 agonists, or approaches that enrich TGR5-active BA species in the ileum while minimizing biliary exposure, are being explored[43].

Newly identified receptors and biased signalling: Microbial conjugates like tryptophan-cholic acid reveal that BAs can engage additional GPCRs such as MRGPRE to stimulate GLP-1 and improve T2D in mice[44]. Other targets (VDR, S1PR2) mediate BA effects on immunity and barrier function. Designing ligands that preferentially activate “metabolically beneficial” pathways (e.g., gut-restricted GLP-1 release and thermogenesis) while avoiding cholestatic or fibrogenic signaling is a key medicinal chemistry goal[44].

Combination and adjunctive strategies

Given the robust efficacy of GLP-1/GIP receptor agonists and SGLT2 inhibitors in OB/T2D, BA-receptor modulators may find their place as adjuncts rather than stand-alone therapies. Intestinal FXR/TGR5/MRGPRE modulation could enhance endogenous incretin release and energy expenditure, allowing lower doses of injectables or providing additional benefit in patients with incomplete response. In MASLD/NASH coexisting with T2D, FXR agonists or related BA-based drugs may serve dual hepatic-metabolic roles[45]. Overall, receptor-targeted BA pharmacology is promising but must balance efficacy with safety and tissue selectivity. Lessons from early FXR trials emphasize the need for nuanced, organ-specific modulation of BA signaling pathways.

7. Biomarkers, Precision Medicine and Future Directions

Because BAs integrate hepatic, intestinal, and microbial function, BA profiles and related microbial signatures are attractive biomarkers for OB/T2D and for response to therapy.

Biomarker opportunities: Serum and fecal BA composition (e.g., primary/secondary ratio, conjugation patterns, specific species such as hyocholic acid) correlate with insulin resistance, β-cell function, and T2D risk[46]. High-throughput LC-MS platforms now make comprehensive BA profiling feasible in clinical cohorts. Combined with 16S or metagenomic microbiome data, these profiles could define “BA–microbiota endotypes” of metabolic disease[47]. Dynamic tests measuring BA and GLP-1 responses to standardized meals—may capture functional capacity of the gut microbiota–BA–incretin axis and predict response to bariatric surgery, BA sequestrants, or FXR/TGR5-targeted therapies[46].

CONCLUSION

In summary, gut microbial BA signaling is not a peripheral curiosity but a central control node for energy and glucose homeostasis. It offers a shared therapeutic axis in OB and T2D, linking diet, microbiota, liver, gut hormones, and peripheral tissues through a chemically rich set of metabolites and receptors. As analytical tools and targeted therapies mature, leveraging this axis could help convert today’s mostly reactive management of OB/T2D into proactive, mechanism-based and personalized intervention.

REFERENCES

1. Bedu-Ferrari, C., Biscarrat, P., Langella, P., Cherbuy, C.: Prebiotics and the Human Gut Microbiota: From Breakdown Mechanisms to the Impact on Metabolic Health. Nutrients. 14, 2096 (2022). https://doi.org/10.3390/nu14102096
2. Cao, C., Yue, S., Lu, A., Liang, C.: Host-Gut Microbiota Metabolic Interactions and Their Role in Precision Diagnosis and Treatment of Gastrointestinal Cancers. Pharmacol. Res. 207, 107321 (2024). https://doi.org/10.1016/j.phrs.2024.107321
3. Bemark, M., Pitcher, M.J., Dionisi, C., Spencer, J.: Gut-associated lymphoid tissue: a microbiota-driven hub of B cell immunity. Trends Immunol. 45, 211–223 (2024). https://doi.org/10.1016/j.it.2024.01.006
4. Alum, E.U.: Circadian nutrition and obesity: timing as a nutritional strategy. J. Health Popul. Nutr. 44, 367 (2025). https://doi.org/10.1186/s41043-025-01102-y
5. Uti, D.E., Atangwho, I.J., Omang, W.A., Alum, E.U., Obeten, U.N., Udeozor, P.A., Agada, S.A., Bawa, I., Ogbu, C.O.: Cytokines as key players in obesity low grade inflammation and related complications. Obes. Med. 54, 100585 (2025). https://doi.org/10.1016/j.obmed.2025.100585
6. Uti, D.E., Omang, W.A., Alum, E.U., Ugwu, O.P.-C., Wokoma, M.A., Oplekwu, R.I., Atangwho, I.J., Egbung, G.E.: Combined Hyaluronic Acid Nanobioconjugates Impair CD44-Signaling for Effective Treatment Against Obesity: A Review of Comparison with Other Actors. Int. J. Nanomedicine. 20, 10101–10126 (2025). https://doi.org/10.2147/IJN.S529250
7. Kim, K.H., Park, D., Jia, B., Baek, J.H., Hahn, Y., Jeon, C.O.: Identification and Characterization of Major Bile Acid 7α-Dehydroxylating Bacteria in the Human Gut. mSystems. 7, e00455-22. https://doi.org/10.1128/msystems.00455-22
8. Ticho, A.L., Malhotra, P., Dudeja, P.K., Gill, R.K., Alrefai, W.A.: Bile acid receptors and gastrointestinal functions. Liver Res. 3, 31–39 (2019). https://doi.org/10.1016/j.livres.2019.01.001
9. Schlicht, K., Pape, L., Rohmann, N., Knappe, C., Epe, J., Geisler, C., Pohlschneider, D., Brodesser, S., Kruse, L., Rohlfing, M.-E., Hartmann, K., Türk, K., Marquardt, J., Beckmann, J., von Schönfels, W., Beckmann, A., Wietzke-Braun, P., Schulte, D.M., Hollstein, T., Demetrowitsch, T., Jensen-Kroll, J., Brix, F., Schreiber, S., Franke, A., Schwarz, K., Waschina, S., Laudes, M.: Prediabetes and type 2 diabetes but not obesity are associated with alterations in bile acid related gut microbe-microbe and gut microbe-host community metabolism. Gut Microbes. 17, 2474143. https://doi.org/10.1080/19490976.2025.2474143
10. Alum, E.U.: Optimizing patient education for sustainable self-management in type 2 diabetes. Discov. Public Health. 22, 44 (2025). https://doi.org/10.1186/s12982-025-00445-5
11. Massafra, V., van Mil, S.W.C.: Farnesoid X receptor: A "homeostat" for hepatic nutrient metabolism. Biochim. Biophys. Acta BBA - Mol. Basis Dis. 1864, 45–59 (2018). https://doi.org/10.1016/j.bbadis.2017.10.003
12. Reddy, T.K., Villavaso, C.D., Pulapaka, A.V., Ferdinand, K.C.: Achieving equitable access to incretin-based therapies in cardiovascular care. Am. Heart J. Plus Cardiol. Res. Pract. 46, 100455 (2024). https://doi.org/10.1016/j.ahjo.2024.100455
13. Yan, K., Yu, H., Blaise, B.: Beyond GLP-1: efficacy and safety of dual and triple incretin agonists in personalized type 2 diabetes care-a systematic review and network meta-analysis. Acta Diabetol. 62, 1359–1370 (2025). https://doi.org/10.1007/s00592-025-02534-y
14. Fuchs, C.D., Simbrunner, B., Baumgartner, M., Campbell, C., Reiberger, T., Trauner, M.: Bile acid metabolism and signalling in liver disease. J. Hepatol. 82, 134–153 (2025). https://doi.org/10.1016/j.jhep.2024.09.032
15. Dang, J.T., Mocanu, V., Park, H., Laffin, M., Hotte, N., Karmali, S., Birch, D.W., Madsen, K.L.: Roux-en-Y gastric bypass and sleeve gastrectomy induce substantial and persistent changes in microbial communities and metabolic pathways. Gut Microbes. 14, 2050636 (2022). https://doi.org/10.1080/19490976.2022.2050636
16. Izah, S.C., Betiang, P.A., Paul-Chima Ugwu, O., Ainebyoona, C., Uti, D.E., Echegu, D.A.: The Ketogenic Diet in Obesity Management: Friend or Foe? Cell Biochem. Biophys. (2025). https://doi.org/10.1007/s12013-025-01878-0
17. Fiorucci, S., Urbani, G., Distrutti, E., Biagioli, M.: Obeticholic Acid and Other Farnesoid-X-Receptor (FXR) Agonists in the Treatment of Liver Disorders. Pharmaceuticals. 18, 1424 (2025). https://doi.org/10.3390/ph18091424
18. Tveter, K.M., Mezhibovsky, E., Wu, Y., Roopchand, D.E.: Bile acid metabolism and signaling: emerging pharmacological targets of dietary polyphenols. Pharmacol. Ther. 248, 108457 (2023). https://doi.org/10.1016/j.pharmthera.2023.108457
19. Haiser, H.J., Seim, K.L., Balskus, E.P., Turnbaugh, P.J.: Mechanistic insight into digoxin inactivation by Eggerthella lenta augments our understanding of its pharmacokinetics. Gut Microbes. 5, 233–238 (2014). https://doi.org/10.4161/gmic.27915
20. Ma, J., Piao, X., Mahfuz, S., Long, S., Wang, J.: The interaction among gut microbes, the intestinal barrier and short chain fatty acids. Anim. Nutr. 9, 159–174 (2022). https://doi.org/10.1016/j.aninu.2021.09.012

21. Theis, B.F., Park, J.S., Kim, J.S.A., Zeydabadinejad, S., Vijay-Kumar, M., Yeoh, B.S., Saha, P.: Gut Feelings: How Microbes, Diet, and Host Immunity Shape Disease. Biomedicines. 13, 1357 (2025). https://doi.org/10.3390/biomedicines13061357
22. Yang, S., Cai, J., Su, Q., Li, Q., Meng, X.: Human milk oligosaccharides combine with Bifidobacterium longum to form the "golden shield" of the infant intestine: metabolic strategies, health effects, and mechanisms of action. Gut Microbes. 16, 2430418. https://doi.org/10.1080/19490976.2024.2430418
23. Song, G., Xie, Y., Yi, L., Cheng, W., Jia, H., Shi, W., Liu, Q., Fang, L., Xue, S., Liu, D., Zhu, J., Zhao, S.: Bile acids affect intestinal barrier function through FXR and TGR5. Front. Med. 12, 1607899 (2025). https://doi.org/10.3389/fmed.2025.1607899
24. Zhuang, S., Li, Q., Cai, L., Wang, C., Lei, X.: Chemoproteomic Profiling of Bile Acid Interacting Proteins. ACS Cent. Sci. 3, 501–509 (2017). https://doi.org/10.1021/acscentsci.7b00134
25. Meacci, D., Bruni, A., Cocquio, A., Dell'Anna, G., Mandarino, F.V., Marasco, G., Cecinato, P., Barbara, G., Zagari, R.M.: Microbial Landscapes of the Gut–Biliary Axis: Implications for Benign and Malignant Biliary Tract Diseases. Microorganisms. 13, 1980 (2025). https://doi.org/10.3390/microorganisms13091980
26. Ejemot-Nwadiaro, R.I., Betiang, P.A., Basajja, M., Uti, D.E.: Obesity and Climate Change: A Two-way Street with Global Health Implications. Obes. Med. 100623 (2025). https://doi.org/10.1016/j.obmed.2025.100623
27. Panzitt, K., Wagner, M.: FXR in liver physiology: Multiple faces to regulate liver metabolism. Biochim. Biophys. Acta BBA - Mol. Basis Dis. 1867, 166133 (2021). https://doi.org/10.1016/j.bbadis.2021.166133
28. Lun, W., Yan, Q., Guo, X., Zhou, M., Bai, Y., He, J., Cao, H., Che, Q., Guo, J., Su, Z.: Mechanism of action of the bile acid receptor TGR5 in obesity. Acta Pharm. Sin. B. 14, 468–491 (2024). https://doi.org/10.1016/j.apsb.2023.11.011
29. Jiang, X., Ren, J., Yu, G., Wu, W., Chen, M., Zhao, Y., He, C.: Targeting Bile-Acid Metabolism: Nutritional and Microbial Approaches to Alleviate Ulcerative Colitis. Nutrients. 17, 1174 (2025). https://doi.org/10.3390/nu17071174
30. Wang, Q., Lin, H., Shen, C., Zhang, M., Wang, X., Yuan, M., Yuan, M., Jia, S., Cao, Z., Wu, C., Chen, B., Gao, A., Bi, Y., Ning, G., Wang, W., Wang, J., Liu, R.: Gut microbiota regulates postprandial GLP-1 response via ileal bile acid-TGR5 signaling. Gut Microbes. 15, 2274124 (2023). https://doi.org/10.1080/19490976.2023.2274124
31. Xie, C., Jiang, C., Shi, J., Gao, X., Sun, D., Sun, L., Wang, T., Takahashi, S., Anitha, M., Krausz, K.W., Patterson, A.D., Gonzalez, F.J.: An Intestinal Farnesoid X Receptor–Ceramide Signaling Axis Modulates Hepatic Gluconeogenesis in Mice. Diabetes. 66, 613–626 (2017). https://doi.org/10.2337/db16-0663
32. Obasi, D.C., Abba, J.N., Aniokete, U.C., Okoroh, P.N., Akwari, A.Ak.: Evolving Paradigms in Nutrition Therapy for Diabetes: From Carbohydrate Counting to Precision Diets. Obes. Med. 100622 (2025). https://doi.org/10.1016/j.obmed.2025.100622
33. Lin, Y., Hu, C., Wang, S., Lin, H.: Bile Acids and Type 2 Diabetes: Roles in Glucose Homeostasis and Therapeutic Opportunities. Metabolites. 15, 401 (2025). https://doi.org/10.3390/metabo15060401
34. Ahechu, P., Zozaya, G., Martí, P., Hernández-Lizoáin, J.L., Baixauli, J., Unamuno, X., Frühbeck, G., Catalán, V.: NLRP3 Inflammasome: A Possible Link Between Obesity-Associated Low-Grade Chronic Inflammation and Colorectal Cancer Development. Front. Immunol. 9, (2018). https://doi.org/10.3389/fimmu.2018.02918
35. Bensussen, A., Torres-Magallanes, J.A., Roces De Álvarez-Buylla, E.: Molecular tracking of insulin resistance and inflammation development on visceral adipose tissue. Front. Immunol. 14, 1014778 (2023). https://doi.org/10.3389/fimmu.2023.1014778
36. Bhat, A.A., Uppada, S., Achkar, I.W., Hashem, S., Yadav, S.K., Shanmugakonar, M., Al-Naemi, H.A., Haris, M., Uddin, S.: Tight Junction Proteins and Signaling Pathways in Cancer and Inflammation: A Functional Crosstalk. Front. Physiol. 9, 1942 (2019). https://doi.org/10.3389/fphys.2018.01942
37. Schlicht, K., Pape, L., Rohmann, N., Knappe, C., Epe, J., Geisler, C., Pohlschneider, D., Brodesser, S., Kruse, L., Rohlfing, M.-E., Hartmann, K., Türk, K., Marquardt, J., Beckmann, J., von Schönfels, W., Beckmann, A., Wietzke-Braun, P., Schulte, D.M., Hollstein, T., Demetrowitsch, T., Jensen-Kroll, J., Brix, F., Schreiber, S., Franke, A., Schwarz, K., Waschina, S., Laudes, M.: Prediabetes and type 2 diabetes but not obesity are associated with alterations in bile acid related gut microbe-microbe and gut microbe-host community metabolism. Gut Microbes. 17, 2474143 (2025). https://doi.org/10.1080/19490976.2025.2474143
38. Hamamah, S., Hajnal, A., Covasa, M.: Influence of Bariatric Surgery on Gut Microbiota Composition and Its Implication on Brain and Peripheral Targets. Nutrients. 16, 1071 (2024). https://doi.org/10.3390/nu16071071
39. Lent-Schochet, D., Jialal, I.: Antilipemic Agent Bile Acid Sequestrants. In: StatPearls. StatPearls Publishing, Treasure Island (FL) (2025)

40. Fan, Y., Liu, Y., Shao, C., Jiang, C., Wu, L., Xiao, J., Tang, L.: Gut Microbiota-Targeted Therapeutics for Metabolic Disorders: Mechanistic Insights into the Synergy of Probiotic-Fermented Herbal Bioactives. Int. J. Mol. Sci. 26, 5486 (2025). https://doi.org/10.3390/ijms26125486
41. Adorini, L., Trauner, M.: FXR agonists in NASH treatment. J. Hepatol. 79, 1317–1331 (2023). https://doi.org/10.1016/j.jhep.2023.07.034
42. Li, P., Wang, Y., Dong, Y., Zhang, X.: Unveiling the gut-liver axis: the behind-the-scenes "manipulator" of human immune function. Front. Immunol. 16, (2025). https://doi.org/10.3389/fimmu.2025.1638197
43. Moon, D.O.: Structure-Based Insights into TGR5 Activation by Natural Compounds: Therapeutic Implications and Emerging Strategies for Obesity Management. Biomedicines. 13, 2405 (2025). https://doi.org/10.3390/biomedicines13102405
44. Lin, J., Nie, Q., Cheng, J., Zhong, Y.-N., Zhang, T., Zhang, X., Ge, X., Ding, Y., Niu, C., Gao, Y., Wang, K., Gao, M., Wang, X., Chen, W., Yun, C., Ye, C., Xu, J., Shaoyong, W., Zhang, L., Shang, P., Luo, X., Zhang, Z., Zheng, X., Sha, X., Zhang, J., Nie, S., Zhang, X., Ren, F., Liu, H., Dong, E., Yu, X., Ji, L., Pang, Y., Sun, J.-P., Jiang, C.: A microbial amino-acid-conjugated bile acid, tryptophan-cholic acid, improves glucose homeostasis via the orphan receptor MRGPRE. Cell. 188, 4530-4548.e25 (2025). https://doi.org/10.1016/j.cell.2025.05.010
45. Tseng, P.-T., Zeng, B.-Y., Hsu, C.-W., Hung, C.-M., Carvalho, A.F., Stubbs, B., Chen, Y.-W., Chen, T.-Y., Lei, W.-T., Chen, J.-J., Su, K.-P., Shiue, Y.-L., Liang, C.-S.: The pharmacodynamics-based prophylactic benefits of GLP-1 receptor agonists and SGLT2 inhibitors on neurodegenerative diseases: evidence from a network meta-analysis. BMC Med. 23, 197 (2025). https://doi.org/10.1186/s12916-025-04018-w
46. Zheng, X., Chen, T., Zhao, A., Ning, Z., Kuang, J., Wang, S., You, Y., Bao, Y., Ma, X., Yu, H., Zhou, J., Jiang, M., Li, M., Wang, J., Ma, X., Zhou, S., Li, Y., Ge, K., Rajani, C., Xie, G., Hu, C., Guo, Y., Lu, A., Jia, W., Jia, W.: Hyocholic acid species as novel biomarkers for metabolic disorders. Nat. Commun. 12, 1487 (2021). https://doi.org/10.1038/s41467-021-21744-w
47. Alum, E.U., Uti, D.E., Ugwu, O.P.-C., Alum, B.N., Edeh, F.O., Ainebyoona, C.: Unveiling the microbial orchestra: exploring the role of microbiota in cancer development and treatment. Discov. Oncol. 16, 646 (2025). https://doi.org/10.1007/s12672-025-02352-2

CITE AS: Winniefred Nankya (2026). Gut Microbial Bile Acid Signaling as a Shared Therapeutic Axis in Obesity and Diabetes. IAA Journal of Biological Sciences 14(1):75-81. https://doi.org/10.59298/IAAJB/2026/1417581