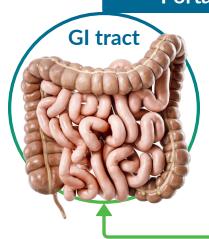
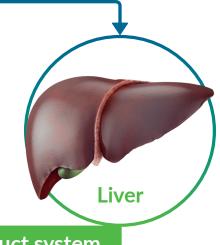
Portal vein



WHAT IS THE GUT-LIVER AXIS?^{1,2}

Bidirectional relationship between the GI tract and liver mediated by blood and bile circulation through the portal vein and biliary duct system



Biliary duct system

How is this bidirectional relationship maintained?^{1,3-9}

Contributor*	In the GI tract	In the liver
Nutrients	Absorbed	Metabolized
Microbiota components/ byproducts and toxins	Produced or released	Surveilled, detoxified, and/or excreted
Immune system	Protects gut from harmful microbiota and their byproducts; provides tolerance to beneficial microbiota	Activated by gut microbiota byproducts and toxins; includes antimicrobial peptides, antibodies (eg, IgA), and proinflammatory mediators
Bile acids [†]	Maintain eubiosis; regulate GI motility and entero-endocrine hormone production	Produced, excreted, and/or recycled
Entero-endocrine hormones	Secreted	Regulate bile acid production

Various contributors with distinct and interacting roles in (or influences on) the GI tract and liver

How does the gut-liver axis function in the healthy state?^{1,3,5-10} Translocation of nutrients, Maintenance of microbiota byproducts, toxins, intestinal barrier integrity entero-endocrine hormones, and reabsorbed bile acids Eubiosis, regulation Metabolism of GI motility and of nutrients, entero-endocrine detoxification of hormone secretion microbial byproducts by bile acids and toxins, and recycling of reabsorbed bile acids Bile acid recycling Synthesis and transport of bile acids (regulated by entero-endocrine hormones), antimicrobial peptides, antibodies (eg, IgA), and liver-derived proinflammatory mediators Biliary duct system **Proinflammatory mediators**



^{*}Select list of contributors and their involvement in the gut-liver axis. For additional details, see Rodrigues SG, et al. Semin Immunol. 2024;71:101859.

[†]Primary bile acids are synthesized from cholesterol in the liver, conjugated with taurine or glycine, excreted into bile, and metabolized into secondary bile acids by the gut microbiota. Primary and secondary bile acids are reabsorbed in the intestines and returned to the liver via the portal vein.⁷

GI = eastrointestinal: IeA = immunoglobulin A

^{1.} Albillos A, et al. *J Hepatol.* 2020;72(3):558-577. **2.** Bruneau A, et al. *Front Med (Lausanne)*. 2021;8:725390. **3.** Hundt M, et al. In: StatPearls Publishing; 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470209/. **4.** Meyer F, et al. *Int J Mol Sci.* 2020;21(15):5357. **5.** Quigley EMM. In: Gershwin ME, et al, eds. *Liver Immunology*. Springer Nature Switzerland AG; 2020:125-137. **6.** Rodrigues SG, et al. *Semin Immunol.* 2024;71:101859. **7.** Tilg H, et al. *Cell Metab.* 2022;34(11):1700-1718. **8.** Trefts E, et al. *Curr Biol.* 2016;39(1):1-12.