Host-microbiota tryptophan metabolism in health and diseases

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The gut microbiota is a crucial actor in human physiology. Many of these effects are mediated by metabolites that are either produced by the microbes or derived from the transformation of environmental or host molecules. A large array of metabolites drives the crosstalk between the host and its microbiome. The three currently most studied categories of metabolites involved in host-microbiota interactions are (1) short-chain fatty acids (SCFAs), produced by bacteria from the fermentation of fibers; (2) bile acids produced in the liver and transformed by the gut microbiota before re-affecting the host; and (3) tryptophan (Trp) metabolites.

In the gut, the three major tryptophan metabolism pathways leading to serotonin, kynurenine and indole derivatives are under the direct or indirect control of the microbiota and are tightly interconnected. Beyond changes in microbiota composition, several key functions are altered in disease and this plays a role in disease onset, chronicity or complication. We showed that the ability of the gut microbiota to produce AhR agonists from tryptophan metabolism, as well as other Trp metabolism pathways are impaired in several diseases including inflammatory bowel disease and metabolic syndrome. More importantly, correcting these functional defects, either pharmacologically or through the administration of bacteria that are natural producers of AhR agonists, induces beneficial effects. Manipulating the gut microbiota to modulate the tryptophan metabolism and particularly the AhR pathway could be of therapeutic interest for many human diseases.