Table S1: Summarizing table of Microbiota-derived metabolites that modulate host immunity in the gut.

Metabolite:		Major Effects:	Ref:
SCFAs		• Maintain intestinal barrier integrity • Induce of tolerogenic DC • Butyrate promotes regulatory T cells and IL22 production	[28,29,31,32,35–37]
Lactate		• Suppresses the inflammation through the activation of GPR81 on DCs and macrophages • Promotes M2 polarization • Inhibits the activation of IECs • Decreases the proliferation of effector T cells and increases the conversion of naive T cells to Tregs	[52,53,54,56]
Succinate		• Activates the SUCNR1 receptor and enhances its synthesis on macrophages • Potent activator of tuft cells and leads to the activation of ILC2s	[61,62,66–68]
B Vitamins	Thiamine	• Required in lymphocyte survival	[86]
	Riboflavin	• Decreases TNF-alpha production by macrophages • Enhances ROS production and phagocytic activity of macrophages • Lessens clinical symptoms and systemic inflammation in patients with Crohn's disease	[90,91,95,96]
	Niacin	• Regulates ROS production by macrophages and neutrophils • Enhances neutrophils recruitment and activity • Promotes T-helper activation	[103–105]
	Pantothenic acid	• Enhances cytokines production and bacterial clearance in *M. tuberculosis* infection	[108]
	Pyridoxine	• Polarizes T-helpers towards a Th1 profile	[122–124]
	Biotin	• Correlates to histological gut inflammation in IBD-mice • Enhances IL-17 and INF-γ production in T lymphocytes	[128,129]
	Folate	• Blood levels correlate to asthma severity and circulating lymphocyte levels in allergic children	[142]
	Cyanocobalamin	• Blood levels correlate to severity of infectious diseases in hospitalized patients	[138,139]
Tryptophan- derived indoles		• Increase the expression of IL10R1 in epithelial cells • Increase the production of IL-22 in IELs • Increase the number of ILC3 producing IL-22	[154,158,160]
Taurine		• Increases the number of lymphocytes in Peyer's patches • Activator of the NLRP6 inflammasome and induces the production of AMPs	[168]
p-Cresol		• Inhibits the proliferation of CD43+ B-cell progenitor • Increases ROS and Phagocytosis in macrophages • Suppresses IFN-γ-producing Th1 cells and favors a Th2 response	[174,175,176]

Histidine	• It is a cytokine and inflammatory mediator in acute inflammation and hypersensitivity • Promotes Th1 response through H1R while H2R activation induces polarization into regulatory T cells • Diminution of IL-18 production through inhibition of NLRP6 inflammasome assembly	[169,179,183–185]
Spermine	• Reduces the expression of pro-inflammatory cytokines produced by monocytes and macrophages	[193,194]
Spermidine	• Reduces monocyte-derived pro-inflammatory cytokines production • Controls the differentiation of naïve T cell to FoxP3+ T cells.	[201,202]
D-amino acids	• Metabolized by the epithelium to generate H_2O_2	
GABA	• Increases the production of IL-17 • Stimulates mucin-1 expression in epithelial cells • Decreases IL-1β, increases tight junction and TGF-β in epithelial cells	[213,214,215]
QSMs	• Elicit proinflammatory effects and modulate the activities of gut-associated T lymphocytes, macrophages, DCs, and neutrophils • Induce Mast cells degranulation and release of ROS, TNF- , and Prostaglandin D2	[221,222]
Catecholamines	• Act as potential inter-kingdom signaling molecules in the gut • Exert autoregulatory functions on immune cells by means of intracellular oxidative mechanisms	[234,245]
CDNs and CTNs	• Induce either STING or RECON and induces antibacterial activity	[249,250,251]
Inosine	• Activates the adenosine 2A receptor and drive Th1 differentiation	[252]
Secondary Bile acids	• Negative regulator of macrophages, DC and NK • Maintain a tolerogenic environment in the liver and in the intestine • Promote generation of colonic RORγt-expressing FoxP3+ Tregs	[255,256,257,258,260]
Sphingolipids	• Preserve the integrity of the intestinal barrier • Bacteroides-derived sphingolipids have anti-inflammatory properties • Prevent accumulation of colonic iNKT	[266,271,270]
Lipoteichoic acids	• Protecting effect on intestinal mucosa • Immunostimulatory properties through TLR2 on monocytes and macrophages • Involve in the antibacterial immune response	[277,279,280,281–283,285,287]