

EPITHELIAL CYP2S1-DEPENDENT REGULATION OF INTESTINAL METABOLOME AND MICROBIOME

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Cyp2s1, an aryl hydrocarbon receptor-regulated enzyme in intestinal epithelial cells, modulates gut microbiota and metabolism, with overexpression exacerbating experimental colitis severity in mice.

KEY POINTS

- Cyp2s1 is predominantly expressed in intestinal epithelial cells and metabolizes xenobiotics like dioxin and endogenous compounds including polyunsaturated fatty acids and retinoic acid.
- Cyp2s1 expression is significantly upregulated by aryl hydrocarbon receptor activation but is consistently reduced in intestinal inflammation, including in biopsies from IBD patients and multiple experimental colitis models.
- Transgenic mice overexpressing Cyp2s1 in intestinal epithelial cells exhibit reduced gut microbial diversity and alterations in fatty acid oxidation and tryptophan metabolism pathways.
- Cyp2s1 overexpression in intestinal epithelial cells exacerbates dextran sulfate sodium-induced colitis severity and reduces colonic group 3 innate lymphoid cells.
- The findings identify Cyp2s1 as a previously unrecognized contributor to IBD pathophysiology and a potential therapeutic target.

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