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Functional Medicine

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RELATION BETWEEN FUT2 GENOTYPE AND INTESTINAL DYSBIOSIS

News & Perspective > Current Opinion in Rheumatology

The Gut Microbiota and Inflammatory Bowel Disease

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DISCLOSURES | Curr Opin Rheumatol. 2015;27(4):388-396.

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"Another Crohn's disease-related gene that may affect epithelial barrier system is that encoding **fucosyl transferase 2** (**Fut2**). Fut2 adds terminal α1, 2-fucose residues on carbohydrate chains expressed on intestinal epithelial cells (IECs). Epithelial fucose has been reported to promote symbiosis between the host and commensal bacteria, because Bacteroides fragilis and B. thetaiotaomicron can forage epithelial fucose for use in extracellular components (…) as an energy source. In addition, several pathogenic microorganisms including Norwalk virus, rotavirus, Salmonella typhimurium, and Helicobacter pylori attach to epithelial fucose, such that epithelial fucosylation is an interface of reciprocal interaction between the host and enteric microorganisms. These findings allow us to speculate on the role of epithelial fucosylation in the regulation of homeostasis of gut microbiota and pathogenic microorganisms.

In fact, humans who are homozygous for a Fut2 nonsense polymorphism and mice that lack Fut2 have aberrant microbiota. Furthermore, mice lacking Fut2 are susceptible to the inflammation induced by infection with pathogenic bacteria such as Citrobacter rodentium and Salmonella typhimurium. Given that the Fut2 nonsense polymorphism is associated with mucosal and systemic inflammatory disorders such as type I diabetes and primary sclerosing cholangitis as well as Crohn's disease, the **dysbiosis** caused by defects in epithelial fucosylation may create an inflammation-prone gut microbiota. (…) Several recent reports including one from our group indicate that commensal and pathogenic bacteria cooperate with mucosal immune cells, especially ILC3s, in the regulation of epithelial Fut2 expression. In this scenario, commensal and pathogenic bacteria stimulate ILC3s to produce IL-22, which signals through IL-22R on IECs to induce expression of Fut2 and subsequent fucosylation of IECs.

These findings show that the epithelial barrier system (mucus secretion, bactericidal molecules production, glycosylation), is crucial to maintaining intestinal homeostasis and preventing deleterious inflammation."