MOLECULAR MECHANISMS OF FREE FATTY ACID RECEPTOR 2-MEDIATED EFFECTS ON GUT INNATE LYMPHOID CELLS

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Intestinal immune cells have been increasingly appreciated as important players in the initiation, propagation and regulation of the autoimmunity directed against the central nervous system (CNS) and pancreatic beta islets, as observed in multiple sclerosis and type 1 diabetes (T1D), respectively. We are particularly interested in the role of intestinal innate lymphoid cells type 3 (ILC3) in autoimmunity. It is our hypothesis that ILC3 play the major regulatory role in the intestine, and that they are able to potentiate regulatory T cells (Treg) and tolerogenic dendritic cells (tolDC), and to inhibit autoreactive effector T helper (Th) cells: Th1 and Th17. We are exploring possibilities to potentiate regulatory properties of intestinal ILC3 cells as a mean to treat autoimmunity. To this end, we use two models of multiple sclerosis: MOG35-55-induced EAE in C57BL/6 mice and spinal cord homogenate-induced EAE in DA rats, and two models of T1D: multiple low dose streptozotocin-induced T1D in C57BL/6 mice and spontaneous T1D in NOD mice. Immune cells from the intestinal lamina propria, Peyers patches, or gut epithelial monolayer are isolated and detailed phenotypic and functional analysis of ILC3, Treg, tolDC, Th1, and Th17 cells, but also of other immune cells of interest, is performed. Finally, different pharmacological agents are applied to mice and rats orally, as the route of choice for delivery to intestinal immune cells. Molecular targets on ILC3 that we are exploring are receptors for short chain fatty acids, aryl hydrocarbons, microbe-associated molecular patterns, and bile acids. Our research contributes both to the basic knowledge on the role of ILC3 in the immune system, and to the discovery of novel therapeutic options for autoimmune and chronic inflammatory diseases. Here, molecular mechanisms of free fatty acid receptor 2-mediated effects on gut ILC will be presented.

Key words: innate lymphoid cells; intestine; autoimmunity; free fatty acid receptor 2.

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