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Eiji Umemoto

University of Shizuoka, Shizuoka, Japan

Pyruvate–GPR31 axis induces LysoDC dendrite protrusion to M-cell pockets for effective immune responses in Peyer's patches

Peyer's patches (PPs) are sites of antigen entry and immunoinduction in the small intestine. In PPs, pathogens are transferred through microfold (M) cells. We analyzed the mechanisms of antigen capture by mononuclear phagocytes beneath M cells. We found that bacterial metabolite pyruvate acted on lysozyme-expressing dendritic cells (LysoDCs), a monocyte-derived phagocyte subset, and induced protrusion of dendrites particularly with "balloon" shapes into basolateral M-cell pockets via its receptor, G-protein coupled receptor 31 (GPR31). Pyruvate administration in wild-type but not Gpr31b-deficient mice increased LysoDC uptake of orally infected Listeria monocytogenes. GPR31 signaling boosted antigen processing and altered gene expression. It also increased LysoDC migration to the interfollicular region, thereby production of pathogen-specific Th1 cells as well as cytotoxic T cells and effector T cell migration to the lamina propria. Furthermore, oral pyruvate administration conferred high resistance to a virulent L. monocytogenes strain in a GPR31-dependent manner. Collectively, the pyruvate–GPR31 axis plays critical roles in orchestrating intestinal protective immunity against pathogenic bacteria. The pyruvate–GPR31 axis may serve as a beneficial target for enhancing mucosal immunity by oral vaccination.

Keywords

Peyer's patch; commensal metabolite; GPCR: dendritic cell; Listeria monocytogenes

Biography

2005-2007 Research Associate, Laboratory of Immunodynamics, Graduate School of Medicine, Osaka University

2007-2012 Assistant professor, Laboratory of Immunodynamics, Graduate School of Medicine, Osaka University

2012-2019 Associate professor, Laboratory of Immune Regulation, Graduate School of Medicine, Osaka University

2019-present Professor, Laboratory of Microbiology and Immunology, School of Pharmaceutical Sciences, University of Shizuoka

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