## GPR31-dependent dendrite protrusion of intestinal $CX_3CR1^+$ cells by bacterial metabolites

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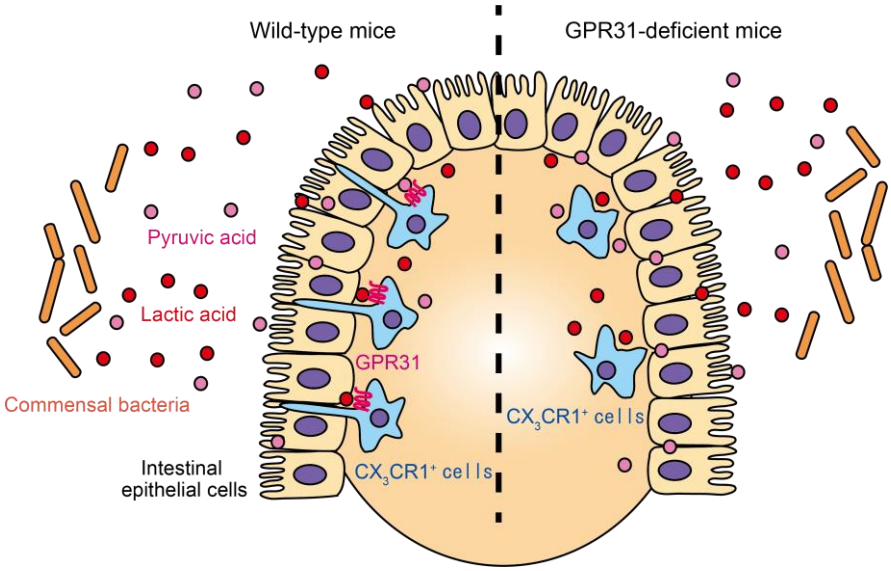
Small intestinal mononuclear cells that express $CX_3CR1$ ($CX_3CR1^+$ cells) regulate immune responses. $CX_3CR1^+$ cells take up luminal antigens by protruding their dendrites into the lumen. However, it remains unclear how dendrite protrusion by $CX_3CR1^+$ cells is induced in the intestine. Here we show that the bacterial metabolites pyruvic acid and lactic acid induce dendrite protrusion via GPR31 in $CX_3CR1^+$ cells. Mice that lack GPR31, which was highly and selectively expressed in intestinal $CX_3CR1^+$ cells, showed defective dendrite protrusions of $CX_3CR1^+$ cells in the small intestine. We purified a GPR31-activating fraction, and identified lactic acid. Both lactic acid and pyruvic acid induced dendrite extension of $CX_3CR1^+$ cells of wild-type mice, but not of *Gpr31b*$^{-/-}$ mice. Furthermore, wild-type mice treated with lactate or pyruvate showed an enhanced immune response and high resistance to intestinal Salmonella infection. These findings demonstrate that lactate and pyruvate, which are produced in the intestinal lumen in a bacteria-dependent manner, contribute to enhanced immune responses by inducing GPR31-mediated dendrite protrusion of intestinal $CX_3CR1^+$ cells.


Wild-type mice
GPR31-deficient mice
Pyruvic acid
Lactic acid
Commensal bacteria
GPR31
CX3CR1+ cells
Intestinal epithelial cells
CX3CR1+ cells