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The crucial role of NF-κB in M cell differentiation

○ Takashi Kanaya and Hiroshi Ohno
Laboratory for Intestinal Ecosystem, RIKEN Center for Integrative Medical Sciences

M cells are located in the follicle-associated epithelium (FAE) that covers Peyer's patches (PPs) and are responsible for the uptake of intestinal antigens. The differentiation of M cells is initiated by receptor activator of NF-κB (RANK) signaling. However, the intracellular pathways involved in M cell differentiation are still elusive. We previously demonstrated that Spi-B transcription factor is essential for the development of functionally mature M cells (*1*). Here we demonstrate that the NF-κB pathway activated by RANK is essential for M cell differentiation using *in vitro* organoids culture. Overexpression of NF-κB transcription factors enhances the expression of M cell-associated molecules, such as Spi-B, but is not sufficient to complete M cell differentiation. Furthermore, we evaluated the requirement for tumor necrosis factor receptor (TNFR)-associated factor 6 (TRAF6). Conditional deletion of TRAF6 in the intestinal epithelium causes a complete loss of M cells in PPs, resulting in impaired antigen uptake into PPs. In addition, the expression of FAE-associated genes is almost silenced in TRAF6-deficient mice. Importantly, the expression of RelB was also observed in the FAE of human PPs, and TRAF6 is required for human M cell differentiation. This study thus demonstrates the crucial role of TRAF6-mediated NF-κB signaling in the development of M cells and FAE (*2*).

【References】

(*1*) Kanaya *et al.* The Ets transcription factor Spi-B is essential for the differentiation of intestinal microfold cells. *Nat Immunol*, 2012.
(*2*) Kanaya *et al.* Development of intestinal M cells and follicle-associated epithelium is regulated by TRAF6-mediated NF-κB. *J Exp Med*, 2018.