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Identification and elucidation of novel M-cell specific molecules for its function and differentiation

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Microfold (M) cells in follicle-associated epithelium (FAE) are specialized antigen-sampling cells that take up various intestinal luminal antigens. Transcription factor Spi-B is known to regulate M-cell maturation, but the molecules that can promote transcytosis within M cells are unidentified, with the exception of glycoprotein 2 (GP2), a receptor for FimH-positive bacteria such as *Salmonella* Typhimurium. From comparing a gene-expression pattern between FAEs prepared from WT and SpiB-deficient mice, we tried to explore molecules which are specifically expressed in mature M cells. Here, we report that mouse allograft inflammatory factor 1 (Aif1) is specifically expressed in M cells and contributes to M-cell transcytosis. Whole-mount staining revealed that Aif1 was expressed in GP2-positive mature M cells, and its expression was dependent on the presence of Spi-B. To investigate the function of Aif1 *in vivo*, we generated Aif1-deficient mice. FAE in *Aif1*$^{-/-}$ mice showed suppressed uptake of particles and commensal bacteria compared with that in wild-type mice. Translocation of *Yersinia enterocolitica*, but not of *S.* Typhimurium, leading to the generation of antigen-specific IgA antibodies, was also diminished in Aif1-deficient mice. Although β1 integrin, which acts as a receptor for *Y. enterocolitica* via invasin protein, was expressed on the apical surface membranes of M cells, its active form was rarely found in *Aif1*$^{-/-}$ mice. Taken together, these findings show that Aif1 is important for bacterial and particle transcytosis in M cells.