Salmonella transforms follicle-associated epithelial cells into antigen sampling M cells to promote intestinal invasion

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As the preferred cell type to translocate across the gut epithelium, S. Typhimurium targets antigen-sampling microfold (M) cells, which represent a small proportion of the specialized follicular associated epithelium (FAE) overlying mucosa-associated lymphoid tissues. Although M cell numbers have been documented to increase during Salmonella infection, the molecular mechanism underlying this increase is unclear. Using in vitro and in vivo infection models we demonstrate that the S. Typhimurium type III effector protein SopB induces an epithelial-mesenchymal transition (EMT) of FAE enterocytes into M cells. This cellular trans-differentiation depends on activation of the Wnt/β-catenin signaling leading to induction of both the growth factor receptor RANK as well as its ligand RANKL. The autocrine activation of RelB expressing FAE enterocytes by RANKL/RANK induces EMT regulator Slug that marks epithelial trans-differentiation into M cells. This study demonstrates a novel host-pathogen interaction in which the pathogen transforms primed epithelial cells to promote host colonisation and invasion.

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