Study on molecular mechanisms of M-cell differentiation and function

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The mucosal epithelium lining the inner surfaces of the body is exposed to various macromolecules and microorganisms. Mucosal membranes are usually a monolayer of epithelial cells, and relatively susceptible to the invasion of microorganisms. Indeed, the mucosal epithelium is the site of invasion for most microorganisms. Therefore, the mucosal membranes are one of the most important places for the immune system to defend the organism from those pathogens. Intestinal epithelial cells are always in contact with enormous numbers of macromolecules and microorganisms through ingestion, and the gut-associated lymphoid tissues (GALT) such as Peyer's patches (PPs) play crucial roles in immunological surveillance and defense at the initial contact site to those pathogens.

PPs are the major site of antigenic macromolecules and microorganisms sampling, which leads to immune responses and/or tolerance. PPs are separated from intestinal lumen by the follicle-associated epithelium (FAE), which contains M-cells (figure). M-cells are specially differentiated epithelial cells. M-cells actively uptake most antigens and microorganisms, and transfer them to PPs for immune response. Thus, passage of those pathogens through M-cells is an essential step for the development of mucosal immunity and the pathology of many infectious diseases. Although the importance of M cells in mucosal and systemic immune responses is obvious, analysis of M cells has been hampered mainly by the limitation in number of M cells (< $1/10^7$ intestinal epithelial cells) and the lack of specific markers for M cells and of *in vitro* M cell models. Recently, an *in vitro* M-cell model has been established, in which the differentiation of M-cells is induced from Caco-2 human colon epithelial carcinoma cells when they are co-cultured with lymphocytes of PPs or Raji B lymphoma cells. We set up the *in vitro* M cell induction protocol to identify molecules involved in M cell differentiation and to understand the cell biology of M cells. We also employ the laser-capture microdissection system to collect M cell-enriched intestinal mucosa for expression profiling analysis using cDNA microarray techniques in search of M cell-specific markers.