

Biological function of paracellular barrier-forming claudins and claudin-deficiency-related metaplasia

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Epithelial cell sheets cover the outer and inner surfaces of every compartment in the body, at every level, from the cell to the body surface, and they function at all of these levels as a permselective barrier. The paracellular barrier, which is established by the formation of tight junctions between epithelial cells, is basically built by the polymerization of claudins. Thus, claudins are thought to play a role in the microenvironment for various biological functions. Analyses of claudin knockout mice are beginning to elucidate the physiological relevance of the paracellular barriers/permeability in many biological systems. Single or multiple claudins have been targeted in different combinations.

Defects in the tight junction (TJ) epithelial paracellular barrier function are thought to be a primary cause of inflammation, but the mechanism remains largely unknown. Here we examined the inflammation reactions associated with the knockout mice of claudin-18, a major component of TJs in the stomach. The *Cldn18*^{-/-} mice were afflicted with atrophic gastritis, which started on postnatal day (pnd) 3, when the intragastric pH was decreased by H⁺ secretion from parietal cells, concomitant with the up-regulation of IL-1 β , COX-2, and KC. These conditions induced spasmodic polypeptide-expressing metaplasia (SPEM) and intestinal metaplasia (IM), although the prolonged acute inflammation did not develop into chronic inflammation. We examined which conditions, such as increased cell proliferation in the *Cldn18*^{-/-} mice, might lead to chronic inflammation. These findings may provide a new paradigm for understanding the regulation of inflammation.

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EDUCATIONS/TRAINING

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POSITIONS AND HONORS

1983-1986	Research Associate, Department of Anatomy, University of Tokyo, Faculty of Medicine, Japan
1986-1990	Research Associate, Department of Ultrastructural Research, Tokyo Metropolitan Institute of Medical Science, Japan
1990-1994	Assistant Professor, Department of Information Physiology, National Institute for Physiological Sciences, Japan
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RECENT PUBLICATIONS

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