Perspective of trans-mucosal delivery using tight junction modulators

Masuo Kondoh, Kiyohito Yagi
(Laboratory of Bio-Functional Molecular Chemistry, Graduate School of Pharmaceutical Sciences, Osaka University)

Passing across epithelial cell sheets is the first step of drug absorption. The epithelial cell sheets function as barriers to prevent the leakage of solutes through the paracellular pathway. Drug delivery systems that overcome the epithelial barrier have been investigated for a long time.

There are tight junctions (TJs) between adjacent cells in the epithelial cell sheets, and TJs prevent the paracellular movement of solutes. A regulation of TJ-barrier is a strategy for drug absorption via the paracellular pathway, and indeed the intestinal absorption enhancers have been developed since 1960s. Biochemical structures of TJs had been unclear, and the drug delivery system based on TJ-components has never been fully developed. The first TJ-component occludin and the first functional TJ-component claudin were identified in 1993 and 1998, respectively. Claudin consists of 24 members, and the expression and barrier-function are tissue-specific among them. These findings provide us new insights into drug delivery through the paracellular route.

In this presentation, we overview the biochemical structures of TJs and the TJs-based drug delivery systems, including our studies using a claudin-4 binder. We discuss the possibility and the problems of future TJs-based strategies for drug delivery.