# How to seal the intercellular space at tricellular contacts

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医学教育図書棟3階 第2講義室

## Abstract

Tight junctions (TJs), one mode of cell-cell junctions in vertebrates, play essential roles in the epithelial barrier function by regulating the passage of solutes via the paracellular pathway. In addition to TJs between adjacent cells, epithelial cells obliterate the extracellular space at tricellular contacts, where the corners of three cells meet, to establish the full epithelial barrier function. Tricellular contacts contain specialized TJs designated tricellular TJs (tTJs), where three closely-attached vertical TJs (central sealing elements) squeeze the extracellular space. However, the molecular mechanisms behind tTJ formation remained elusive for a long time. So far two types of integral membrane proteins, tricellulin and angulin family proteins, including angulin-1/LSR, angulin-2/ILDR1, and angulin-3/ILDR2, are known as molecular components of tTJs. Recent studies in a renal epithelial cell line MDCK using the genome editing-mediated gene disruption have clarified how angulin and tricellulin are involved in tTJ formation: angulin plays a central role in the tricellular plasma membrane contacts independent of tricellulin, while tricellulin is required for the connection of short TJs to the central sealing elements to generate complete tTJ structures. Furthermore, human genetics and knockout mice studies have gradually reported that the impairment of tTJ proteins causes various pathological conditions. This lecture will explain the molecular organization and physiological impact of tTJs, a new topic in the field of epithelial barrier function.

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