CDB SEMINAR

Jerrold R. Turner

Department of Pathology

The University of Chicago

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16:00~16:50 A7F Seminar Room

Tight Junction Remodeling Participates in Cytoskeletally-mediated Barrier Regulation: The Unique Role of Zonula Occludens-1

Summary

The tight junction is composed of transmembrane and membrane-associated proteins previously thought to form stable complexes. Our recent data (Shen et al., J Cell Biol, 2008) indicates that this is not the case. While claudin-1 is stably anchored at the tight junction, the majority of occludin diffuses rapidly within cell membranes. ZO-1 is also highly dynamic and exchanges between membrane and intracellular pools by an energy-dependent process. To determine whether this continuous molecular remodeling contributes to function, we assessed the effects myosin light chain kinase (MLCK) inhibition, which enhances barrier function, on tight junction protein dynamics. MLCK inhibition had no effect on exchange of tight junction-associated actin, occludin, or claudin-1, but the ZO-1 immobile fraction was increased by MLCK inhibition. In contrast, a ZO-1 mutant lacking the actin binding region (ABR) was not immobilized by MLCK inhibition. Moreover, expression of the free ABR limited exchange of full-length ZO-1 (in the absence of MLCK inhibitors) and free ABR expression prevented barrier enhancement induced by MLCK inhibition. The data demonstrate that ZO-1 stabilization at the tight junction is dependent on the ABR and contributes to cytoskeletally-mediated barrier regulation.

Host:
Shigenobu Yonemura
Electron Microscope Laboratory, CDB
yonemura@cdb.riken.jp
Tel:078-306-3106
(ext:1314)