## The association with tight junction and stratum corneum formation

## Hiroaki Iwata

Gifu University Graduate School of Medicine, Department of Dermatology

The tight junction (TJ) is an intercellular junction complex that seals adjacent epithelial cells and plays a crucial role in epithelial barrier function. TJs consist of several proteins, including those of the transmembrane claudin family, occludin and the scaffold zonula occludens (ZO) family. The distribution of TJs is distinct among stratified squamous epithelia, such as between skin and oral buccal mucosa. However, how TJs are associated with stratum corneum have not been elucidated. We show that epithelial turnover and proliferation dictate TJ distribution in the squamous epithelia. Human samples and mouse pharmacological models revealed that slower epithelial turnover/proliferation led to the confinement of TJs in the uppermost part of squamous epithelia. In contrast, TJs were dispersedly distributed in faster cell turnover/proliferation conditions. Cell culture experiments and mathematical modeling corroborated the TJ arrangements. These findings demonstrate that TJ formation is dependent on epithelial cell dynamics, the confinement of ZO-1 within a single layer of squamous epithelia is indicative of slow epithelial proliferation and turnover rates. Our findings do not fully elucidate the functional significance of ZO-1 distribution, but our study does suggest that ZO-1 reflects the proliferation and turnover of epithelia. Our study implicates that TJ expression can be a therapeutic output of diseased epithelia.