O-18.6 Short talk

Visualizing Permeation Enhancement of the Intestinal Epithelium Using Label-Free Live-Cell Coherent Anti-Stokes Raman Scattering (CARS) Microscopy

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The barrier function of epithelial tissues is essential for homeostasis. While excessive permeability is linked to disease, controlled modulation is desirable for drug delivery. Diverse chemical permeation enhancers (PEs) have been proposed to enable oral delivery of peptide therapeutics, but understanding their mechanisms/effects on the epithelium is crucial to ensure safety. Conventional permeability studies rely on indirect methods like transepithelial resistance measurements, transport assays, cytotoxicity tests, and fixation-based immunostaining, which provide limited spatial information and/or may alter cell physiology. CARS microscopy is a chemically sensitive, label-free imaging technique that enables high-resolution, real-time, live-cell visualization. Here, we present a CARS-based strategy to directly monitor epithelial monolayer dynamics under PE treatment. Z-stacks were acquired over 3 hours at various doses of paracellular (P-PE) and transcellular (T-PE) enhancers. P-PEs induced an expansion of the paracellular space, indicating tight-junction modulation, while T-PEs preserved cell-cell junctions but altered lipid content. This study highlights CARS microscopy's potential for directly assessing PE-induced epithelial changes at subcellular resolution, which could be extended to other cellular components involved in permeability modulation and other body barriers.