

2147**Topic Category:** 4110-ASIP Regulation of the epithelial barrier and intercellular junctions**First Author:** Hanna Ungewiß

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Dsg2 regulates intestinal epithelial cell adhesion and barrier function via EGFR

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Rapidly renewing epithelial tissues such as the intestinal epithelium require precise modulation of intercellular adhesion to preserve barrier integrity during cell division and differentiation. Previously, we have shown that Desmoglein 2 (Dsg2), an adhesion molecule of desmosomes, beside its adhesion function, regulates intestinal barrier properties via p38MAPK signaling. Here we show that Dsg2 and epidermal growth factor receptor (EGFR) co-localize at the apical part of cell-cell contacts in polarized enterocytes using confocal and stimulated emission depletion (STED) microscopy. DLD1 cells deficient for Dsg2 display EGFR mislocalization and reduced protein levels of activated as well as total EGFR. Atomic force microscopy (AFM) revealed EGFR-Dsg2 interaction both under cell-free conditions as well as on living enterocytes, which was confirmed by co-immunoprecipitation. Moreover, EGFR inhibition reduced cell cohesion and barrier reformation. In line with this, we demonstrate that Src activity is required for barrier formation and localization of EGFR and Dsg2 to cell-cell contacts. Thus, our study reveals a new mechanism by which Dsg2 regulates barrier properties via EGFR.

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