

**P023** Mechanisms of dissociation of E-cadherin-mediated junctions in enterocytes undergoing anoikis: the role of the epidermal growth factor receptor

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The intestinal epithelium is constantly renewed. At the villus tip, enterocytes are shed into the intestinal lumen and die probably by anoikis, the apoptosis triggered by loss of adhesion. We have previously demonstrated that the loss of E-cadherin from cell-cell junctions is a key-event in the onset of anoikis in enterocytes (Fouquet et al, 2004, J. Biol. Chem 279: 43061-43069). Here, we show that the detachment of intestinal epithelial sheets from the basal lamina triggers E-cadherin endocytosis, and that this process depends on the tyrosine-kinase activity of the epidermal growth factor receptor (EGFR). EGFR activation is detected in detached enterocytes prior to E-cadherin disappearance. Accordingly, the specific inhibition of EGFR by AG1478 during enterocytes detachment leads to the maintenance of E-cadherin at the cell-cell contacts, together with its cytoplasmic partners  $\beta$ - and  $\alpha$ -catenins, paralleled by an improvement of cell survival. We show that the phosphatidylinositol-3 kinase is also involved in the disassembly of E-cadherin-mediated junctions and subsequent anoikis. Finally, we evidence EGFR activation in the intestinal epithelium *in vivo*, in single cells the frequency and the position of which are consistent with their close exfoliation.