A new mouse model for studying EGFR-dependent gastric polyps.

Abstract:

Hyperactivation of the epidermal growth factor receptor (EGFR) in gastric cells due to excess of its ligand transforming growth factor-? (TGFA) is associated with hyperplastic lesions in Ménétrier's disease patients and in transgenic mice. Other EGFR ligands, however, have never been associated with stomach diseases. Here, we report that overexpression of the EGFR ligand betacellulin (BTC) results in a severe, age-dependent hyperplasia of foveolar epithelium. The stomach weight of affected mice reached up to 3g representing more than 10% of total body weight. The preexisting corpus mucosa was severely depleted, and both parietal and chief cells were replaced by proliferating foveolar epithelium. The lesions were more severe in male as compared to female transgenic mice, and partially regressed in the former after castration-mediated androgen removal. The gastric hyperplasia fully disappeared when BTC-tg mice were crossed into the Egfr(Wa5) background expressing a dominant-negative EGFR, indicating that the phenotype is EGFR-dependent. This is, to our knowledge, the first report of hyperplastic gastric lesions due to the overexpression of an EGFR ligand other than TGFA. BTC-tg mice are therefore a new promising model for studying EGFR-dependent gastric polyps.