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Fibroblast growth factor 10 alters the balance between goblet and Paneth cells in the adult mouse small intestine

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Abstract

© 2015 the American Physiological Society. Intestinal epithelial cell renewal relies on the right balance of epithelial cell migration, proliferation, differentiation, and apoptosis. Intestinal epithelial cells consist of absorptive and secretory lineage. The latter is comprised of goblet, Paneth, and enteroendocrine cells. Fibroblast growth factor 10 (FGF10) plays a central role in epithelial cell proliferation, survival, and differentiation in several organs. The expression pattern of FGF10 and its receptors in both human and mouse intestine and their role in small intestine have yet to be investigated. First, we analyzed the expression of FGF10, FGFR1, and FGFR2, in the human ileum and throughout the adult mouse small intestine. We found that FGF10, FGFR1b, and FGFR2b are expressed in the human ileum as well as in the mouse small intestine. We then used transgenic mouse models to overexpress Fgf10 and a soluble form of Fgfr2b, to study the impact of gain or loss of Fgf signaling in the adult small intestine. We demonstrated that overexpression of Fgf10 in vivo and in vitro induces goblet cell differentiation while decreasing Paneth cells. Moreover, FGF10 decreases stem cell markers such as Lgr5, Lrig1, Hopx, Ascl2, and Sox9. FGF10 inhibited Hes1 expression in vitro, suggesting that FGF10 induces goblet cell differentiation likely through the inhibition of Notch signaling. Interestingly, Fgf10 overexpression for 3 days in vivo and in vitro increased the number of Mmp7/Muc2 double-positive cells, suggesting that goblet cells replace Paneth cells. Further studies are needed to determine the mechanism by which Fgf10 alters cell differentiation in the small intestine.

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Keywords

Differentiation, Fgf10, Fgfr2b, Small intestine