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"Downregulation of primary cilia promotes colon inflammation and carcinogenesis"

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A master regulator of signaling pathways are primary cilia (PC), which act as sensory antennae and are supposed to extrude most mammalian cells. PC contain a scaffold of microtubules that is stabilized by posttranslational modifications. We previously described an unexpected role of the tubulin glycylase TTLL3 in the regulation of colon tumorigenesis. Specifically, we discovered that the absence of TTLL3 leads to decreased numbers of PC in colonic crypts. When exposed to chemically induced colon carcinogenesis, *Ttll3*$^{-/-}$ mice are more susceptible to tumor formation.
To test for a potential role of PC in colon homeostasis and pathology we analyzed PC presence in murine colon by immunohistochemistry and observed that the number of colonic cilia decreases during colitis as well as colon carcinogenesis. Moreover, we found that in the colon mainly fibroblasts, but only few epithelial cells express PC. Analysis of conditional knock-out mice, in which cilia are partially depleted in colonic fibroblasts, revealed that cell-type specific deletion of PC in the colon does not affect colon homeostasis, but significantly increases the susceptibility to chemically induced colitis, as well as colon carcinogenesis. Finally, an analysis of biopsies from colorectal cancer patients displayed lower numbers of cilia in tumoral compared to peritumoral regions. All together, these findings suggest a link between the presence of primary cilia, colitis and colon carcinogenesis.