PTPRT is a tumor suppressor that regulates intestinal stem cell proliferation

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Abstract

Protein tyrosine phosphatase receptor-type T (PTPRT) is frequently mutated in a variety of human cancers including colon cancer. We demonstrated that PRPRT normally functions as a tumor suppressor using three different colon tumor models: (1) PTPRT knockout mice are highly susceptible to carcinogen azoxymethane-induced colon tumor; (2) PTPRT knockout increase incidence of AOM-DSS-induced colon tumors; and (3) PTPRT knockout increase the size of colon tumors in the Apc^{min} mouse genetic background. Recently, intestinal stem cells marked by Lgr5 are shown to be potential cell original of colon cancers. Interestingly, we found that Lgr5+ intestinal stem cells in PTPRT knockout mice are more proliferative than in the wild-type (WT) mice. Using a phospho-proteomics approach, we identified and validated STAT3 as a direct substrate of PTPRT. Moreover, phospho-STAT3 is up-regulated in the intestinal crypts of PTPRT knockout mice compare to WT mice. These studies suggest that PTPRT-regulated STAT3 signaling pathway that plays important roles in intestinal homeostasis and colorectal tumorigenesis.