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TRPV1 regulates EGFR signaling via PTP1B to suppress intestinal tumorigenesis in mice

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The molecular mechanisms that control oncogenic events in the intestinal epithelium are not fully understood. Here, a novel feedback loop in intestinal epithelial cells (IEC) between the EGFR and transient receptor potential cation channel, subfamily V, member 1 (TRPV1) is described. It was found that TRPV1 is expressed by IEC and that it is intrinsically activated upon EGFR stimulation. This subsequently negatively regulates EGFR-induced epithelial cell proliferation via the activation of Ca2+/calpain and protein tyrosine phosphatase 1B (PTP1B), respectively. The *in vivo* relevance of this negative feedback on EGFR signaling was demonstrated in the mouse model of multiple intestinal neoplasia (Min), which showed that genetic deficiency of Trpv1 increased adenoma formation. Treatment with an EGFR kinase inhibitor reversed this pro-tumorigenic phenotype, further supporting the functional association between TRPV1 and EGFR signaling in IEC. Similar to, and in conjunction with a COX-2 inhibitor, the administration of a TRPV1 agonist suppressed intestinal tumorigenesis in Apcmin/+ mice, suggesting a novel approach for tumor prevention. Our findings implicate TRPV1 as a novel regulator of growth factor signaling in the intestinal epithelium through PTP1B that suppresses intestinal tumorigenesis.

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