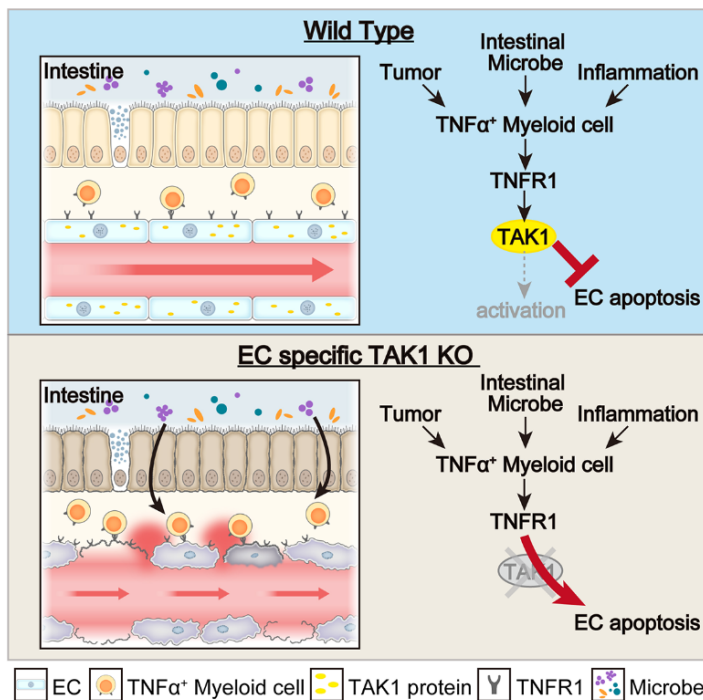


TAK1 Prevents Endothelial Apoptosis and Maintains Vascular Integrity

Keywords: Inflammation, tumor, tumor blood vessels, intestinal bacteria

TNF α is a pleiotropic cytokine which has potential to induce apoptosis under inflammation. How endothelial cells (ECs) are spared from this fate in inflammatory environments where TNF α is present is not known. Hisamichi Naito, Nobuyuki Takakura (Signal Transduction, IFRc and RIMD) and their research group showed that TGF β -activated kinase 1 (TAK1) ensures EC survival and maintains vascular integrity upon TNF α stimulation. Endothelial-specific TAK1 knockout mice exhibit intestinal and liver hemorrhage due to EC apoptosis, leading to vascular destruction and rapid death. This EC apoptosis was induced by TNF α from myeloid cells responding to intestinal microbiota. TNF α secretion associated with inflammation also induced vascular defects in inflamed organs.

Additionally, they determined TAK1 deletion in tumor ECs resulted in blood vessel and hence tumor regression. Our results illuminate mechanisms ensuring survival of intestinal and liver ECs under physiological conditions and ECs of other organs under inflammatory conditions that could be exploited for anti-angiogenic therapy to treat cancer.



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