How intestinal cancer stem cells evade anti-angiogenic therapy

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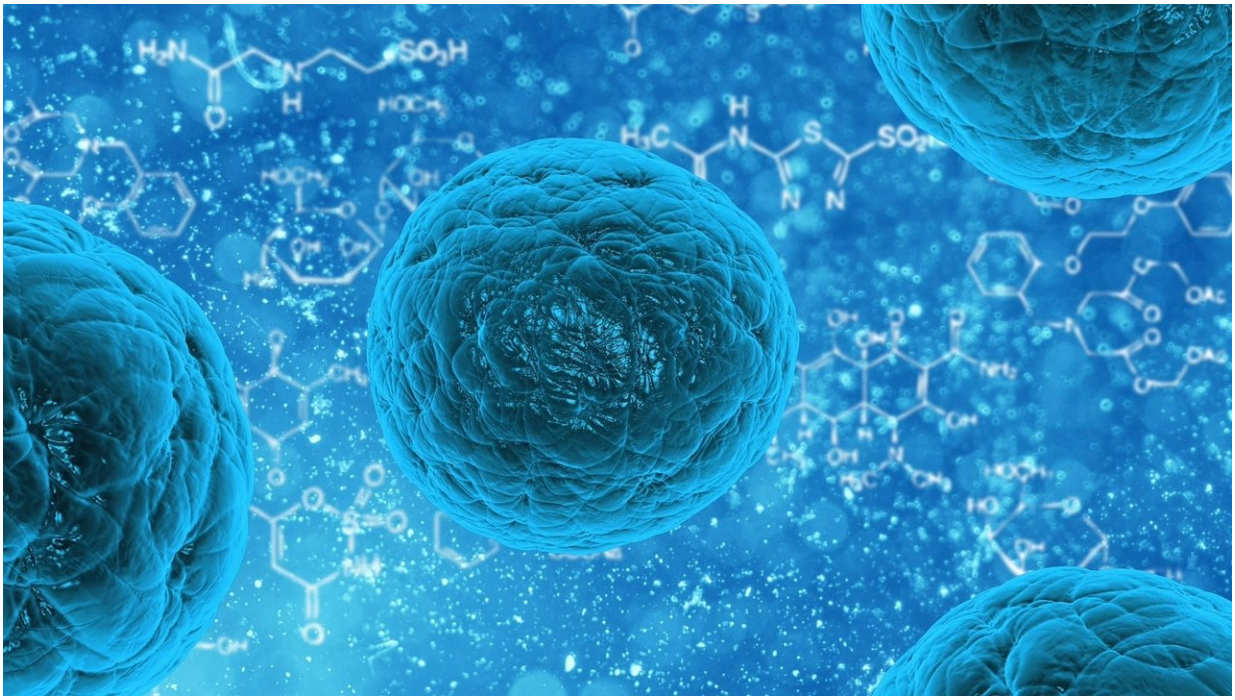

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A team led by Ludwig Lausanne's Tatiana Petrova, Jeremiah Bernier-Latmani and alum Christoph Cisarovsky identified a novel mechanism by which stem cells in intestinal tumors generate new blood vessels and evade anti-angiogenic therapy. Vascular endothelial growth factor A (VEGFA) is an important supporter of both healthy and malignant angiogenesis. But anti-VEGFA therapies have had mixed success against

many cancers, including colorectal cancer (CRC).

In CRC tumors that resist anti-VEGF-A therapy, intestinal stem cells—or epithelial progenitor cells—tend to signal strongly through the WNT pathway compared to those that are susceptible to the therapy. Petrova and her team explored in mouse models how such WNThigh cells, both normal and cancerous, maintain their vascular support. They reported in a May paper in *Nature Cardiovascular Research* that both types of progenitor cells are nestled in intestinal niches that are rich in oxygen and surrounded by VEGFA-independent vessels.

The proliferation of cancerous epithelial progenitor cells induces the production of a small protein named apelin, which triggers the migration of endothelial cells from distant veins towards the progenitor cell niche, where they fill in existing blood vessels. This supports the coordinated growth of the epithelial progenitor cells and that of the blood vessel network independent of VEGFA. Loss of apelin inhibits progenitor cell proliferation, niche oxygenation and tumor growth, suggesting a new approach to treating CRC tumors that resist VEGFA blockade.

More information: Jeremiah Bernier-Latmani et al, Apelin-driven endothelial cell migration sustains intestinal progenitor cells and tumor growth, *Nature Cardiovascular Research* (2022). DOI: 10.1038/s44161-022-00061-5

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