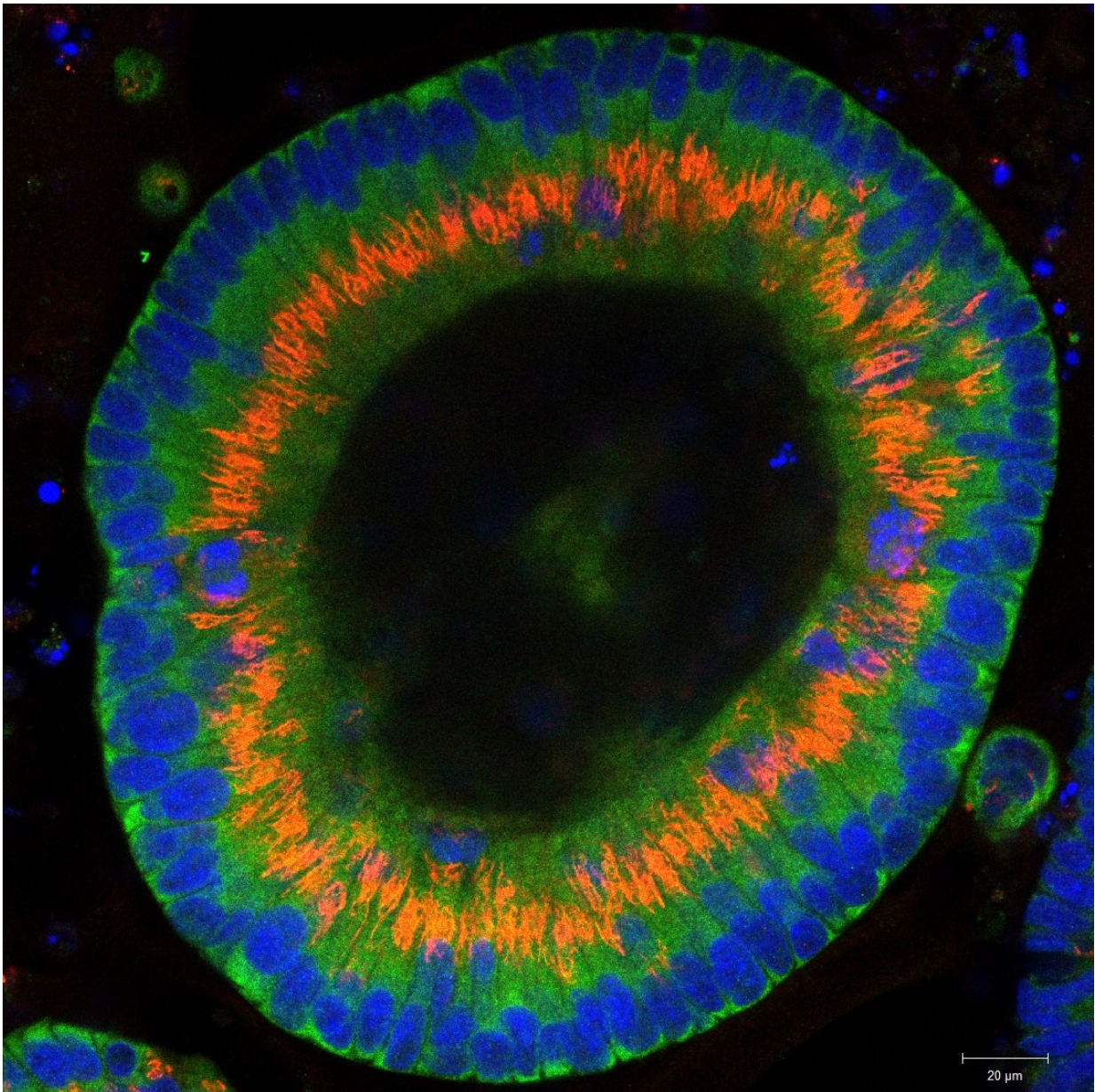


Hedgehog signaling proteins keep cancer stem cells alive

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Colon cancer cells grow into three-dimensional organoids in the culture dish.
Credit: Dr. Joseph Regan / Charité - Universitätsmedizin Berlin

Researchers from Charité - Universitätsmedizin Berlin have discovered that the survival of cancer stem cells is dependent on the Hedgehog signaling pathway. Targeting this pathway had previously shown no effect on the growth of colorectal cancer. Now, Charité scientists have demonstrated that using different drugs to target a specific aspect of the pathway may yield better treatment outcomes for patients. Results from this research have been published in the journal *Cell Reports*.

Colon cancer is the third most common cancer and fourth most common cause of death worldwide. Colon tumors consist of cell types that play different roles in the growth of the tumor. The development and spread of cancer is thought to be caused by a subpopulation of [cells](#) that possess stem cell characteristics, including the capacity for self-renewal, differentiation and therapy resistance. These cancer stem cells are also thought to be the source of [cancer recurrence](#) following initial treatment success.

As part of the OncoTrack project, Dr. Joseph Regan and his colleagues at the Charité Comprehensive Cancer Center (CCCC), working with scientists from the Max Planck Institute for Molecular Genetics, the Medical University of Graz and Bayer AG, investigated a treatment option aimed at treating cancers via the targeted elimination of cancer stem cells. Potentially capable of significantly improving treatment outcomes, this approach requires an in-depth understanding of both the relevant cellular communication pathways within the stem cells, and of the genes regulating them.

As part of the current study, the researchers carried out genetic

sequencing of the colon cancer stem cells and performed functional studies using both mouse models and 3-D cell cultures from patient-derived cancer cells. Their research revealed that [cancer stem cell survival](#) is controlled by a specific feature of the Hedgehog signaling [pathway](#) (SHH-PTCH1), which allows cells to respond to external signals in addition to inhibiting [stem cell differentiation](#).

"The targeted inhibition of the Hedgehog signaling pathway, used in combination with other standard treatments to shrink tumors, may provide a new strategy for the elimination of cancer stem cells and the prevention of cancer recurrence," explains Dr. Regan. Similar targeting of the Hedgehog signaling pathway has also produced promising results in other preclinical studies on pancreatic and [breast cancer cells](#). He adds: "Future research will set out to better define the downstream signaling components of the pathway and further investigate how Hedgehog signaling controls cancer stem cell survival."

More information: Joseph L. Regan et al, Non-Canonical Hedgehog Signaling Is a Positive Regulator of the WNT Pathway and Is Required for the Survival of Colon Cancer Stem Cells, *Cell Reports* (2017). [DOI: 10.1016/j.celrep.2017.11.025](#)

Provided by Charité - Universitätsmedizin Berlin

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