



Reconstructing cancer

Using human colon organoids to model carcinogenesis



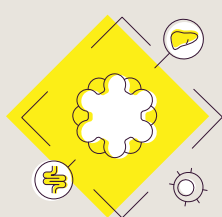
Understanding colorectal cancer

Colorectal cancer (CRC) remains one of the **deadliest cancers**. To develop improved therapies, it is important to understand the details that drive carcinogenesis, or the conversion of normal cells into cancer cells.



Specific mutations drive CRC

In the case of CRC, it is well-established that carcinogenesis is driven through a relatively ordered sequence of mutations in specific genes, known as the 'adenoma-carcinoma sequence'. In recent years, scientists have used CRISPR-Cas9 genome editing to experimentally introduce mutations associated with this sequence into colon epithelial organoids. They proved that introduction of these mutations can transform organoids into full-blown cancer cells capable of metastasizing.



A new organoid model

Excitingly, a paper published in *Nature Cancer* by the group of Prof. Hans Clevers has now demonstrated that it is also possible to mimic the adenoma-carcinoma sequence simply by placing selective pressure on well-defined oncogenic pathways. This research shows that by using sequential clonal selection and niche factor deprivation of mismatch repair-deficient organoids, tumor organoids that recapitulate the acquisition of CRC driver mutations could be generated.



Hope for the future

This research provides scientists with a **valuable new experimental model** for further studies on CRC – both for understanding the mechanisms that kick-start oncogenesis & potentially for finding therapies that can intervene in the process.

Read the whole article!

Mizutani et al. *Nature Cancer* (2024).

<https://doi.org/10.1038/s43018-024-00841-x>

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