Patient cancer cells help to test treatments

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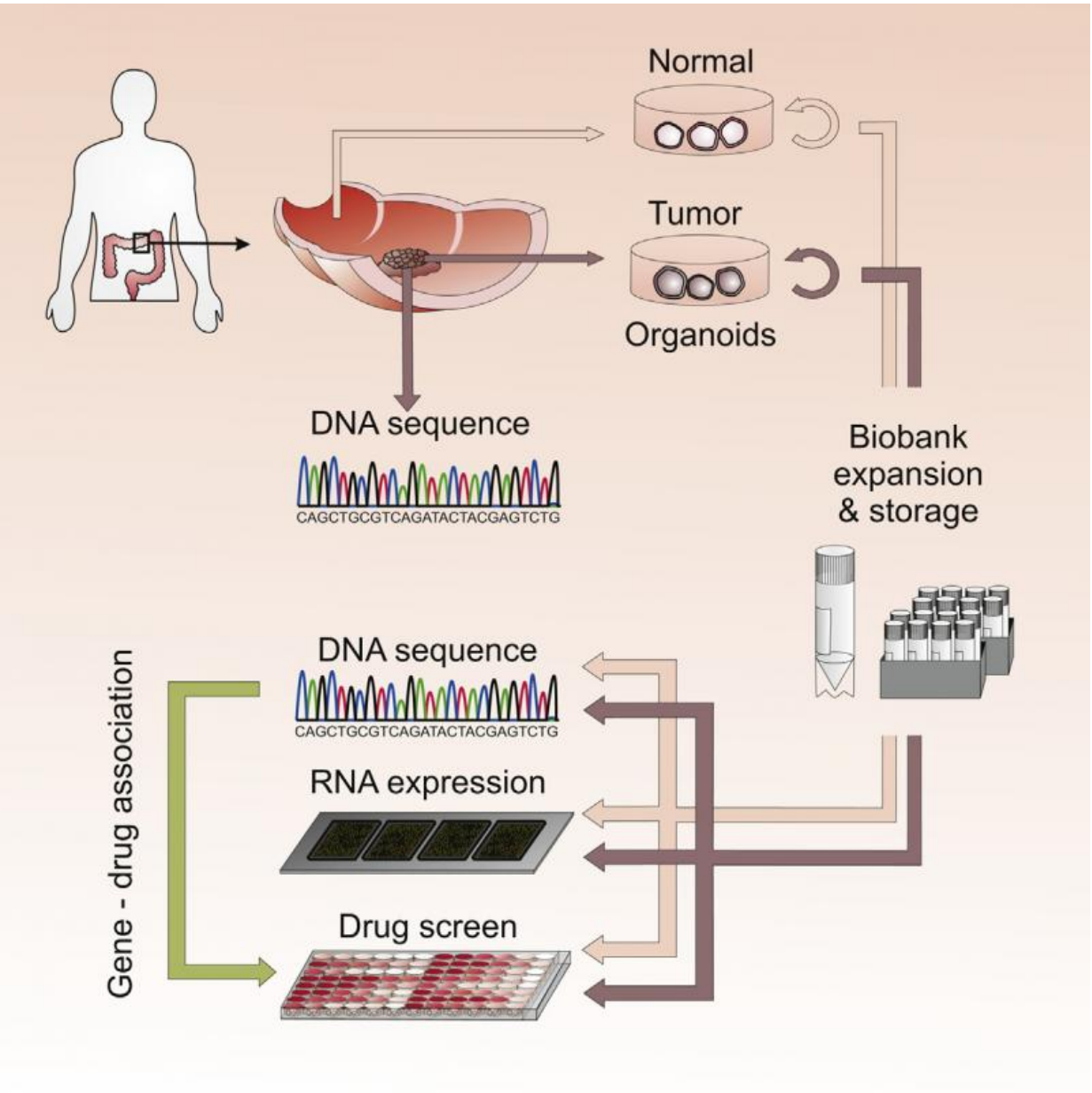

3-D organoid cultures derived fromhealthy and tumor tissue from

colorectalcancer patients are used for a highthroughput drug screen to identify genedrugassociations that may facilitatepersonalized therapy. Credit: van de Wetering et al./*Cell* 2015

A study, published today in *Cell*, demonstrates the power of organoids to capture, in three dimensions, the multiple mutations that occur in tumours. Organoids, small clusters of cells that accurately mimic the behaviour of human tissue, can be used to test cancer drugs and, eventually, to identify effective personalised treatments for patients.

Until now, cancer drug screening has primarily been carried out using two-dimensional cell lines grown in dishes, or in mouse models. Organoids, which more closely resemble human tumours than cell lines, and are less time and resource intensive than mouse models, offer researchers a middle ground between existing approaches.

These exciting findings are the result of an international collaboration involving research teams in the UK, Netherlands, and the US.

"Every tumour is different, even those that arise in the same organ. They each have a mixture of cells with different mutations that subsequently determine if a treatment will be effective," explains Dr Hayley Francies, a first author from the Wellcome Trust Sanger Institute. "Organoids, much to our delight, replicated the features of patient tumours. This gives us a more realistic environment in which to test new and existing drugs, and to explore combination therapies."

Researchers at the Hubrecht Institute, The Netherlands, have pioneered the use of organoids, which have important applications in cancer research, stem cell biology and regenerative medicine. The organoids used in the study were derived at the Hubrecht Institute using stem cells

from colon tissue. Stem cells, which are found in most tissues, are responsible for growth and repair, so they replicate constantly. When isolated in culture, the cells continue to grow, forming small cell-clusters that retain their tissue identity.

Samples from healthy tissue and cancerous tissue were taken from 20 patients with colorectal carcinoma and used to form the organoids. The organoids were then exposed to a range of colorectal cancer treatments as part of the Sanger Institute's high-throughput drug screen, which is testing hundreds of different drugs against cancer cell lines.

"This exciting new tool has the potential to transform the way we develop and deliver cancer treatment," says Dr Mathew Garnett, a senior author at the Sanger Institute. "We feel fortunate to have been part of this collaborative scientific effort. We are now building a biobank of organoids at the Sanger Institute that will help to illuminate the complex interactions between the multiple genomic alterations in tumours that determine which drugs work and which don't."

Organoids could ultimately be used in the clinic to predict how a patient will respond to treatment. However, researchers say that more work to speed up and standardise the process of producing and testing organoids is needed before this is possible. In the short term, organoids are likely to speed up the process of developing new cancer treatments and reduce costs.

"Often, the jump from studying a cancer treatment in cells to performing a successful patient trial is too wide," says Professor Hans Clevers, a senior author at the Hubrecht Institute. "Organoids are so experimentally tractable that they can answer many of our questions about cancers, bridging this gap. Not only can organoids save time and resources, we hope that they will one day let us see how treatments will work in an individual's unique cancer."

More information: Wetering M, Francies HE, Francis JM et al. (2015).Prospective derivation of a living organoid biobank' of colorectal cancer patients. *Cell*. DOI: 10.1016/j.cell.2015.03.053