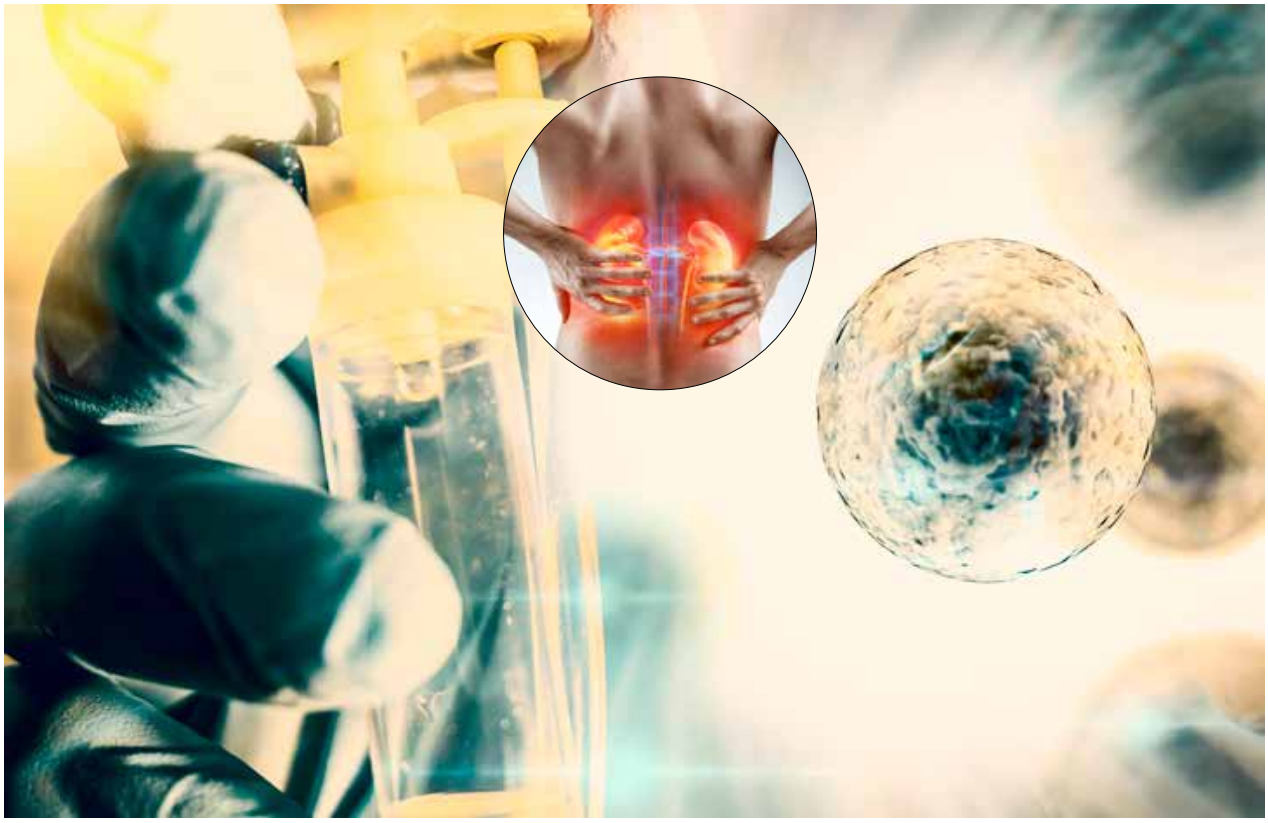
Organoids grown from stem cells boost cancer research

Organoids grown from stem cells enable new ways to model a variety of diseases such as cancer. At the University of Oulu, new techniques to engineer embryonic tissue are used to find cancer genes.



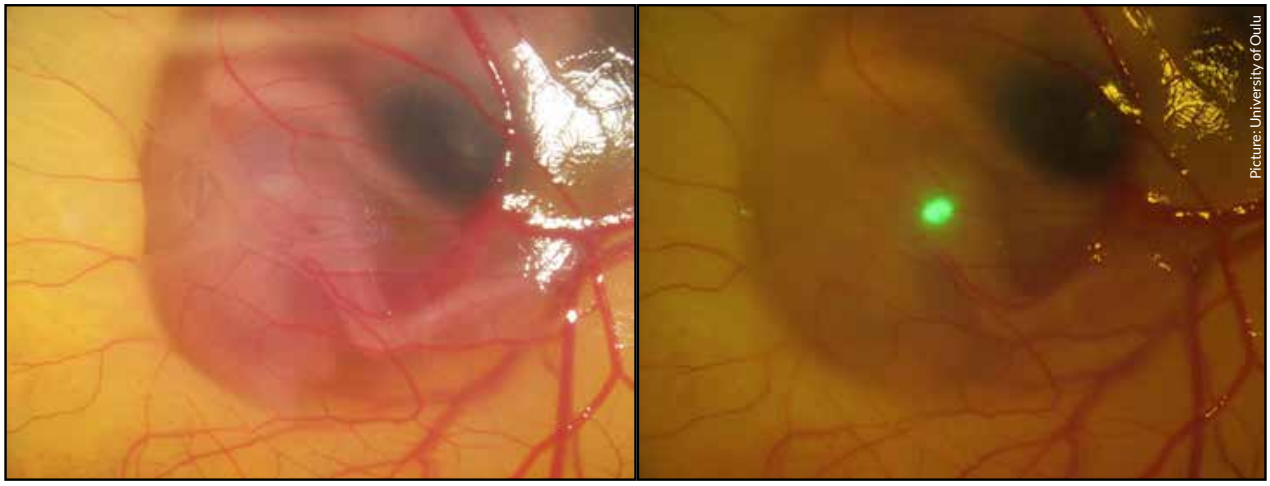
Professor of Developmental Biology **Seppo Vainio's** research group uses organoids to study the genes that cause kidney cancer. Stem cells can be manipulated to create organs – such as three-dimensional cell cultures resembling kidneys – that include nearly all the cell types found in real organs. Organoids can also be clusters of cancer cells grown from the cells harvested form a patient's cancer tumour. Organoids are created with a few cells harvested from tissue or with stem cells.

"We can create models of the development of internal organs like kidneys. Our toolkit also includes methods to create, or replicate, the gene-level changes caused by different diseases found in human embryonic stem cells. This is based on gene targeting techniques," says Vainio.

Finding cancer genes with organoids

Of all kidney cancers, 90 per cent are caused by renal cell carcinoma. Factors causing the disease include smoking, obesity and genetics. In particular, the research at the University of Oulu focuses on the similarities between kidney development and cancer development. The research group studied gene expression to determine whether some of the genes involved with kidney development are also involved with cancer development. A variety of organoids were experimented with. Some were created with renal cells and cancer cells from mice and some were a combination of mouse renal cells and human cervical cancer cells.

"When we combined the embryonic renal cells and the renal cancer cells to create a single organoid, the embryonic renal cells did not create the tubular structures typical of kidneys. However, when we blocked the expression of certain genes associated with kidney growth in the cancer cells, cancer cell growth slowed down and we found that the tubular structures developed normally," says researcher **Anatoliy Samoylenko**.



Tumour growing due to a xenograft dyed with a green fluorescent protein. In the first image, a tumour growing on the leg of a chicken embryo appears as a red dot. In the second image, the same location is illuminated with a fluorescent lamp. The tumour is dyed with a fluorescent protein and appears as a green dot.

The research group found that deactivating certain cancer cell genes resulted in the embryo being able to produce new structures normally. The organoid model developed at the University enables a new way of examining the detrimental signals that cancer cells send to their surroundings.

Embryonic stem cells have revolutionised disease-oriented research, and stem cells can be used to create in vivo models. Organoids can be used to identify the initial stages of tumour growth, cell proliferation and specialisation, cell migration and cell death.

Organoids are a major development for biomedicine

According to researcher **Ilya Skovorodkin**, organoid research is a revolutionary development.

"True science starts with experimentation. In a way, classical medicine can never be a true scientific endeavour, since you cannot use people as test subjects."

Skovorodkin says that organoids will change this. They enable studying human diseases with experiments. They can be taken advantage of in the development of new medicines and treatment methods.

"Naturally, we are still far from being able to study all the interaction that goes on within an organism. However, we can start by studying the cell-cell interaction and the way cells signal each other."

Organoids can be kidneys, hearts or cancers in miniature form.

"In the best-case scenario we are able to harvest cells from a patient in connection with an autopsy or from the patient's skin, for example. The cells can be reverted to their embryonic state and then they can be used to create miniature organs. This enables us to experiment. What kind of medicine would be best for this patient? Our primary focus is on organ development and embryonic kidney development in particular. Organoids are a very impressive tool. The laboratory in Oulu was one of the first laboratories to have the capability to create a kidney organoid."

According to Skovorodkin, the next step in biomedicine is to create an organoid with blood circulation.

"With a single organoid, we can study cell-cell interaction and how organs work. But in real life, organs are connected to the whole organism via blood circulation. Blood circulation brings cells all the materials they need, and interaction happens with cells and organs. We can already grow blood vessels of chicken embryos in organoids."

Skovorodkin aims to model the interaction between cells and organs. Microfluidics, or the control of microscopic fluid and gas flows, can be used to create artificial blood vessels and to study blood circulation in organs.

This type of modelling would significantly benefit cancer research.

"A cancer does not grow in isolation; it is always connected to the whole organism through blood circulation."

According to Professor Vainio, the aim is that organoids could be used with 3D bioprinting techniques to find new cell and tissue therapies.

"Organs that will not be rejected are greatly needed for transplantation. Successful attempts at this have already been made," Vainio says.

In Finland, biobanks are responsible for the legality and information safety of human sample collection. The biobanks encode each sample, which ensures that donors stay anonymous.

"But the need to apply for licences has increased the bureaucracy of getting samples and their clinical data for use in research."

Vainio says that the aim is to improve legislation to allow safeguarding the anonymity of private individuals in research activities such as creating human organoids and the patient records related to them. Currently, university hospitals and the Finnish Social and Health Data Permit Authority

FINDATA are responsible for the administration of clinical test results of operational patient care.

"Researchers can reuse the data on gene-level changes associated with certain human diseases observed in stem cells and the organoids grown from them. This is basic research and produces experimental data such as image analysis data and gene-level data. CSC – IT Center for Science already provides the framework needed to store such digital material."

According to Vainio, anonymisation is not as relevant when data on experimental cell lines is produced, which is why it would be possible to manage such data through CSC.

"If there was a need to link this data to patient records, it could be done with FINDATA cooperation. Creating organoids from samples donated by patients, for example, could also be made subject to licence in Finland."

Ari Turunen

MORE INFORMATION:

University of Oulu
https://www.oulu.fi/en

Development Biology Laboratory
https://www.oulu.fi/en/research-groups/developmental-biology-laboratory-organogenesis-extracellular-vesicles

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