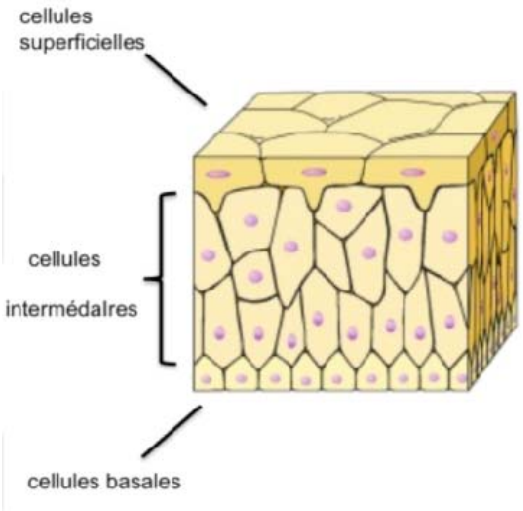
Press release from Toulouse University Hospital (CHU de Toulouse)
Toulouse, 14th February 2017

Innovation: the first bladder organoid made from its own stem cells

Science fiction has become reality at Toulouse University Hospital: a number of teams[1] working together have created the world's first bladder organoid. They have reconstructed a 3-dimensional bladder model from stem cells taken from a human bladder…but how and for what purpose?

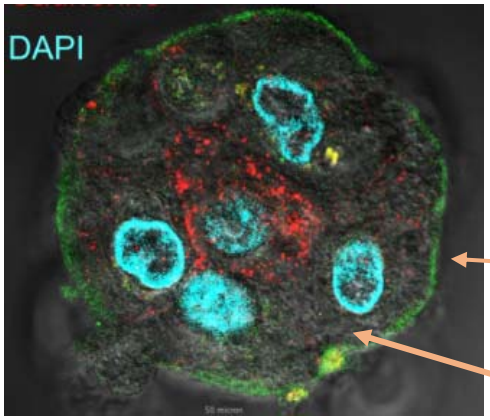
Groundbreaking research

Many researchers around the world are already working on reconstituted human organoids, with colon, prostate, lung, breast and pancreas organoids developed to date, but this is the first time a human bladder organoid has been created. Until now it has proven impossible to reconstitute the epithelium of the bladder (the tissue that lines the interior of the organ) in its true form, which consists of three superimposed layers.



The main obstacle in reconstituting the bladder epithelium has been the inability to culture all three layers. Previously, only cells from the outermost layer (the superficial cells) were able to be cultured and although this is useful for diagnosing the causes of inflammation (such as cancer, functional pathologies, etc), it is not sufficient for the production of a functioning organoid. However, the researchers at Toulouse University Hospital have overcome this challenge by culturing stem cells taken from human

bladders. Using the correct conditions they were able to manipulate the stem cells to reconstitute the complete epithelial cellular environment in its true three-dimensional form. Their model has been validated, with the organoid epithelial cells shown to have the same characteristics as their human bladder counterparts.



These results form the end of the first phase of this study, which aimed to reconstitute the three-dimensional epithelium of a healthy bladder. They were presented to the French Association of Urology in November 2016 by the team of Professor Xavier Gamé, a surgeon in the Urological Surgery Team at Rangueil Hospital. In collaboration with others, his team realized this goal by developing a specific technique for bladder stem cell extraction and culture, in collaboration with the INSERM and the Urosphere platform at Toulouse that is dedicated to experimental urology research.

The next three phases of the study aim to:

- Reconstitute an epithelium from diseased cells in order to produce a diseased organoid model, to help our understanding of conditions such as malignant tumors.
- Test drugs on these diseased models, with the long-term aim of reducing the need for in vivo animal testing.
- Apply this to the clinic, with the ultimate aim of endoscopic removal of a patient's bladder stem cells being used to develop personalized medicine

In the early phases of this work the stem cells are being taken from bladders which have been removed by cystectomy, but later in the study the aim is to remove stem cells from the bladder endoscopically.

A step closer to personalized medicine

Medical research is becoming more and more focused on personalized medicines, however all patients with bladder cancer are currently treated with the same chemotherapy and have unpredictable outcomes. Some benefit from positive effects but others see no improvement in their condition.

The reconstitution of a diseased bladder for each patient from their own stem cells will allow for the testing of different drugs to find the best combination for that patient. Thus, the patient will benefit from a customized regimen that is optimized to meet the needs of their own cells.

Funding

This project, named ORGANOCAN, recognized by the Cancer-Bio-Santé (CBS) cluster, won the Fonds Unique Interministériel Prize in 2014, thanks to which funding was provided by the Banque Publique d'Investissement (BPI), the former Midi-Pyrénées region and the Toulouse Métropole.

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