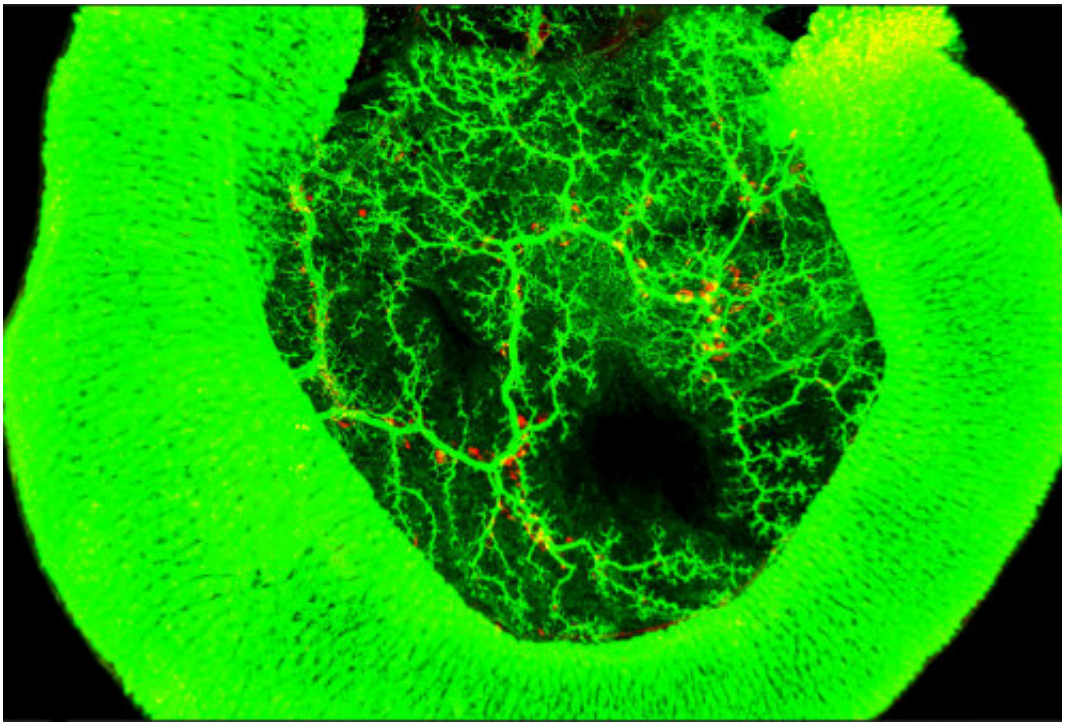
MedicalXpress

Enzyme ducts in the pancreas are formed like rivers

August 28 2018



A pancreas coloured with fluorescent antibodies. Photo: Assistant professor Dror Sever. Credit: University of Copenhagen

Applying methods for analyzing road systems and rivers, researchers from the University of Copenhagen have studied the formation of the pancreatic network of ducts transporting digestive enzymes in mice. The network resembles the structure of road networks and the formation patterns of rivers. The new results can help researchers gain a better

understanding of disorders like cystic fibrosis.

When rivers are formed and branch into smaller streams, those with the strongest current expand, while others run dry and eventually disappear. The same happens with the formation of human organs, according to researchers from the Faculty of Health and Medical Sciences at the University of Copenhagen in collaboration with physicists from the Niels Bohr Institute. They have studied the pancreas in mouse embryos and looked at how the organ develops from the embryo stage until the mouse is born. The new research results have been published in the scientific journal *PLOS Biology*.

A well-functioning pancreas is essential to the ability to digest food. The organ produces enzymes that help the body digest and assimilate nutrients. The enzymes are led to the intestines via a network of ducts. It is the formation of this network the researchers have studied and analysed. The methods they have used to analyse the different developmental stages of the organ were originally designed to analyse road and river networks.

"We discovered that even though the shape of the pancreas varies from mouse to mouse, the network of the pancreas is the same across mice at a given developmental stage. At the early developmental stages, the network of ducts resembles a road network in a city, where it is easy to get from one place to another and you can take several roads to reach the same destination. Everything is connected in a superfluous manner. It is convenient, but everything comes at a price. It means that you have to maintain a lot of roads."

"Toward the end of the development, the structure of the network is far more economical and optimal with regard to delivering digestive enzymes to the intestines. The flow of fluid running through the pancreas network to the duodenum causes the ducts with the largest flow

to expand and the unnecessary ones to be eliminated—just like the formation of river beds," says co-author Professor Anne Grapin-Botton from the Novo Nordisk Foundation Center for Stem Cell Biology (DanStem).

The Pancreas Does "Test Runs"

The researchers coloured the network of ducts using fluorescent antibodies to monitor the development of the network and to learn how the ducts were connected. This revealed to the researchers that the pancreas at an early stage begins to practise and prepare for birth. The organ does this, among other things, by doing 'test runs' and sending secretion through the network.

"Our study shows how the organ, already at the foetal stage, is able to prepare its form and structure to such a degree that it is ready to work optimally after birth. The organ's 'test runs' make it possible to optimize the network of ducts to secure the most efficient delivery of enzymes to the intestines. The process that we have uncovered in the pancreas may also prove relevant to other similar organs like the salivary gland," says Professor Grapin-Botton.

This new knowledge of the pancreas may also lead to better understanding and development of treatments for diseases involving abnormal formation of the duct network. This is seen in patients with the hereditary disorder cystic fibrosis, among others, which around 15 children are born with in Denmark each year. The disorder, which develops differently from person to person, prevents the enzymes from the pancreas from reaching the intestines, because the network does not work properly.

"I hope this improved understanding of how the organs form these networks of ducts will enable us to discover how diseases affecting the

pancreas emerge. E.g. cystic fibrosis. Patients suffering from some types of diabetes also show cystic or enlarged ducts in the pancreas and other organs such as the kidneys and liver. This study is a step in the direction of better understanding the link between enlarged ducts and diabetes," says Professor Grapin-Botton.

More information: Svend Bertel Dahl-Jensen et al, Deconstructing the principles of ductal network formation in the pancreas, *PLOS Biology* (2018). DOI: 10.1371/journal.pbio.2002842

Provided by University of Copenhagen