Scientists announce revolutionary culturing technique for liver and pancreas

January 22 2015

The International Society for Stem Cell Research (ISSCR) has awarded Dr. Hans Clevers, senior author on two important papers published recently in the scientific journal *Cell*, the society's McEwen Award for Innovation. The papers describe the development of a culturing system for human liver stem cells, as well as stem cells from pancreatic cancer, discoveries with the potential to revolutionize liver transplantation and aid in the fight against pancreatic cancer, respectively.

Clevers is a professor at the Hubrecht Institute and president of the Royal Netherlands Academy of Arts and Sciences. He shares the McEwen Award for Innovation with Dr. Irving Weissman, Stanford School of Medicine, for the identification, prospective purification and characterization of somatic (adult) tissue-associated stem cells and advancement of this research toward clinical applications.

"These new discoveries by Hans Clevers extend the work for which he was awarded the McEwen Award, the ISSCR's most prestigious award," Dr. Rudolf Jaenisch, ISSCR president, said. "The innovative approach Dr. Clevers took in the gut has borne fruit and proven the basis of these significant advances in the liver and pancreas, which hold great promise for the study of and treatments for diseases impacting these organs."

Organoids

Until recently, it appeared impossible to keep healthy or diseased tissue

from patients alive under laboratory conditions, let alone multiply it. However, in 2009, the research group headed by Clevers described a revolutionary culturing method that allowed the culturing of mini-guts from single mouse intestine stem cells. These organoids are functional miniature organs that can grow in tissue culture. The same research group now adds a culturing system for liver stem cells and stem cells from pancreatic cancer to their record. In the future, cultured stem cells could conceivably replace donor organs for transplantation. They also offer prospects for personalized medicine, the development of treatments specifically geared to individual patients.

Cultured Liver Stem Cells

The technology described in *Cell* can be used for the long-term replication in the laboratory of minute amounts of tissue harvested from a healthy or diseased liver. Over a period of four months, the equivalent of a full-grown liver can be cultured from a single liver stem cell. All analyses show that this cultured tissue is genetically the same as healthy liver tissue and is very stable.

The cultured human mini-livers have already been successfully transplanted in mice with liver damage. This is the first step toward using this cultured liver tissue to replace donor livers for transplantation. As such, this technology could solve the worldwide shortage of donor livers. Moreover, this technology offers future potential for personalized medicine. Organoids could, for instance, be grown from the tissue of patients suffering from genetic liver diseases, so that drugs could be tested on this patient material first, before being administered to the patients themselves. Examples of such diseases are alpha-1 antitrypsin deficiency and Alagille Syndrome.

Pancreatic Stem Cells

Clevers' research group additionally reports on a technology for the long-term laboratory culturing of healthy and diseased pancreatic stem cells, which was not possible before. His group worked with Dr. David Tuveson of Cold Spring Harbor Laboratory in New York.

The study in *Cell* shows that the sensitivity or resistance of the tumor tissue of individual patients to a wide range of cancer drugs can be determined in the laboratory. As a next step, this method can therefore be used to prescribe individualized therapy for each cancer patient.

The technology described was then used to create a "living biobank" of cultured pancreatic tumors from a large group of patients with pancreatic cancer. This allows the culturing of organoids from multiple patients, which in turn makes it possible to study larger populations. Established with support from the Dutch Cancer Society/Stand up to Cancer campaign (KWF/Sta Op Tegen Kanker), this biobank is open to cancer researchers and companies worldwide wanting to develop new cancer drugs and treatments.

Pancreatic cancer is one of the deadliest forms of the disease. Only six percent of patients survive for over five years. There is no effective therapy.

Provided by International Society for Stem Cell Research