"Manmade" Liver Close

K. Pomeroy reports on the research being conducted at Keio University toward the development of bioartificial livers.

An ultimate goal of regenerative medicine is generation of organs derived from cells... although realizing this goal in vitro is hindered by the sheer difficulty of organogenesis, making this goal a distant one. So, in addition to work by Professor Yamanaka Shinya of Kyoto University and others involving induced pluripotent stem cells, work such as cell generation of rat pancreases in mice by interspecific blastocyst injection of pluripotent stem cells has been moving forward. However, a way to form a three-dimensional integrated structure from layers of cells may have been opened up by a joint international effort involving Japanese, Korean and U.S. researchers approaching the complex issue from an engineering angle.

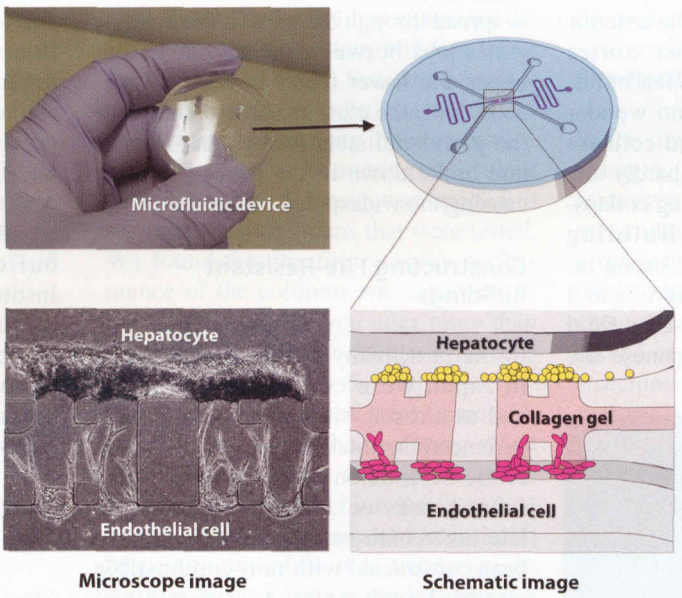
The work entails rat liver cells being utilized to produce layers through use of microfluidic devices (chips) to try realizing a 3-D integrated structure, aimed at future production of a "manmade" liver. The problem had been that although cells have been replicated in the past, a method of producing an "intra-organ network" of capillary blood vessels to keep these cells alive within a larger structure was required. Taking place now is work which involves hepatic stellate cells for intrusion of blood vessels plus endothelial cells and pericytes so said blood vessels can keep liver cells (hepatocytes) alive within an "artificially tailored organ"... a scheme that in theory can be also applied to other organ cells, so as to create new organs.

Assistant Professor Sudo Ryo, of the Department of System Design Engineering at Keio University, is handling the cell-related aspects of the collaborative effort. His "systems study" (scrutinizing "self-repairing" biological systems like the liver) is based upon his post-doctoral research at Massachusetts Institute of Technology (MIT), where he worked with Professor R.D. Kamm of the Department of Biological Engineering and Mechanical Engineering for some two and a half years, until March of 2009. Dr. Sudo has since then continued the work at Keio University, where he started his academic career under Professor Tanishita Kazuo in whose laboratory the international endeavor is still ongoing.

This endeavor is grounded in biochip and micrometer-level platform (microchannel) research which originated at MIT, starting from the 1990s. Dr. Sudo's Massachusetts colleague, Dr. Seok Chung of Korea (currently assistant professor at Korea University and part of the international cooperation for advancing "microfluidics and tissue engineering"), is an expert in preparing finely detailed workings of the microchannel "stamp" utilized to produce the platform used at Keio today. At MIT, Dr. Sudo looked after the "cell" side despite the fact that he is an engineer by training. He studied for about a year at Sapporo Medical University to familiarize himself with liver cell biology during his Master's study.

In a gist, the effort that has proceeded with biomechanics in mind is at a stage where the precursor liver cells are being washed under flows of proteins and chemical concoctions to enable the building of larger cell-based structures ultimately targeting the construction of an organ, while taking gravity and other factors under consideration. The next step is to arrange for the intrusion of miniscule vessels into the 3-D object and to ensure that the hepatocytes, known for their regenerative capacity, can keep reproducing themselves within the "manmade home" without being "starved to death, asphyxiated, etc." due to too much carbon, lack of oxygen and the like. Dr. Sudo says for this more time (seven years) is needed.

Nevertheless, once the liver—which although it is capable of "rejuvenating" itself is known to be a complex structure as well as an organ which is replete with a variety of vital functions—is (re-)created, the heart, kidneys and other important organs that must be surgically removed can perhaps be replaced anew, without regard to the donor status too.



COURTESY OF ASSISTANT PROFESSOR SUDO RYO

Microfluidic device (top) with images of blood vessel (endothelial) cells growing within reach of liver cells (hepatocytes) (bottom)

K. Pomeroy is a journalist and columnist specializing in science and technology.