Research team makes progress toward 'printing' organs

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Each year, pharmaceutical companies invest millions of dollars to test drugs, many of which will never reach the market because of side effects found only during human clinical trials. At the same time, the number of patients waiting for organ transplants continues to increase. In the past 10 years, this number has nearly doubled. Now, a new study led by a University of Missouri-Columbia physics researcher might present new solutions to both problems with the help of a very special printer.

For the past four years, Gabor Forgacs, the George H. Vineyard Professor of Physics in the MU College of Arts and Science, has been working to refine the process of “printing” tissue structures of complex shape with the aim of eventually building human organs. In the latest study, a research team led by Forgacs determined that the process of building such structures by printing does not harm the properties of the composing cells and the process mimics the naturally occurring biological assembly of living tissues.

In the study, the team used bio-ink particles, or spheres containing 10,000 to 40,000 cells, and assembled, or “printed,” them on to sheets of organic, cell friendly “bio-paper.” Once printed, the spheres began to fuse in the bio-paper into one structure, much the same way that drops of water will fuse to form a larger drop of water.

“If you wait for a long time, eventually all the small spheres will fuse into one large sphere,” Forgacs said. “To prevent that from happening, we can remove the bio-paper and stop the fusion process once the

desired shape has formed. Through this bio-printing process, we were able to build, for the first time, functional tissue structures."

In the past, there have been two concerns with printing extended tissue structures using large amounts of cells. First, scientists needed to determine how to get specific cells to the correct locations within the structures. Second, even though the right cells might be in the right place within the structure, there was a problem of function. How do you make an organ start working?

As the Mizzou research team found in the study, there appears to be no need to worry about either of these concerns. As the tissue structure begins to form, the cells go through a natural process called "sorting," which is nature's way of determining where specific cells need to be. For example, an artery has three specific types of cells – endothelial cells, smooth muscle cells and fibroblast cells, each type needing to be in a specific location in the artery. As thousands and thousands of cells are added to the bio-paper under controlled conditions, the cells migrate automatically to their specific locations to make the structure form correctly.

The team also found that nature was the answer to the second question. In the study, scientists took cells from a chicken heart and used them to form bio-ink particles, which were then printed on to thick sheets. Heart cells must be synchronized for the heart to beat properly. When the bio-ink particles were first printed, the cells did not beat in unison, but as the cellular spheroids fused, the structure eventually started beating just as a heart does.

"This study shows that we can use multiple cell types and that we do not have to control what happens when the cells fuse together," Forgacs said. "Nature is smart enough to do the job."

The study is being published in an upcoming edition of *Tissue Engineering* and was funded by a $5 million grant from the National Science Foundation. Forgacs also has become involved with a company, Organovo, Inc., which is interested in licensing the technology. He also plans to work with drug companies to provide them with tissues they can use to test drugs, prior to human clinical trials.

Currently, drugs are tested first on animals and then go through a human clinical stage. Because of the major differences in biological function, humans often have different reactions than animals. Forgacs believes that providing human tissue structures that resemble organs to the drug companies will make drug testing cheaper and much more efficient.

Source: University of Missouri-Columbia