Right This Way, Mr. Smith. Your New Kidneys Are Ready.

David Gennert

We have all seen the image of the naked lab rat with a human ear growing out of its back at some point in our lives. The Vacanti mouse is iconic and intriguing, sure, but what relevant breakthroughs has this peculiarity led to in recent years?

The field of tissue engineering–the creation of biological tissues outside their normal environments–has seen tremendous advancements lately. Laboratories across the world are investigating the possibilities that lab-grown tissues can offer, both in research for a better understanding of how organs function and in developing treatments for debilitating diseases that wreak havoc on individual organs.

As one of the many such breakthroughs recently, June 2010 saw a team from Harvard Medical School and Children's Hospital Boston publish their results on the development of a system that mimics lung tissue on a one-inch microchip. Their "lung-on-a-chip" model uses cultured human lung cells and capillary tissue on an engineered matrix to recreate human lung tissues with near identical properties, such as chemical permeability and the activation of an immune response in the chip's blood vessels.[1]

The Harvard researchers responsible received a $3.3 million grant in October to develop this system to test drugs that target lung tissue. The hope for this system, and many others in development, is to facilitate the creation of new pharmaceuticals. The organ-on-a-chip opens the door to a method of testing drugs in a way that eliminates the need for animal testing while providing a system that uses real human cells. As Harvard researcher Kevin Parker said, "With this kind of tool, we can do all sorts of toxicity studies on new drugs and move to a… [new] model about how the lung and the heart work together."[2]

What if, though, a patient appears with a condition that has damaged an organ beyond what any amount of drugs can repair? An estimated 20 Americans die every day while waiting for an organ transplant, and this is something researchers in tissue engineering hope to address with the advent of lab-grown organs.[3]

The waiting list for transplantable organs has many downsides–waiting for years for a decent match, receiving "new" organ that has been used for years already, and the deadly risk of organ rejection. Tissue engineers are trying to address all these problems with organs made from the patient's own cells. From the start, an organ created from a patient's own cells will have the molecular signature recognized by the patient's immune system as native tissue, eliminating the chance of rejection. Also, accumulated damage to a donor's organs from years of use will no longer pose a problem, since the implantable tissue will be new and never exposed to damaging factors.

"Tissue engineering is paving the way to patient-specific implantable tissues grown outside the human body."

Doris Taylor of the University of Minnesota describes the future of the clinical implementation of such a breakthrough as becoming another commercial pharmaceutical product. She imagines "manufacturing facilities" that produce organs en masse, customized for specific patients.[3]

The method of creating functional organs outside the body is a very complicated one that only recent research has shown to be a viable, productive process. One challenge facing researchers in the field is the need to create an extracellular matrix where tissue can grow. The human body is not only made of cells, but rather, a large portion of the body is a matrix of proteins whose main function is to connect, anchor, and support every cell in the body. In order to grow functional tissue in vitro, a matrix must be created to mold the growing tissue into the proper structures and cell types.

Joseph Vacanti (the same researcher who developed the "earmouse") of Massachusetts General Hospital and Robert Langser, of the Massachusetts Institute of Technology, have spent a great deal of their research developing artificial extracellular matrix, called a scaffold because it functions as a base on which tissue can be grown. Langser has developed a material called biorubber scaffold that is able to mimic extracellular matrix very efficiently. It is strong, inexpensive, and it also has the ability to be reabsorbed into the body once its function is complete, making it an ideal material to be used as tissue engineering scaffold.[3]

Tissue engineers can take this type of artificial scaffold and "seed" the matrix with a patient's own cells. Within days, all the surfaces of the matrix will be coated in cells specific to the type of matrix and growth conditions, giving the tissue engineers the ability to grow tissues in any shape of virtually

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any tissue type that is ready to be implanted into a patient.

Already, this sort of tissue replacement procedure has been carried out with human patients, and the potential of this method is only recently becoming realized. Claudia Castillo is a resident of Barcelona, Spain, who was one of the pioneering patients in this field of medical research.

In early 2008, a case of tuberculosis devastated her windpipe. It was damaged beyond repair, and doctors knew she needed a transplant. It was then decided that she would be one of the first patients to receive a transplanted organ composed of her own cells. The medical team that treated Ms. Castillo removed the trachea from a cadaver and washed all the donor's cells away. This left the natural extracellular scaffold without cells that could then be reseeded with Ms. Castillo's own cells. Four days after doctors seeded the trachea scaffold with cells taken from her own body, the new trachea was transplanted into Ms. Castillo. Incredibly, after only four days of recovery, she was able to return home. Since the implant was composed of her own cells, there was virtually no danger of autoimmune rejection, something that most transplant recipients must treat with lifelong dependence on immunosuppressant drugs.[3]

This one case highlights an interesting development in the construction of transplantable tissues. Artificial scaffolds take time and resources to create, yet this case shows that the scaffold from a living being can be stripped down and reseeded with another person's cells. Harold Ott, currently at Massachusetts General Hospital, has been leading the field in the creation of cell-free scaffolds derived from organs that have been removed from other individuals.[3]

After much research and trial and error experimenting, Ott came across a chemical solution that was able to dissolve all the cells in an organ while leaving the scaffold perfectly preserved. Stripping away the cells leaves a translucent, white scaffold in the exact shape of the organ, down to tiny channels where blood vessels permeate the tissues. Using a rat heart, Ott was able to strip off all cells of the organ and reseed the scaffold with cells from another rat. Only eight days after reseeding, the heart was visibly beating spontaneously, proving that tissues can be regrown on natural scaffold from a different individual than the donor of the seed cells. Ott has also recreated viable rat lungs using the same technique, and says researchers can now "build literally any organ."[3]

Doris Taylor, now similarly working on the development and implementation of natural scaffolds, explains that the scaffolds do not even need to be from humans in order to create transplantable tissues. Holding the cell-free scaffold of a pig kidney, which is of remarkably similar size and complexity as a human kidney, she says "we can cover this with human cells, and, in theory, build you a kidney."[3]

The complexity and specificity of these therapeutic systems inevitably lead to the question of who will receive access to these revolutionary therapies? A failing set of kidneys may be treated quickly with very high efficacy, but what will the cost be of these patient-specific treatments? When the technology makes lab-grown tissues a commercially viable medical treatment, steps will have to be taken to ensure a fair process that grants access of such a life-saving procedure to those who need it. One can easily imagine a situation when only wealthy individuals can afford to donate cells to a manufacturer who then keeps a stock of various organs on hand for the individual in case of need later in life. These issues may have to be resolved quickly, too, since Taylor speculates, "We're not decades away from building something complicated. We're more like years away."[3]

References

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Vitamin D: Friend or Foe?

The Institute of Medicine recently held a panel that found that vitamin D supplements were unnecessary for most Americans. This new finding conflicts with what physicians and scientist have been saying for years- that those who consume more vitamin D have better health outcomes. One of the reasons for this current disagreement lies in the types of trials used. Nutritionist and scientist who helped set this standard based their findings on randomized clinical trials. The panel, however, gave priority to clinical studies. The panel, like many physicians, suggest that randomized clinical trials take place in real-world environments, where it is impossible to control for important factors, such as how much vitamin D the placebo group actually receives. So should you continue taking your vitamin D supplements? We may have to wait for the Endocrine Society's official report to learn the answer to this one.

References

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