Mayo Clinic researchers study how body can repair itself

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At Mayo Clinic's Center for Regenerative Medicine, physicians and researchers have a dazzling array of tools at their fingertips: transplants, genomics, computerized data analysis and biomedical engineering. But the core idea is simple: stimulating or restoring the human body's innate ability to heal itself.

Recent discoveries in cellular biology and genomics have led scientists to the threshold of what transplant cardiologist Dr. Brooks Edwards called the "single most-exciting advance" in his 35 years at Mayo.

"Our goal is that, by the time I retire, we're not going to need to wait for a tragic accident and a young person to donate a heart or a liver or a kidney. We're going to be regenerating those organs," said Edwards, 56. "So then if I'm on a transplant list ... I'll be using my cells or some kind of cell-based therapy to either strengthen my own heart, or regenerate my own heart, or even grow a new heart."

Edwards predicted that solid organ transplants - say, a liver grown from a patient's own cells - will take place within a decade. And there will be different solutions for different patients - ranging from bioengineered human cells and pig cells, to mechanical devices and materials such as biocompatible polymers.

"It's going to be a cafeteria," said Edwards, who is director of the transplant center and deputy director for regenerative medicine applications at Mayo. "There's going to be a variety of tools in the

toolbox."

Mayo has been involved in stem cell research and prospective therapies for two decades. The clinic's three campuses - in Minnesota, Florida and Arizona - make up the largest integrated transplant program in the country, performing 1,600 to 1,700 transplants a year, Edwards said. About half involve blood or bone marrow, which he called types of stem cell transplants.

In January 2012, Mayo's board of governors funded the centers for Regenerative Medicine, Individualized Medicine and Science of Health Care Delivery to drive the latest research from the laboratory to the bedside and to analyze its cost-effectiveness.

Dr. Gianrico Farrugia, director of Mayo's Center for Individualized Medicine, traces the roots of the latest advances to the sequencing of the human genome 10 years ago.

The breakthrough produced a lot of hype and unrealistic promises, he said. But two years ago, Mayo redid its strategic plan and realized that there was no way it could remain true to its core mission - that the needs of the patients come first - without incorporating genomic medicine into routine care and documenting its value.

"At that point we said, 'OK, now is the point to stop talking about the promise of genomic medicine and start talking about the practice of genomic medicine,'" Farrugia said.

It already has produced changes in the way Mayo physicians care for patients. For instance, Mayo has instituted a protocol that blocks a physician from prescribing certain drugs that are known to have adverse side effects for people with certain genotypes until the patient has been tested for a genetic conflict.

Last September, the center established a clinic that initially will focus on advanced cancers and undiagnosed diseases. Patients in a 200-person breast-cancer study are having their genomes sequenced, and pieces of their tumors are preserved and inserted into mice for ongoing tests against certain drugs. A similar project is underway targeting prostate cancer.

Genomics, Farrugia said, could allow doctors to target specific types of tumors with custom cocktails - including so-called orphan drugs that were abandoned because they didn't help a broad-enough population to be marketable.

Now, Farrugia said, "What we give you is dependent on your tumor and on your own genetic makeup."

Regenerative medicine is closely related to individualized medicine, said Dr. Robert Simari, who chairs the Cardiovascular Cell Therapy Research Network for the National Heart, Lung, and Blood Institute.

At Mayo, Simari co-directs Mayo's cardiac valve and vascular regeneration efforts and oversees a project that he hopes will lead to the fabrication of custom heart valves and other parts for defective hearts.

The project started two years ago, when a patient from the Middle East asked if stem cell technology could be used to create a valve, Simari said. He assigned Dr. Daniel Spoon, 33, to spearhead research on whether valves could be fabricated on what resembles a fancy inkjet printer, with a goal of having a working valve implanted in sheep by August 2014. Spoon said the work is on track.

The project illustrates the confluence of computer science, genomics and medicine.

Printing a heart valve essentially involves two parts: creating an anatomically correct scaffold and coating it with bioengineered stem cells - possibly from a patient's skin or heart muscle.

The scaffold can be made by removing the cells from a pig's heart valve, a process known as decellularization, which leaves a framework of collagen and elastin. Or an exact replica of the patient's own valve can be made using advanced imaging technology and then manufacturing a duplicate from biocompatible products.

Last month, Mayo installed a three-dimensional "bio-plotter," made by a German company, that is capable of printing both the scaffold and the cells in a sterile solution. Spoon said it's one of just three bioprinters in the United States capable of doing both.

Researchers have found that while it's easy to remove cells from a heart valve, it can be difficult to "recellularize" it. Blood flow and pressure in the heart kill the cells, Spoon said.

Spoon and his colleagues developed a way to inject the cells into the scaffold. But the key to keeping them alive may be a state-of-the-art "bioreactor" that Mayo developed in conjunction with a company in Massachusetts. Mayo hired Brandon Tefft, a 30-year-old biomedical engineer, to help design a bioreactor that would mimic conditions in the heart at rest. The bioreactor's unique design will let researchers gradually increase the pressures on the valves, Spoon said, "and it's our hypothesis that will enable us then to take them from static conditions to large animals."

Simari called the study a "shakedown cruise" for a procedure that could be used to create custom valves, especially for children who need valves that can grow as their bodies grow. He said that could happen in five to 10 years, though it may take longer for adults, because they already have

good alternatives that last 10 to 15 years.

In the meantime, Simari said he expects the research to spin off related technologies, such as printing heart patches and blood vessels. The printing of tendons, ligaments and cartilage could come even sooner, he said.

Dr. Dennis Wigle, 46, is a thoracic surgeon who oversees a massive library of genomic data, cells, tissue, blood and other specimens in what Mayo calls its Regenerative Medicine Biotrust.

While replacing diseased organs via transplantation remains the only option in many cases now, Wigle said, nearly everyone believes that the future lies in regenerative and individualized medicine, and the Biotrust is a critical component.

"We can decellularize a lung to use as a matrix and recellularize it. No one has actually done it in a human yet, but we've seen in mice and rats what's coming down the line," Wigle said. "We're at the science-fiction stage, but we're getting to where it's almost ... an engineering problem."

The new directions for medicine are so complex, Wigle said, that they require cross-collaboration of physicians, research scientists, engineers, mathematicians, data analysts, and so on.

He added: "One person sitting at a desk with a big notepad in front of them can't do this anymore."