Scientists

Organizing Organs

Anthony Atala

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Anthony Atala's pioneering work in regenerative medicine and stem cell research caught our attention. Curious to know more, *BioTechniques* contacted him to find out about the ambition, character, and motivations that led to his success.

What led you to investigate tissue regeneration?

I'm a pediatric urological surgeon by training; my interest in regenerative medicine was first piqued in 1990 when the standard of care for adult patients with bladder cancer was to fashion a reservoir made out of intestine to replace the bladder. But the intestine was designed to absorb nutrients from food and excrete the waste, whereas the bladder only excretes and does not absorb. This surgery resulted in the patients absorbing things that they should have been excreting, leading to chemical imbalances, stones, perforations, and increased tumors. As a pediatric urologic surgical specialist, I needed to apply this same procedure to children who had an 80-year life expectancy, leaving the child with a long life of potential medical challenges because intestinal tissue simply didn't belong there. Then I thought the ideal solution would be to put in an organ that had the same qualities as the bladder. Why not make an organ using the patient's own cells?

How did you begin working towards that goal?

We started looking at various tissues and organs to see if we could transplant

something that actually belonged to the patients. Back then the challenge was to get primary human cell types to grow outside the body. We spent several years just trying to sort out the cell and molecular biology necessary to establish the cultures and grow cells with consistent properties and phenotypes in large quantities. Once we were able to do that with a few tissue types, we wondered if these cells could actually reconstitute different tissues when implanted in vivo. That required specific biomaterials that matched the structural, architectural, and biological properties of the tissues we were trying to replace. Creating bone requires a very different biomaterial than creating blood vessels. For the blood vessel, the biomaterial must be elastic and resilient, but bone must be strong enough to withstand large amounts of pressure. We usually use a combination of biomaterials to create the properties we're seeking and to match the cell type. Our next step was to put these cultures and biomaterials into in vitro and in vivo experimental models to see if the cells would reconstitute tissue. Sure enough, they were able to do that.

What types of cells do you use for creating these tissues?

We piece out the cells that we need from a very small biopsy of the patient's tissue of interest. We never use differentiated cells because they will not grow. Our first preference is to target the patient's own organ-specific progenitor cells because those cells will need minimal manipulation. Our second choice is a stem cell population from the same patient. For example, we can take a mesenchymal cell line from bone marrow to grow into bone or cartilage. Our goal is to put the tissue right back into the same patient, so we prefer autologous stem cell populations because they're not going to be rejected by the patient's immune system. If we can't get a native stem cell population, then we will use outside stem cell sources that have a decreased rejection potential.

The biopsy is taken 6–8 weeks prior to surgery. The selected cells are seeded onto the biomaterial one layer at a time and then later placed in a bioreactor to help the tissue take form. Then we deliver the tissue or organ to the surgeon for implantation into the patient.

Can cells be used from diseased organs?

Since we use the progenitor cells and not the differentiated cells, we can use cells from diseased organs. Let's say we're working with a patient with kidney failure. He still has progenitor cells within the kidney that are normal and can be used. This will not be the case when dealing with a single-gene disease such as cystic fibrosis or muscular dystrophy, because every cell will be the same. But single gene mutations make up less than 1% of diseases. In most cases, it's okay to use the patient's own tissues.

What is the most important current research question in your discipline?

How can we create solid organs that function adequately? The simplest tissues to build are the flat structures such as skin. Tubular structures such as blood vessels or tracheas are more complex because they need two cell types. Hollow organs like the bladder, uterus, or stomach have 2 cell types, but have a much higher interaction with the brain as they must contract on demand, so they fall into a third level of complexity. The solid organs usually have more than 2 cells types and require a lot more vascularity because there are so many more cells per centimeter than in any of the other tissue types. Vascularizing the tissues is a challenge that we are working to resolve.

Interviewed by Kristie Nybo, Ph.D. Image courtesy of Wake Forest University Baptist Medical Center.

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