Learning for Life Summary 10-14-2020

Topic: Regenerating Our Bodies with Nanoscience

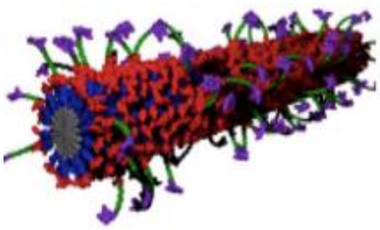
Speaker: Samuel I. Stupp PhD

Regenerative medicine is a relatively recent concept. The term was first used in 1999 and is defined as a branch of translational research in tissue engineering and molecular biology which deals with the recreation of the structure and function of tissue and organs that are lost due to trauma, aging, disease and congenital anomalies. Advances in science have increased our lifespan, but not always our "health span", meaning that we may live longer but with a decline in quality of life due to disease and degeneration of our physical bodies that impact wellness. Physicians have been substituting human structures and functions using inert materials like metal and advanced plastics for over fifty years (e.g. joint replacements and blood vessel grafts), but now with rapid advances in molecular biology which allows scientists to manipulate genes, proteins, tissue formation and stem cells combined with the burgeoning field of biotechnology (the use of living organisms to create products) the possibility of regenerating human tissues and organs is on the horizon! Some exciting opportunities in the not-to-distant future:

- The reversal and prevention of paralysis, blindness or hearing loss through regeneration of spinal cord nerves
- Heart regeneration after infarcts
- Curing Parkinson and Alzheimer's by providing new neurons. Would also help to minimize stroke dysfunction
- Cell therapies for diabetes
- Utilization of new cartilage, muscle, tendons, ligaments, and intervertebral discs.
- Kidney regeneration (life without dialysis)
- Universal repair of all bone fractures
- New teeth

In order for regeneration to happen, scientists learn from human development when tissues and organs form and grow. Stem cells are cells with the potential to develop into many different types of cells in the body. They are present in the human body throughout the lifespan, but their number does decline as we age. Gene expression and protein signals stimulate stem cells to differentiate and mature into all the different cell types in our body, so the ability to target our adult stem cells and trigger them to differentiate into heart cells or cartilage cells has clear implications for repair of a damaged heart or joint capsule. Many attempts have been made to utilize stem cell therapy in various conditions, but success has been quite mixed. With the intention of improving the utility of stem cells in the field of regenerative medicine, Dr. Stupp applied the principles of nanoscience to stem cell treatment.

Nanotechnology is about designing, synthesizing, manipulating and organizing nanostructures (a tiny structure with a dimension of only a few nanometers) to generate smart materials and devices. A Cell is a great example of highly orchestrated array of nanostructures. The extracellular matrix consists of biologic materials that provide structural and biochemical support to surrounding cells. What if we could make that extracellular matrix out of nanostructures that we can engineer in order to stimulate the stem cell to mature into a particular type of desired cell, like cartilage? Sam's lab was able to use amino acids, sugars and fats (all safe materials which will degenerate after time in the human body) to create a molecule that will self-assemble into a nanofiber with biological signals at the end of the molecule. (see image below)



These nanofibers mimic the natural extracellular matrix of cells. They have millions of the signals required to stimulate the receptors on the stem cells which, when stimulated, will push the cell to differentiate. The nanostructures are liquids but when you put them in the body, they become magical gels at the site where you want the generation to occur.

A breakthrough occurred in 2004 when the lab took neural stem cells from the brains of embryonic mice and exposed them to nanofibers with an artificial signal and they could make new neurons! Subsequent experimental applications continued with a partnership with the University of Wisconsin School of Veterinary Medicine to create new cartilage in the joints of sheep and the development of a nanofiber that travels in the body to the site of bleeding and stops it.

However, the dream was to regenerate neurons in spinal cord injury patients. Every year between eleven and thirty-one thousand patients suffer spinal cord injuries in the United States with an estimated health care cost of over 40 billion dollars each year. A second major breakthrough occurred in the lab just about one year ago. The intensity of motion of the nanofibers is a critical variable to signal the stem cell receptors most effectively, and the team discovered a way to control the motion of the molecules in the nanofibers they were using as the extracellular matrix. Sam demonstrated the effects of this by showing a video of a paralyzed mouse that received an injection of the nanomaterials into its spinal cord. After 12 weeks, the mouse that had received the nanofiber gel that was able to sustain more motion had significantly better outcomes and more physical movement.

The implications of the work of Sam Stupp's lab are numerous and include the ability to regenerate nerves in the brain and spinal cord, replace knees with injections that create cartilage, repair fractures with injections that replace bone and even replace organs like the kidney in the future.

Take home points:

1. Regenerative medicine is a field of science that combines tissue engineering with molecular biology to recreate the structure and function of tissue and organs that are lost due to trauma, aging, disease and congenital anomalies.
2. Dr. Stupp's lab has used Nanotechnology in order to create an injectable cellular environment where scientists and soon physicians can target the stimulation of stem cells to repair damaged tissues and organs.
3. The applications for human health are extensive. The team has already demonstrated that they can generate many types of cells including neurons utilizing this technology.