Regenerative Medicine
Advances from the Convergence of Biology & Engineering

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BREAKTHROUGHS IN BIOSCIENCE/REGENERATIVE MEDICINE

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ON THE COVER

The image, which was a winner in the 2012 FASEB BioArt Competition, shows a three-dimensionally woven biomaterial scaffold. Multiple layers of resorbable fiber bundles have been woven into a porous structure. The scaffold is then seeded with cells that grow to become new tissue as the fibers are resorbed. Farshid Guilak, PhD, (Washington University in St. Louis and Cytex Therapeutics, Inc.) and Frank Moutos, PhD, (Cytex Therapeutics, Inc.) developed this scaffold in hopes of growing replacement cartilage to resurface joints.

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Throughout history, we have dreamed of healing untreatable wounds, replacing a disfiguring scar with healthy skin, growing replacement lungs in the laboratory, reawakening the body’s dormant ability to regenerate, and replacing a leg lost to injury or disease. Those are, in fact, the ultimate goals of the interdisciplinary field called regenerative medicine.

Dreams of regeneration took shape in ancient myths and legends. Greek mythology told of how the god Prometheus, chained to a rock, regrew his liver overnight after an eagle pecked at it each day.

What is fascinating is that the human liver can actually regenerate itself from just a small portion— as little as a quarter of its original size. Skin and bone can also partially regenerate themselves as part of daily living and also after minor injuries. Unfortunately, most of our organs and tissues have only limited abilities to repair themselves and restore lost function. Instead, we require prosthetics or organ transplants when we have lost or injured essential body parts.

The abilities of the human liver, skin, and bone to regenerate pale in comparison to some members of the animal kingdom. Great thinkers from Aristotle and Voltaire to
Charles Darwin and Thomas Hunt Morgan, the “father of genetics,” marveled at enviable examples of regeneration in other animal species (Figure 1). For example, salamanders and sea stars can perfectly regenerate lost limbs and arms. Zebrafish can replace lost fins to exact proportions, and a family of flatworms called planaria can completely restore their entire body from a tiny segment. Scientists continue to uncover the biological principles that underlie these animals’ regenerative abilities in hopes of learning how to stimulate regeneration in humans.

In general, regenerative medicine utilizes two approaches: (1) reawakening the body’s own dormant ability to renew and repair tissues from within, or (2) growing replacement tissues in the laboratory to implant in the body, an area called tissue engineering. Some tissue engineering applications, such as those for skin and cartilage, already have US Food and Drug Administration (FDA) approval for clinical use. Others, including tissue-engineered bladders and trachea (windpipe) are in pilot studies in humans, and many more are being evaluated in laboratory animals in preparation for human studies.

In the past twenty years, rapid advances in medicine and surgery, developmental and stem cell biology, biochemistry and bioengineering, and the material and physical sciences have propelled the field forward, thanks largely to key funding from the National Institutes of Health (NIH), National Science Foundation (NSF), the Department of Defense (DOD), and the Armed Forces Institute for Regenerative Medicine (AFIRM). Almost every week, researchers report new successes in the laboratory, fueling optimism that we may indeed attain the age-old dream of regeneration, at least for some of our tissues.

**EXCEPTIONAL REGENERATION IN NATURE**

A flat worm, called a planarian, performs the most remarkable regeneration in all the animal kingdom. It can restore any tissue following any injury, re-growing its head, central nervous system, vascular system, muscles—the entire body—from just a tiny piece, all with the proper front-to-back orientation. An early 19th century scholar called planaria “immortal under the edge of the knife.”

To discover planaria’s secrets in regeneration, late 19th and early 20th century scientists used their best available tool at the time—the microscope—and saw a mass of rapidly dividing cells quickly forming at the site of the planarian’s injury. Those cells developed into all the various specialized cells of the missing tissue.
WHAT MAKES STEM CELLS SPECIAL?

AN ENDURING MYSTERY OF LIFE is how a single cell (a fertilized egg) can divide and give rise to all the tissues and organs of a living, breathing, acting, and thinking human being. Much remains unknown, but developmental biologists do know that part of the answer lies in stem cells.

Most cells in our body are specialized to perform a limited set of jobs, and when they divide, they produce two copies of themselves. They are called differentiated cells and are considered mature, adult cells (even in a young child). A stem cell, however, is immature and undifferentiated, without a distinct, specialized function in a given tissue. A stem cell can either duplicate itself, or it can make one copy of itself (“self-renewing”) and another copy of a differentiated, specialized cell. Stem cells can divide indefinitely, whereas differentiated cells can only divide a limited number of times before they die.

Stem cells come with a spectrum of powers. Embryonic stem cells (ESCs) are the first cells produced by a fertilized egg and are totipotent meaning they can produce any type of cell in the body. Totipotent cells can give rise to an entire organism. Pluripotent stem cells are just slightly more mature than ESCs but still very powerful. They can also develop into many cell types in the body, but they cannot reproduce an entire organism.

Adult stem cells in our tissues are multipotent. They can divide and differentiate into several specialized cell types in one or more tissues, but they cannot produce all the cell types in the body. Tissues also harbor progenitor cells, which are partially differentiated cells that can self-renew to a limited extent and can make several of the cell types required by their tissue of origin.

Stem cells and progenitor cells are often hard to identify and isolate because they are rare and may reside in specialized niches in the tissue environment. Researchers have the most success harvesting adult stem cells from skin, bone marrow, adipose tissue (fat), amniotic fluid, and hair follicles.

Adult stem cells and progenitor cells are usually dormant, or non-dividing. But when they sense that a tissue has worn down or been injured, they kick in to replace tired, injured, or diseased cells.

Collectively, these are the cells that can refresh our skin as it flakes off each day, replace the cells lining our intestines that encounter caustic digestive juices, and repair wounds. Aging slows down the power of stem cells, leaving us less resilient and less able to heal ourselves.

NATURAL REGENERATION IN HUMAN TISSUES

What about humans? Some of our organs and tissues can regenerate to some extent. As mentioned, the liver can restore its full size from as little as a quarter of its original size. Skin can repair scrapes, cuts, and burns. Bones can re-fuse fractures. Bone marrow cells, as well as cells lining the intestine, and the cornea also undergo continuous cell renewal. Previously, researchers assumed that stem cells drive this regeneration, but, given discoveries in animal regeneration, they now think differentiated cells also play a role.

A skin wound exemplifies the body’s general response to an injury. Skin—our largest organ—protects us from disease, infection, dehydration, and other threats. It is laced with blood vessels that carry oxygen and immune cells and with nerves that allow us to sense our external environment. When a layer of skin is scraped off, immune cells first detect the injury and re-
Recruit various cell types to stop the bleeding, plug the defect, and rid the area of debris and damaged cells. Platelets, the sticky cells circulating in the blood, arrive at the wound and clump together to form a clot. Next, stringy proteins called fibrin replace the clot, forming scar tissue that fills in the gap in the skin. Cells called fibroblasts begin producing collagen and other proteins that provide a supportive scaffold and a nurturing environment for new skin cell growth. The scaffold components attract molecules that emit growth signals that stimulate new capillaries and nerve cells, bringing oxygen and sensation to the new tissue. In successful healing, these events remodel the scar tissue, replacing the fibrin scars with normal skin.

For deep or extensive skin wounds, however, remodeling may be impaired, resulting in a permanent scar. Severe wounds and burns may leave scars that limit flexibility and movement and may damage or destroy nerves, creating either chronic pain or a disabling loss of sensation.

Similarly, chronic liver damage, such as from alcohol abuse, impairs healing in that organ. Again, fibrous scar tissue forms instead of healthy new tissue, causing cirrhosis of the liver. Cirrhosis blocks the blood flow in the liver and slows the processing of nutrients, hormones, drugs, and toxins. Likewise, damage to the heart muscle following a heart attack leaves scarring that reduces its ability to pump blood throughout the body.

When natural regeneration fails, tissue engineering holds the promise of restoring function.

**TISSUE ENGINEERING**

The modern approach to tissue engineering was pioneered by Joseph Vacanti, MD, then a surgeon at Boston Children’s Hospital specializing in pediatric surgery and organ transplants, and Robert Langer, ScD, a chemical engineer at MIT (Figure 4). Early in his career, Vacanti concluded that the major challenge in his field was the shortage of donor organs for transplantation and also of healthy tissue for reconstructive surgery. He conceived of developing implantable constructs that act as permanent replacement structures in the body to restore lost function. In the late 1980s, he teamed up with Langer, who was creating new synthetic materials with biologically compatible properties for building new blood vessels. In hindsight, this collaboration kicked off a new convergence of the fields of engineering, the physical sciences, and life sciences that has inspired ongoing innovation and discovery.

Specifically, Vacanti and Langer began combining living cells with three-dimensional scaffolds made of a synthetic polymer to create new tissues and organs in the laboratory. They developed the approach of creating a supportive scaffold, seeding it with stem cells...
or other cells, and coaxing them to grow and fill in the scaffold to create a simulated tissue (Figure 5).

The body’s cells naturally produce scaffolds when they secrete collagen, fibrinogen, and other proteins. These components are collectively called the extracellular matrix (ECM). The ECM contains growth factors and other signaling molecules that direct and regulate cell growth. Basically, the scaffold gives the tissue its shape, contains space for cells to grow, and provides the nurturing conditions cells need to thrive.

Tissue engineering requires materials that are biocompatible and sometimes biodegradable in the body, such as naturally derived polymers isolated from animal or human tissues. Alternatively, synthetic molecules can be tailored with specific physical properties to suit particular biomedical applications. Cellular and molecular biologists have determined which signals direct stem cells to differentiate towards the desired cell type and to control cell growth as the tissue develops in the lab.

In the body, the scaffold structure naturally includes channels for blood vessels that carry oxygen and important nutrients to the cells, as well as for nerve cells. Stem cells generally live in a special supportive niche within the scaffold. Tissue engineers are working to recreate these channels and stem cell niches for a specific tissue type.

The material properties of the scaffold also affect the type of tissue that will develop. Gordana Vunjak-Novakovic, PhD (Figure 6), a biomedical engineer at Columbia University who has conducted seminal work in this area, has discovered that scaffold design can “unlock”
SCAFFOLDS: VARIATIONS ON A THEME

THE CONVERGENCE OF CELL BIOLOGY, engineering, and material science has led to many innovations in scaffold design. Here are three important new developments.

DECELLULARIZED SCAFFOLDS: It is very challenging to recreate the complex structure of an organ’s scaffold from scratch in the lab. One solution is to use a donor organ and wash away all the cells, leaving just the extracellular matrix. The remaining matrix provides the ready-made structure for the tissue scaffold. It also conveniently retains the many protein factors and molecular signals that guide the growth of stem cells from the patient’s body. When the scaffold is seeded with cells from the patient, those cells have the perfect environment to encourage proper tissue growth. Decellularized scaffolds are rapidly advancing the tissue engineering of solid organs and may soon enter human testing.

CELL-FREE SCAFFOLDS: Another challenge is keeping cells alive in the scaffold outside the body, especially in thick-engineered tissues that have not developed their own blood supply. To solve this problem, researchers have made progress in promoting the growth of blood vessels simultaneously with tissue cells. Another solution is to omit the step of seeding the cells in thicker scaffolds. Instead, the scaffold itself recruits the necessary cells into it once it is implanted in the body. Researchers first infuse the scaffold with the signaling molecules that are predicted to attract the cells and also add growth factors that stimulate the desired tissue development. To regenerate bone, for example, cell-free scaffolds made of calcium phosphate cements, collagen gels, or collagen sponges are combined with clinically approved bone morphogenetic protein-2, a factor that promotes bone growth and is thought to attract bone stem cells and osteoblasts to the site. Cell-free scaffolds are also being safety tested in human studies to repair cartilage and ligament tears that heal poorly following a surgical graft of a ligament.

SPHEROIDS: Another solution to the challenge of simulating the proper extracellular matrix for engineered tissue is to have the cells create their own matrix. First, the cells are nurtured in a bioreactor (a device used to grow cells or tissues) so that they form three-dimensional cellular groups called spheroids. The three-dimensional structure stimulates cells to secrete the materials and signals that make up the matrix.

the biological potential of the seeded cells. For example, stiff scaffolds skew fibroblastic cells towards developing into bone. Spongy scaffolds encourage fat-forming cells. Stretchy scaffolds stimulate neurons to form connections and transmit electrical signals as they do in the brain. In heart tissue constructs, applying electrical signals promotes contraction of cardiac muscles, and these mechanics are important for development.

For lung tissue, the flow of air and blood, as well as mechanical stretch, helps form the functional architecture of the tissue.

Following the production of engineered tissue in the laboratory, the goal is to graft it into a patient’s body. Once implanted, the body’s own endogenous (native) cells begin making their own ECM, growth factors, and other components of the maturing tissue. Researchers hope
to one day bypass the need to grow cells in the lab. Instead, they envision implanting a well-designed scaffold that will, on its own, attract the necessary cells to restore the form and function of the missing or injured tissue. Alternatively, it may be possible to bypass the need for scaffolds altogether by adding the right mix of cells, molecular signals, and growth factors to awaken the kind of regenerative power seen in salamanders and zebrafish.

**CONSTRUCTING SKIN**

In the United States, 15-20 thousand patients are hospitalized each year for acute burns from fire, electricity, or chemicals; the battlefield also causes life-threatening burns and skin wounds. With over 50 years of research on skin grafts and artificial and tissue-engineered skin, people can now survive burns to 90 percent of their bodies with quick and intensive treatment.

The standard treatment for severe burns is an autologous skin graft, meaning surgeons remove a layer of healthy skin from an unaffected part of the patient’s body and transplant it on the burned area. Then, the intact skin cells and capillaries of the graft will become integrated with the underlying tissue. In some cases, however, there may not be sufficient healthy skin to cover a burned area. In the mid-1970s, researchers began addressing this problem by removing some of the patient’s keratinocytes—an abundant cell type in the outer layer of the skin—and growing these cells in thin sheets in the lab. Later, they developed a multi-layered scaffold to encourage growth of the deeper layer of skin. Beginning in 1981, researchers created thicker skin using a scaffold made of collagen gel containing fibroblasts. They seeded this scaffold with keratinocytes and then stacked the engineered tissue layers together to produce deeper layered skin (Figure 7).

FDA approved the first tissue-engineered skin in 1998. Today, FDA has approved more than 20 commercially
available forms of tissue-engineered skin, which is the largest regenerative medicine product line. Now, researchers are learning how to regenerate nerves, hair follicles, and sweat glands in the engineered skin to restore full-function following severe burns or wounds.

**TUBULAR ORGANS**

Success in tissue-engineered skin laid the groundwork for manufacturing other organs. The complexity of tissue engineering increases from flat tissue (such as skin) to hollow organs (like the bladder) to solid or multi-component organs with multiple tissue types (like the heart – with its four chambers, valves, inner and outer linings, muscles, blood vessels, nerves, and connective tissues).

To create scaffolds for organs that are hollow or tubular, tissue engineers essentially design flat sheets of tissue that can be rolled to form the basic architecture. In 2006, Anthony Atala, MD (Figure 8), director of the Wake Forest Institute for Regenerative Medicine, used this method to produce the first human therapeutic application of a hollow organ, the bladder. Patients who had their bladders removed received replacement organs made of a rolled scaffold seeded with cells taken from their muscles and bladder lining. The engineered bladders functioned moderately well during the 2-5 year follow up and remain functional today. Atala continues to work to improve the method with newer technologies.

Around that same time, Atala’s group began a pilot study implanting tissue-engineered vaginas in young women who were born with a syndrome that caused underdeveloped sexual organs. In 2014, the researchers reported, “All patients are sexually active and have functional variables in the normal range for desire or arousal, lubrication, orgasm, satisfaction, and painless intercourse.”

Atala’s group and others have been employing tissue engineering methods for other tubular organs, including the trachea, urethra, anal sphincter, and penis. Atala’s strategy is to conduct long-term pilot studies to ensure the technology is doable, long lasting, and reproducible before advancing to formal clinical trials.

**BONE ENGINEERING**

Among solid organs, bones have a promising natural capacity for regeneration and are a major focus for tissue engineering. They constantly remodel themselves in response to the mechanical stress, tension, and pressure they encounter each day. Bones undergo a balancing act between two types of specialized cells: osteoclasts that break down bone tissue and osteoblasts that secrete new bone material. When bones do not heal, surgeons have traditionally removed bone from elsewhere in the patient’s body and transplanted it to the site of the wound. Alternatively, patients may receive bone segments from cadavers, in an allograft procedure. However, the allografts are treated to prevent rejection and infection, and this treatment reduces bone healing.

Bone engineering may offer an alternative. Researchers first construct a scaffold with the proper size and shape to replace the defective bone (Figure 9). Then they seed the scaffold with bone-forming osteoblasts and/or adult stem cells that eventually become osteoblasts. The scaffold material may resemble bone minerals or may use natural or synthetic polymers infused with bioactive growth factors involved in bone formation. The scaffolds may be designed to degrade in the body once the osteoblasts replace the synthetic material with minerals and other natural components of bone.

Tests in animals show that resurfacing the scaffolds with nanoscopic grooves and chemical coatings that resemble the surface of native bone promotes the cellular response and the production of growth factors in the surrounding tissue. Researchers are also using 3D printing to perfect this surfacing technique, which will be studied in animal models before advancing to human trials.

**MENDING BROKEN HEARTS**

Engineering a scaffold for a complex functional organ like the heart, brain, or pancreas is a more challenging problem than for something like bone and skin. Unlike
these body parts, heart, brain, and pancreas cells do not divide frequently. However, in the past decade or so, researchers have discovered that even these stable organs do have cells that divide. Regeneration can happen, but just too slowly to repair the acute damage following heart attacks or severe brain injuries or disease.

The heart is a good example of what happens in response to damage of a complex organ, and it follows a similar healing process as the skin. In a heart attack, the blocked coronary arteries deprive the beating cardiac muscle of sufficient oxygen. The heart muscle cells, called cardiomyocytes, die. The resulting inflammation activates repair mechanisms and produces collagen, fibrin, and other materials that form the scaffold for the cardiomyocytes. Although cardiomyocytes can replace themselves, they do it much too slowly to improve function. Instead, fibroblasts deposit ECM components, which cause myocardial scarring. This scar tissue displaces new heart muscle and impairs the ability of heart muscles to contract, which weakens blood circulation and may lead to aneurysms or heart failure.

In the zebrafish and salamander, the response to heart damage initially resembles what happens in humans, but the end result is quite different. In 2002, Kenneth Poss, PhD (Figure 10), a cell biologist then at Harvard Medical School and now at Duke University, removed the lower section of the ventricle from an adult zebrafish heart. His research, partially supported by NIH, showed that a blood clot first formed over the injured region. Next, fibrin scar tissue replaced the red blood cells. In two months, however, new cardiomyocytes replaced the scar with heart muscle, and the heart looked and beat as well as it did prior to injury (Figure 11).

Heart regeneration also happens in newborn mice, contrary to previous assumptions that mammals could not heal their own hearts. Newborn mice can regenerate the heart as completely as zebrafish—but only up until seven days of age. This limited period of regenerative ability offers the welcome opportunity to learn what occurs at day seven to shut down regeneration and to figure out how to restart it.
One possibility is that mouse cardiomyocytes stop dividing after seven days because of a rise in oxygen saturation as breathing capacity increases. Oxygen deprivation, which damages heart muscle, has been shown to stimulate the repair signals leading to cardiomyocyte proliferation in both mice and zebrafish.

Another possibility involves microRNAs, which are small molecules known to modulate expression of genes. A 2013 study, for example, found a microRNA (MiR-195) that turns off genes thought to be involved in self-renewal. MiR-195 is active in seven day and older mice, possibly explaining why their heart muscle cells no longer self-renew. Conversely, this molecule is less active following a heart attack in neonatal mice, which may allow self-renewal genes to function. Researchers are excited because they might be able to manipulate this and similar molecules that regulate gene activity to stimulate heart regeneration in older mice and other animals. They can then apply that knowledge to human hearts.

In April 2016, Poss’s lab reported a genetic regulatory region that is only active when tissues regenerate in both zebrafish and mice. He used this piece of regulatory DNA to drive expression of growth factors to promote regeneration of the zebrafish fin and heart. This exciting discovery suggests that, just as earlier researchers hoped, there might be common underlying biological principles for regeneration that scientists could tap into.

REAWAKENING THE HUMAN HEART

So, are tissue engineers trying to build scaffolds to seed with cardiomyocytes for transplanting into people to replace scar tissue with healthy heart muscle tissue? That’s one approach. Another approach is to try to heal the heart from within using a regenerative medicine strategy called cell therapy, which is also applicable to other organs and tissues.

With heart-related cell therapy, physicians try to halt the progression of cardiac muscle damage by harvesting a patient’s stem cells, multiplying them in the lab, and infusing them back into the heart (Figure 12). Heart cell therapy is being evaluated in human clinical trials. Worldwide, several thousand patients have safely received this therapy, and their condition often appears to stabilize. It was thought that once in the environment of the damaged heart the stem cells would detect molecular signals telling them to become new heart muscle cells. New research, however, suggests that the stem cells themselves are not directly causing the observed clinical improvement in heart attack patients. Instead, the cells may act indirectly by inducing signals that prompt other cells to begin proliferating and regenerating—a phenomenon that is observed in zebrafish and mice.

For example, recent studies in young mice show that after an injury most of the new cardiomyocytes attempting to repair the damage come from de-differentiated mature cells. The signals that stimulate cardiomyocytes to proliferate come not just from the site of injury but also from an organ-wide response. The cells lining the inner and outer walls of the heart and the blood vessels all release cell-to-cell communication signals that change the behavior of the cardiomyocytes. In turn, these signals activate genes that are usually only functioning during development.

The laboratory of Nobel Laureate Shinya Yamanaka, MD, PhD, at Kyoto University made another breakthrough in stem cell research. Yamanaka had developed induced pluripotent stem cells (iPSCs), which are differentiated adult cells reprogrammed to revert to pluripotency. Yamanaka later found that iPSCs that have undergone 20 days of differentiation towards cardiac muscle cells perform better when implanted in the heart than more developmentally immature, stem-like iPSCs.

FIGURE 12 / STEM CELL THERAPY FOR THE HEART

Scientists are studying whether stem cells integrate in the heart and whether they develop into functioning new heart muscle cells. Image courtesy of the McGowan Institute for Regenerative Medicine
LETS RESEARCH THIS!

WHAT CAN SPEED THE TRANSITION OF NEW DISCOVERIES into clinical breakthroughs? One way is to probe these important questions.

- **HOW ARE STEM CELLS** functioning and differentiating once engineered tissues are implanted in the body? Do they engraft, or integrate, with the surrounding tissue? Do they survive, proliferate and differentiate into functioning components of the tissue?

- **WHAT ENVIRONMENTAL CUES** within a tissue induce cells to regenerate? How does an injury to a tissue activate those cues? How can scientists manipulate those signals to stimulate natural regeneration?

- **ARE THE STEM CELLS** used in tissue engineering or cell therapy indeed stem cells? Different labs use different protocols for classifying and purifying stem cells, making it problematic to compare and replicate results. Solving this problem could accelerate FDA approval for human therapeutic applications.

- **ARE INDUCED PLURIPOTENT STEM CELLS (iPSCs)** safe for human therapeutic applications? What is the optimal stage of development for these cells for seeding scaffolds or infusing into organs for different tissue types?

(Figure 13). This discovery may accelerate progress in human heart regeneration, since the more differentiated iPSCs cells are easier to control than stem cells.

Again, researchers now realize that both the organ-wide communication signals and the efficiency of more differentiated tissue cells in inducing spontaneous regeneration also apply to other organs and tissues. This is expected to streamline the quest for simplified strategies to regenerative medicine in general. Similar approaches are being evaluated in clinical trials for repairing common knee injuries, restoring teeth and gums, and many other applications. Ultimately, regenerative medicine may move even beyond cell therapy. Instead of infusing cells into the damaged organ or tissue, clinicians may just infuse the cocktail of molecules prompting the repair signals that will reawaken the inner salamander, zebrafish, or planarian in us all.

THE ROAD AHEAD

Successive generations of scientists have made stunning discoveries about the biology of regeneration. Although there are many questions remaining, the synergy of researchers in biology and engineering has provided new tools for searching for solutions. Rapid advancements in genetics, molecular biology, and live cell imaging now allow researchers to identify the origin of some of the cells that initiate regeneration and to follow them as they diverge into specialized cells. Researchers can analyze and manipulate cell signaling molecules, growth factors, and proteins that promote these processes. Tissue engineers have a growing inventory of biocompatible materials that can host these cells and molecules in implantable structures formed to integrate into the body. This progress has been made possible by basic research on the fundamental biology of creatures like the planarian, zebrafish, and mouse. As we discover how these organisms naturally

**FIGURE 13 / DIRECTING iPSCs TOWARDS CARDIOMYOCYTES** Yamanaka tested the hypothesis that allowing iPSCs to differentiate towards cardiomyocytes might improve engraftment in the heart. He compared the engraftment efficiency of the cells at different stages of maturation in mice. He found that iPSCs that have undergone 20 days of differentiation engrafted better than either more immature stem cells (Day8) or more differentiated cardiomyocytes (Day30)—as indicated by the thicker heart muscle wall—and also restored cardiac function better. Image credit: Funakoshi et al. Enhanced engraftment, proliferation, and therapeutic potential in heart using optimized human iPSC-derived cardiomyocytes. Scientific Reports 6, Article number 19111 (2016)
rebuild their bodies, we discover ways to rebuild the human body.

Regenerative medicine is making huge strides due to the investment of taxpayer dollars by NIH, DOD’s Congressionally Directed Medical Research Program, and NSF. NIH has both a Regenerative Medicine Program and a Tissue Engineering Program, and DOD has the AFIRM program. These and other programs and organizations have helped fund the breakthrough convergence of basic researchers, surgical scientists, biomedical engineers, biochemists and biophysicists, material scientists, and cell, developmental, and molecular biologists all working towards the goal of regenerative medicine. This funding is also assisting in building the complex infrastructure needed for cell growth, biomaterials development, high-resolution imaging, and cutting-edge genetic and molecular analyses.

More and more applications of regenerative medicine are being tested in animals, entering human trials, and gaining approval for clinical use. The field of regenerative medicine is still young, but scientists have already made great progress up a steep learning curve.

In the future, regenerative medicine and tissue engineering will come to the aid of wounded warriors, dying patients waiting for life-saving organ transplants, victims of traumatic accidents, and people with debilitating or disfiguring birth defects. It will benefit people suffering spinal cord and brain injuries and countless others needing physical restoration and medical renewal. We may never achieve the remarkable abilities of the “immortal” planarian, but with the advances of the past twenty years, we have an unprecedented potential to fulfill the human longing for regeneration that the ancient Greeks saw in Prometheus.

ADDITIONAL SUGGESTED READING


Cleveland Clinic “Stem Cell Therapy: Helping the Body Heal Itself” https://my.clevelandclinic.org/services/heart/disorders/heart-failure-what-is/stemcells


