Cover Page

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Wake Forest Institute for Regenerative Medicine

Legislative Report

July 1, 2011 to June 30, 2012

Program Activities, Objectives and Accomplishments and Itemized Expenditures

Report to
Joint Legislative Commission on Governmental Operations and
Fiscal Research Division
S.L. 2011-145 Section 14.12.(b)

Introduction

The U. S. Department of Health and Human Services (HHS) calls regenerative medicine the "next evolution of medical treatments." In its 2007 report, *2020: A New Vision - A Future for Regenerative Medicine*,[1] HHS concluded that the field not only "holds the realistic promise of regenerating damaged tissues and organs in the living body, " but "empowers scientists to grow tissues and organs in the laboratory and safely implant them." In recognition of this pivotal role, the National Institutes of Health in 2011 established the Center for Regenerative Medicine to provide the infrastructure to support and accelerate the clinical translation of stem cell-based technologies, and to develop widely available resources to be used as standards in stem cell research. Regenerative medicine is not just a future promise, but is already making its mark on health care. Skin and cartilage substitutes are available through regenerative medicine techniques and laboratory-grown bladders, tracheas, blood vessels and other tissues have been implanted in patients.

In addition to the medical benefits, regenerative medicine also represents the potential for economic benefit through the growth of companies and research institutions dedicated to its technologies. According to industry analysts, regenerative medicine is at an inflection point, poised for explosive growth.[2] Between 2008 and 2011, the global market for regenerative medicine products increased three-fold and the number of companies offering products and services doubled. In 2011, regenerative medicine companies generated $3.5 billion in sales and employed almost 14,000 people.[3]

What is Regenerative Medicine?

Regenerative medicine is an interdisciplinary field bringing together scientists in molecular biology, genetics, cell biology, physiology, pharmacology, biomaterials and nanotechnology working collaboratively to deliver therapies that repair, replace or regenerate organs and tissues. The field is composed of the sub-disciplines of tissue engineering, cell therapies, and an area often called healing therapies.

Tissue engineering is the science of growing replacement tissue in the laboratory to replace damaged or diseased tissue and organs. The process usually starts with a three dimensional structure called a scaffold that is used to support cells as they grow and develop. Skin, blood vessels, bladders, trachea, esophagus, muscle and other types of tissue have been successfully engineered; some of these tissues have already been used in treating human disease.

Cell therapies apply living cells to an organ or tissue to promote healing and regeneration from within. Cell therapies are an exciting area of research since it is simpler to heal existing tissues and organs than to replace them. Cell therapies are being delivered today for cartilage reconstruction, bone reconstruction, and in inflammatory and immune response problems. In the future, cell therapies hold promise for treating liver disease, diabetes, neural disorders, renal failure and other chronic conditions.

Healing therapies are similar to cell therapies in that the goal is to restore the function of an existing tissue or organ. However, rather than using cells alone, non-cellular components are used to accelerate the regeneration

[1] *2020—A New Vision: A Future for Regenerative Medicine*, U.S. DHHS (2007).
[2] *Regenerative Medicine at an Inflection Point* BNA Insights, 5 LSLR 476 (2011) E. Herriman
[3] *Progress in the Tissue Engineering and Stem Cell Industry: Are we there yet?* Tissue Engineering: Part B, 18:155 (2012), A. Jaklenec et al.

process. Various strategies are currently being studied with good results, including using biomaterials to aid in cell recruitment for regeneration, and using small molecules to trigger a regenerative effect.

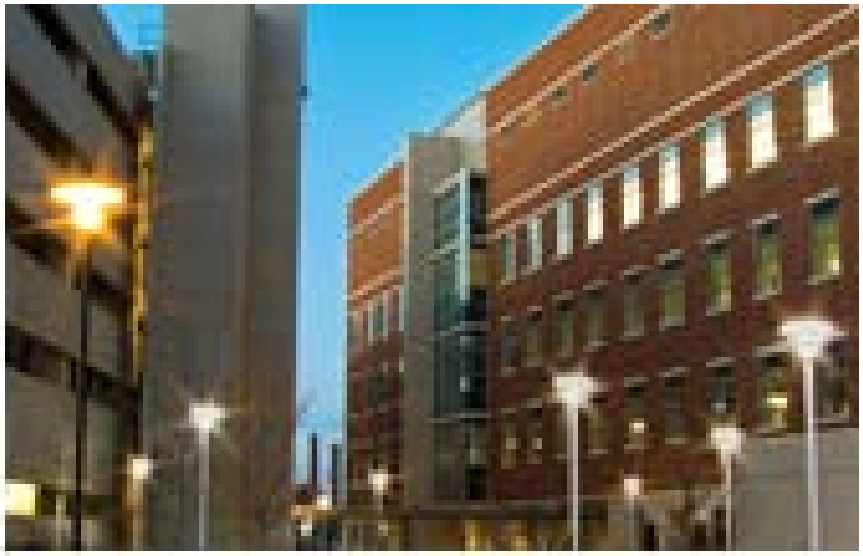
A common misconception about regenerative medicine is that it requires use of stem cells that come from human embryos. This is not accurate. In fact, the goal of many regenerative therapies is to use a patient's own cells. These cells can include adult stem cells (found in many organs and tissues, including brain, bone marrow, and the blood) and progenitor cells (an immature type of cell found in almost every organ in the body). In cases where a patient's own stem cells cannot be obtained, there are several other sources of stem cells. For example, scientists at WFIRM discovered a type of versatile stem cells in amniotic fluid.

About WFIRM

The ***Wake Forest Institute for Regenerative Medicine*** (www.wfirm.org) is an international leader in translating scientific discoveries into therapies to benefit patients. Its physicians and scientists were the first in the world to engineer laboratory grown organs that were successfully implanted into humans. Today, this team, which has grown to almost 300 scientists and staff, is working to engineer replacement tissues and organs and develop healing cell therapies for more than 30 different areas of the body.

Once a new technology has been thoroughly tested and is ready for clinical studies, WFIRM is equipped for efficient "translation" from the bench to the bedside. A current good manufacturing practices (cGMP) facility, which manufactures replacement tissues and organs under guidelines of the U.S. Food and Drug Administration, ensures that a reproducible process is in place. And when the technology is ready to be licensed to a company that can commercialize it for widespread use, WFIRM has the unique infrastructure and community resources to create companies and develop partnerships to expedite the delivery of the technology to patients.

WFIRM is part of Wake Forest Baptist Medical Center and is located in Piedmont Triad Research Park in downtown Winston-Salem, North Carolina. With its high-tech research and innovation center, Wake Forest Biotech Place, a former R.J. Reynolds Tobacco Co. processing plant, the Piedmont Triad Research Park has been heralded as a shining example of how a community can transform itself into a knowledge-driven economy. When complete, the entire redevelopment will convert more than a million square feet of rehabbed historic buildings into a vibrant, urban community, making it the largest urban research park in the nation. As a premier tenant in the Park, WFIRM is seen as an integral factor in drawing private sector business to the region.



Role of State Funding

Government/academic initiatives play a pivotal role in realizing the promise of regenerative medicine. State funding can help accelerate the translation of scientific discoveries through pre-clinical and clinical trials, manufacturing and commercialization strategies, and the U.S. Department of Health and Human Services recommendations include a government/academic model, citing the success of the approach in growing the nation's semiconductor industry from $8 billion to $170 billion in a 10-year period.

State support is also vital to help leverage economic benefits of regenerative medicine. According to a study by Battelle and the Biotechnology Industry Organization, despite challenging state fiscal conditions, states continue to make investments designed to encourage the growth of the bioscience sector, a key driver of economic growth.[4]

Regenerative Medicine Initiatives Selected State Programs

California Institute for Regenerative Medicine (CIRM)
CIRM was created in 2004 through a ballot measure that authorized the sale of $3 billion in general obligation bonds to finance regenerative medicine research and related research facilities in California. CIRM has awarded grants totaling $1.1 billion since its first round of awards in 2006.

New York State Stem Cell Science (NYSTEM)
NYSTEM is $600 million, 11-year initiative of the State of New York to provide funding stem cell biology research and development. The fund was created through legislation authorizing the Empire State Stem Cell Trust Fund and is administered by the New York State Department of Health.

Maryland Stem Cell Research Fund
Established through the Maryland Stem Cell Act of 2006 to promote stem cell research and development, the Maryland Stem Cell Research Fund has awarded $68.4 million in research grants to date.

Connecticut Stem Cell Research Fund
Started in 2006, the Connecticut Stem Cell Research Fund commits $100 million over a 10 year period to stem cell research. The Fund is administered through the Connecticut Commissioner of Public Health.

North Carolina's Leadership Role

The State of North Carolina is among the states providing critical state support. The State has initiated a recurring annual investment to allow WFIRM to better develop and translate its discoveries to patients. State support of regenerative medicine will help North Carolina maintain its leadership position in this sector by accelerating the clinical translation of scientific discoveries, enabling regenerative technologies to be developed and manufactured in North Carolina and increasing its economic base by manufacturing and job creation in North Carolina.

While regenerative medicine research initiatives are under way globally, few areas have the critical mass and infrastructure that North Carolina has to engage in the full spectrum of activities required to move from basic research to commercialization and the clinic. Examples of the state's competitive advantages include the following:

- ***World-renown organization***. North Carolina is home to an international leader in regenerative medicine – the Wake Forest Institute for Regenerative Medicine. WFIRM is the largest dedicated regenerative medicine organization in the world in terms of number of direct employees and its continuing accomplishments have meant a growing reputation in regenerative medicine for North Carolina.

- ***Proven track record***. Several regenerative medicine therapies developed by North Carolina scientists are already in patients, and others are in the pipeline, ready to begin testing in patients within the next few years.

[4] Battelle/BIO *State Bioscience Initiatives* 2010

Projects range from treatments designed to help wounds heal to using skin cells to treat burns. The team was the first in the world to successfully engineer human organs in the laboratory and implant them in patients.

- ***Strong collaborations***. North Carolina scientists are involved in numerous collaborations – which make for stronger science – throughout the nation and world. WFIRM has collaborative agreements with institutes in 10 different countries, and collaborations with numerous universities.

- ***GMP manufacturing facility***. Through WFIRM, regenerative medicine researchers have access to a current good manufacturing practices production facility that allows for the preparation of tissues and cell therapies under U.S. Food and Drug Administration guidelines. This facility helps accelerate clinical translation and commercialization.

- ***AFIRM leadership role***. By leveraging state funds, WFIRM was selected to co-direct the Armed Forces Institute for Regenerative Medicine, a $100 million virtual institute that develops regenerative therapies for our wounded warriors. This project has brought significant funding to North Carolina scientists to rapidly develop new treatments that will benefit both wounded warriors and civilians. This last year, WFIRM was selected by the current four major partner institutions to lead the Warrior Restoration Consortium as prime contractor in response to the AFIRM II solicitation. The Warrior Restoration Consortium proposes a comprehensive program of $75 million in research over 5 years, with more than 60 projects in 5 program areas, with more than 40 participating institutions.

Armed Forces Institute of Regenerative Medicine

Accelerating Regenerative Technologies to the Wounded Warrior

The use of improvised explosive devices in Iraq and Afghanistan has caused a significant increase in severe blast trauma. More than 6,500 U.S. military fatalities and more than 49,500 injuries have been reported.[5] While advances in body armor, quicker evacuation from the battlefield, and advanced medical care have improved survival rates, many of the injured come home to face challenges of overcoming severe limb, head, face, and burn injuries that can take years to treat and usually result in significant lifelong impairment. The Department of Defense established the Armed Forces Institute of Regenerative Medicine (AFIRM) in 2008 with the mission of developing new products and therapies to treat severe injuries suffered by U.S. service members. There were two consortia established within AFIRM to accelerate the delivery of regenerative medicine therapies to these severely injured U.S. service members: one headed by Wake Forest University (the Wake Forest-Pittsburgh University Consortium or WFPC) and one headed by Rutgers University (the Rutgers-Cleveland Clinic Consortium or RCCC). While these two consortia are distinct and separate entities, they have the same and complementary mission — accelerate regenerative technologies to the wounded warrior. WFIRM in its role as a consortium co-leader has continued to grow a national network of regenerative medicine leaders in advancing the AFIRM mission.

[5] http://www.defense.gov/news/casualty.pdf (August 2012)

Five Major Program Areas within AFIRM

There are five areas of research emphasis within AFIRM-WFPC focused on developing regenerative therapies to address burn, craniofacial, and compartment syndrome related injuries, limb and digit regeneration and healing without scarring.

Craniofacial Regeneration Program

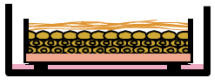
Craniofacial trauma is among the most debilitating forms of injury facing civilian and military populations due to the important aesthetic and functional role of the craniofacial complex. Blast injuries and injuries from high velocity projectiles, such as those encountered on the battlefield, present a range of therapeutic challenges and often require a staged repair. A significant need exists for the development of novel regenerative medicine approaches for the generation of both soft and hard tissues to overcome the current clinical barriers to craniofacial reconstruction. Like all programs within AFIRM, this program consists of several multidisciplinary, multi-institutional collaborative research teams to address the core issues associated with traumatic injuries.

Burn Program

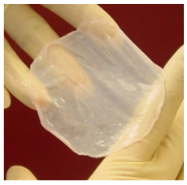
Unquestionably, one of the most visible and life threatening injuries to military service personnel are severe burns. The current standard of care for burn injuries remains early excision and autografting, and has not fundamentally changed in over 30 years. The multi-institutional, and multi-disciplinary Burn Program's principal "thrust" is to significantly advancing the operative management of burn injuries, as burn wound "closure" remains the single greatest threat to the burn-injured warfighter. All six of the originally funded AFIRM projects, and the three added clinical trials, in the Burn Program complement each other and offer significant potential for synergy, which has been and will be leveraged at every opportunity. In addition to an ongoing 100-patient trial using a cell spraying technology, a second burn project recently received Orphan Drug Status from the FDA and is expected to complete the Phase II clinical trial within 12 months.

Skin Spraying Technology for Burn Repair
AFIRM Clinical Trial in North Carolina

- Using a small piece of skin, the skin cells can be converted into a spray form that be applied over a larger area (80% of the body) with good results.



Culture under organotypic conditions



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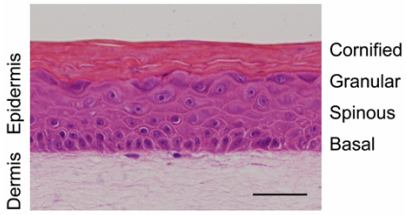


Scarless Wound Healing Program

Military trauma creates not only large wounds but also large scars. These scars are often very visible and can draw unwanted attention to the wounded warrior. In some instances the scars become so thick that they can limit movement of joints and greatly restrict the patient's ability to move. The costs associated with treatment of tissue fibrosis in the U.S. are estimated to be over $4 billion per year. Current treatment regimens involving surgery, silicone sheeting, anti-inflammatory medications and laser/radiation have been disappointing. This is largely due to

a lack of understanding of the fibrotic process. The pathophysiology of scar formation suggests the need to regulate numerous aspects of the wound environment, including cells, extracellular matrix, mechanics and biochemical signaling.

The WFPC approach encompasses a broad continuum of technologies aimed at modulating the tissue response to injury. Collectively, these projects represent a collaborative effort to address every aspect and stage of wound repair in a single research program, with the overarching aim of developing a more effective wound management paradigm. Thus the WFPC Scarless Program is composed of a synergistic combination of seven leading research groups focusing on every aspect of scarless wound healing. Industrial partners have contributed to the initiation of two clinical trials. This program utilizes complementary approaches (device, pharma, biotechnology) to balance short- and long-term objectives.

Compartment Syndrome and Limb & Digit Programs

Tissue wounds to the extremities are among the most common battlefield injuries sustained by troops during Operations Iraqi Freedom and Enduring Freedom. Particularly common trauma injuries caused by improvised explosive devices are blast and projectile injuries. Thus there is a need to develop technologies which address both limb and digit salvage and the consequences of amputated parts. While some times the damage is obvious other times injuries are complicated by compartment syndrome (CS). In CS, trauma related tissue swelling creates increased compartment pressures and this leads to ischemia and infarction of tissues. CS dramatically amplifies the battlefield injury and quickly leads to permanent muscle, nerve and vascular cell death. Soldiers that develop CS have prolonged recovery times and rarely recover complete muscle function, and they usually do not return to active duty at the same level of performance. Most CS injuries of the extremities result in permanent disability.

This program aims to develop regenerative medicine technologies using a number of approaches from autologous and progenitor cells that offer a safe and potentially effective new therapeutic avenue to amplify the body's endogenous regenerative response to injury, to hand transplants, to biomaterials approaches — all with the goal to improve the functional recovery of the injured soldier. The regenerative medicine technologies, which have already been used by AFIRM investigators and others safely and effectively for civilian tissue injuries, provide a promising approach to solve an important unmet need in the treatment of battlefield injuries.

Clinical Trials Underway

During the fourth year of operation, WFPC has continued to advance technologies to clinical trials. The following table shows the number of Department of Defense nationwide approved trials currently under AFIRM-WFPC.

Current AFIRM Clinical Trials
A Comparative Study of the ReCell® Device and Autologous Split-thickness Meshed Skin Grafting in the Treatment of Acute Burn Injuries (Phase III) (J. Holmes MD)
Human Upper Extremity Allotransplantation; (A. Lee, MD)
Autologous Adipose Derived Stem Cell Therapy For Soft Tissue Reconstruction After Facial Trauma (P. Rubin, MD)
Structural Fat Grafting for Craniofacial Trauma: Effect of Concentrating Endogenous Stromal Cells in the Fat Graft using the Tissue Genesis Cell Isolation System Device: (P Rubin, MD)
Clinical Evaluation of the Neodyne Dressing for Diminished Scarring (G. Gurtner, MD)

Beyond these clinical trials, a string of clinical trials nearing the enrollment phase are coming to fruition. Utilizing well-established, proven research investigators, the AFIRM has been able to expand the rehabilitative medicine knowledge base, develop models of injury, and test advanced technology products.

Future AFIRM Programs: AFIRM II and the Warrior Restoration Consortium

This spring, the U.S. Army Medical Research and Materiel Command, with the Office of Naval Research, the Air Force Medical Service, the Office of Research and Development - Department of Veterans Affairs, the National Institutes of Health, and the Office of the Assistant Secretary of Defense for Health Affairs announced the continuation of AFIRM and solicitated applications for the AFIRM II program. AFIRM II, expected to be funded in 2013, will include progams in the areas of extremity renegeration, craniomaxillofacial regeneration, skin regeneration, composite tissue allotransplantation, and genitourinary repair. WFIRM was selected by the current four major partner institutions to lead the Warrior Restoration Consortium as prime contractor in response to the AFIRM II solicitation. The Warrior Restoration Consortium proposes a comprehensive program of $75 million in research over 5 years, with more than 60 projects in 5 program areas, with more than 30 participating institutions.

Mission Driven Accomplishments

WFIRM's mission is to improve patients' lives by developing regenerative medicine therapies and support technologies. As such, WFIRM's goals have been focused on clinical translation with emphasis on innovation, teamwork and development of platform technologies that address the current scientific challenges. Additional core resources provided by the State of North Carolina have allowed projects within the federally funded AFIRM to accelerate progress and aid in increasing the visibility of North Carolina to military and federal leadership. State support has been leveraged to attract top scientists from around the nation to North Carolina. The State award has supported the work and training scientists and synergized the growth and productivity of WFIRM.

Good Manufacturing Practices—A Key to Translation

An important key to translating a therapy to the patient is to have strict quality control over the manufacturing process. A central FDA compliant current good manufacturing practices (cGMP) processing facility was designed and built to target completion to support clinical trials specifically for AFIRM. The construction of the central cGMP facility, physically located at WFIRM, is part of the commitment from the state of North Carolina to support the clinical programs for AFIRM. The cell processing facility complies with good manufacturing practices as defined in Title 21 of the Code of Federal Regulations and section 520 of the Food, Drug, and Cosmetic Act. This facility supports the clinical studies developed in the AFIRM program. The facility of approximately 4,000 square feet is fully equipped for processing and cryopreservation of human cell and tissue products as well as providing biomaterial design and fabrication. The facility includes cell culture/constructs and cell/bioreactor processing laboratories with a class 10,000 air handling capability. Other

spaces include cell and materials testing and scaffold fabrication laboratories, quarantine room, cryopreservation room, and a quality control/analytical lab.

Development continues on multiple cell therapy, tissue engineered and manufacturing and banking stem cell banks of adult and fetal derived stem cells projects, including muscle precursor cells for treatment of urinary incontinence, tissue engineered muscle repair for cleft lip deformities, and peripheral blood progenitor cells for articular cartilage regeneration. Preclinical process development and regulatory submissions are underway for a number of earlier stage projects including development of a bioengineered cornea, use of particle oxygen generators for wound healing, and self-seeding heart valves.

Current GMP Clinical Development Projects	
CELL THERAPY AND TISSUE ENGINEERING	
Project	***Indication***
Muscle precursor cell therapy	Urinary incontinence
Tissue engineered muscle repair	Cleft lip deformities
Peripheral blood progenitor cell therapy	Articular cartilage regeneration
Autologous islet cell transplantation	Chronic pancreatitis
STEM CELL BANKING ***Preclinical and Clinical Applications***	
Amniotic fluid stem cells	
Muscle precursor cells	
Placental stem cells	
Adipose derived stem cells	

Integrated Intellectual Property and Technology Transfer

WFIRM's strategy has been and continues to be solving the technical challenges that hamper clinical translation through innovation. Robust intellectual property protection is essential to the effective commercialization of these innovations. WFIRM faculty members have been very productive in generating intellectual property. The WFIRM patent portfolio includes approximately 200 patents and applications generated from over 150 invention disclosures.

WFIRM has integrated intellectual property into the day-to-day operations through a dedicated technology transfer team that operates within the Institute. The arrangement promotes frequent and informal communications, better flow of information and closer working relationships between the researchers, commercialization team and technology transfer staff, all of which contribute to higher quality protection and better prospects for faster, more effective commercialization, building portfolios around key technology areas.

Collaborations

WFIRM strongly believes that collaborative teamwork is the key to success. Collaborations create opportunity for scientific exchanges at the very highest levels, extend the translation of clinical techniques to the most appropriate places and increase the visibility and reputation of WFIRM and the State of North Carolina.

WFIRM currently has established numerous collaborative relationships within the region, nationally and internationally. Local and regional collaborations have been a particular focus for WFIRM, strengthening the State and promoting economic development. Research activities with these collaborators have been extremely productive.

Regional Academic Collaborations

Collaborations continue with *North Carolina State University Center for Comparative Medicine and Translational Research* and *North Carolina State University Edward P. Fitts Department of Industrial and Systems Engineering*. Each of these collaborations is directed at bringing together advances in regenerative medicine with cutting edge science in other disciplines to reduce cost and improve effectiveness. Both collaborations expand training opportunities to develop the North Carolina work force infrastructure.

Piedmont Triad Industry Collaborations

WFIRM continues to emphasize collaborations with its local industry neighbors. Of note this year is the expanding collaboration with ***Ocular Systems Inc***., a Piedmont Triad Research Park company, with the goal of commercializing an endothelial cell product for cornea transplantation, using technology developed by WFIRM. The goal is to grow replacement corneal tissue in the lab using "banked" cells and a scaffolding material. With this approach, in which scientists multiply donor corneal cells, cells from a single donor could benefit multiple patients, helping to increase the availability of tissue to patients who need transplants. In the planning phase is a new venture to take the bioengineered cornea through preclinical development, regulatory approvals, and then to market.

International Collaborations

WFIRM has established research collaborations with leading laboratories in regenerative medicine research from around the world. Collaborations include the following institutions:

Austria	Ludwig Boltzmann Institute, Wien
China	Shanghai Tissue Engineering Research Center, Jiao Tong University School of Medicine, Shanghai
	Beihang University, Beihang
	Nantong University, Nantong
Egypt	Kasr Al Ainy Teaching Hospital, Cairo University, El Manial
	Assuit University, Assuit
Germany	European Center for Medical Technologies and Applications, Cologne
	Institute for Tissue Engineering and Regenerative Medicine ITERM, Lukas Hospital, Neuss
	Aachen University Institute of Applied Medical Engineering, Aachen
Hungary	University of Szeged Institute of Surgical Research, Szeged
Ireland	National University of Ireland at Galway and Regenerative Medicine Institute of Ireland at Galway
Israel	Rambam Medical Center, Haifa

Japan	Tokyo Woman's Medical University, Institute of Advanced Biomedical Engineering & Science, Tokyo
Korea	Kyungpook National University and Kyungpook National University Hospital Daegu Korea Institute of Science and Technology, Seoul
Switzerland	University Hospital Basel, ICFS, Basel
Taiwan	Taipei Medical University, Taipei

Education and Outreach

Consistent with its philosophy of making regenerative medicine training widely accessible, WFIRM maintains a wide variety of educational offerings, from traditional graduate and post-graduate education to programs for the general public.

Tours and Lectures

WFIRM maintains a very active outreach program through all levels of the community to provide high school, middle school students, and the general public with opportunities to learn more about regenerative medicine. Recent activities include:

- Host to more than 500 visitors per year from all walks of life to the WFIRM facility
- Contributions to exhibits in several prominent local (SciWorks), regional (UNC Museum of Science), national (Chicago Museum of Science and Industry), international (Science Museum, London, England) museums and prominent technology forums (Wired Nextfest, TED)
- Presentations by WFIRM faculty at lay events throughout the Triad, the State, and nationally
- Keynote participation in State science and technology outreach, including programs through NC Science Festival and NC Association for Biomedical Research to educate students about biotechnology

Connecting the Future with the Past WFIRM hosts two significant collections highlighting the history of medicine, giving visitors the opportunity to appreciate the progress of medical science.

- Collections of medical artifacts amassed by former Bowman Gray professor and local obstetrician Dr. Jack Monroe. Included are a number of decorative bleeding bowls, bowls with a sliced-out portion to fit under the patient's neck or elbow when a vein was slit, the oldest dating back to 1690, and a metal trepanner, a device used to drill into the skull, to relieve swelling caused by a kick to the head.
- The History of Medicine in Pictures, a series of prints from the 1950s, donated by Dr. Jesse Meredith, emeritus chair of surgery at Wake Forest Baptist Medical Center.

Traditional Degree Programs

The outstanding research infrastructure, highly collaborative nature and expertise of WFIRM faculty and cutting-edge integrated training program prepare students for research careers in regenerative medicine. WFIRM students interact and exchange ideas on a daily basis with scientifically and culturally diverse students, post doctoral

fellows, technicians and faculty in regenerative medicine. Current enrollment is 28 pre-doctoral (PhD) students and 50 postdoctoral fellows. During the last year, 10 WFIRM students obtained doctoral degrees with dissertations in regenerative medicine, a foundational generation of new scientists with the interdisciplinary training needed to create the future.

Volunteer Program

- Open to high school students, undergraduate students and postdoctoral fellows from around the world
- 100 volunteers at any point in time
- Hands-on experience in regenerative medicine techniques
- Volunteers work on a variety of funded projects supervised by faculty and with a laboratory mentor

Summer Research Scholars Program

- Highly competitive 10-week program open to undergraduate science and engineering and medical students.
- Students are assigned to one of a broad range of funded projects focused on various aspects of tissue engineering and regenerative medicine.
- Program concludes with research day of student presentations attended by family members, mentors and faculty.

Forsyth Tech Intern Program

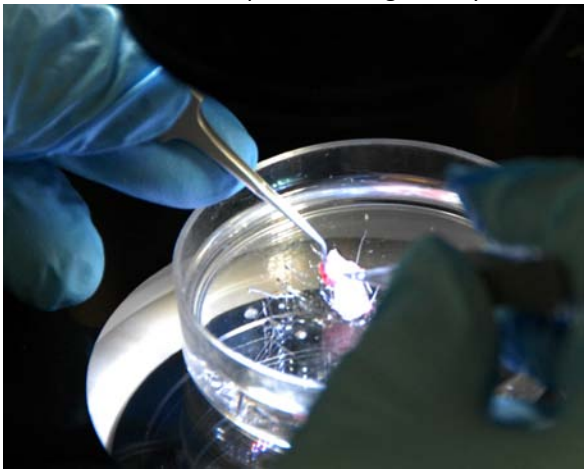
- Internships for Forsyth Technical Community College students pursuing careers in biotechnology
- Hands-on experience in regenerative medicine techniques that satisfies the FTCC program requirements
- Students have gone on to science jobs in industry and medicine and to higher education

Post-Baccalaureate Program

- Post-baccalaureate research program for minority students (PREP Scholars) funded by the National Institute of General Medical Sciences (Principal Investigator Dr. Debra Diz)
- Research, coursework and entrance exam preparation for under-represented minority students interested in careers in the biomedical sciences

Research Awards

WFIRM faculty submitted more than 80 research proposals totaling over $125 million to 20 different agencies, foundations, and companies during fiscal year 2012. New and continuing awards provided over $30 million in grant funding. Included in the FY12 proposals were a number of major collaborative projects, such as the proposal to the Space and Naval Warfare Systems Center Chemical, Biological Defense Innovations and Technologies Xvivo Capability for Evaluation and Licensure Program. The goal of this program is to develop an *in vitro* platform of human organ constructs – a "body on a chip" – that could accurately predict human safety and effectiveness of potential medical countermeasures against biological and chemical agents. WFIRM was the lead institution on a proposal that brings together leading experts from a range of disciplines and includes six different institutions.

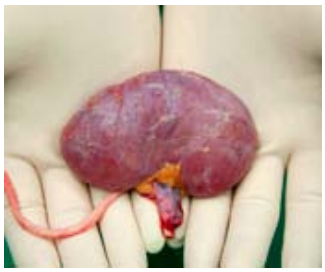


News and Publications

Scientific Publications

WFIRM authors published 126 peer-reviewed papers in 81 different scientific journals during fiscal year 2012. Notable reports include:

Kidney organ engineering



WFIRM researchers reached an early milestone in a long-term project that aims to build replacement kidneys in the lab to help solve the shortage of donor organs. In proof-of-concept research, the team successfully used pig kidneys to make "scaffolds" or support structures that could potentially one day be used to build new kidneys for human patients. The idea is to remove all animal cells – leaving only the organ structure or "skeleton." A patient's own cells would then be placed on the scaffold, making an organ that the patient theoretically would not reject. While this is one of the first studies to assess the possibility of using whole pig kidneys to engineer replacement organs, the idea of using organ structures from pigs to help human patients is not new. Pig heart valves – removed of cells – have been used for more than three decades to provide heart valve replacements in human patients.

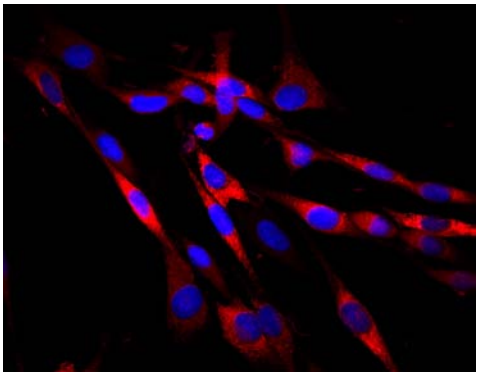
Production and Implantation of Renal Extracellular Matrix Scaffolds From Porcine Kidneys as a Platform for Renal Bioengineering Investigations. Orlando G, Farney AC, Iskandar SS, Mirmalek-Sani SH, Sullivan DC, Moran E, Aboushwareb T, Paolo DC, Wood KJ, Stratta RJ, Atala A, Yoo JJ, Soker S. Ann Surg. 2012 Aug;256(2):363-370.

Bioengineered heart valves

WFIRM researchers demonstrated the feasibility of eliminating time-consuming and technically demanding process of seeding patient cells on heart valves. This process begins with a pig valve, which, today, is commonly used to replace human heart valves. While these valves function quite well, they are not always long-lasting. The goal is to remove all cells from the valve, and replace them with a patient's own cells *after* implantation, by coating the scaffold with an antibody that attracts certain cell types. The scaffold would then be implanted in the body, where it would theoretically "self-seed" with a patient's cells.

Bioengineered self-seeding heart valves. Jordan JE, Williams JK, Lee SJ, Raghavan D, Atala A, Yoo JJ. J Thorac Cardiovasc Surg. 2012 Jan;143(1):201-8.

Hemophilia treatment



Gene therapy combined with stem cell transplantation successfully reversed the severe, crippling bleeding disorder hemophilia A in large animals. A single injection of genetically-modified adult stem cells in two sheep converted the severe disorder to a milder form, opening the door to the development of new therapies for human patients.

Phenotypic correction of hemophilia A in sheep by postnatal intraperitoneal transplantation of FVIII-expressing MSC. Porada CD, Sanada C, Kuo CJ, Colletti E, Mandeville W, Hasenau J, Zanjani ED, Moot R, Doering C, Spencer HT, Almeida-Porada G. Exp Hematol. 2011 Dec;39(12):1124-1135.e4.

Muscle tissue engineering

Research revealed that exercise is a key step in engineering muscle cell implants with the potential to repair muscle damage from injury or disease. In mice, these implants more successfully prompt the regeneration and repair of damaged or lost muscle tissue, resulting in significant functional improvement. The technology was

originally developed under the Armed Forces Institute of Regenerative Medicine (AFIRM) program. A longer-term goal is to use the implant - in combination with other tissue-engineered implants and technologies being developed as part of AFIRM -- to treat the severe head and facial injuries sustained by military personnel.

Further development of a tissue engineered muscle repair construct in vitro for enhanced functional recovery following implantation in vivo in a murine model of volumetric muscle loss injury. Corona BT, Machingal MA, Criswell T, Vadhavkar M, Dannahower AC, Bergman C, Zhao W, Christ GJ. Tissue Eng Part A. 2012 Jun;18(11-12):1213-28.

Popular Media Reports

WFIRM's work has been featured in media outlets around the world, including:

BBC	CNN.com
Discovery Magazine	Huffington Post
PBS Newshour	National Journal
Popular Science	Reuters TV
Scientific American	Time Magazine

Selected News Coverage

- Anthony Atala, M.D., professor and director of the Wake Forest Institute for Regenerative Medicine, is profiled in *The Lancet*, one of the world's leading independent general medical journals. Dr. Atala was elected this year to the prestigious Institute of Medicine, considered one of the highest honors in the fields of health and medicine.
  http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)61600-0/fulltext?rss=yes

- The work of Dr. Atala and the Wake Forest Institute for Regenerative Medicine made several "best of 2011" lists:
  - Time Magazine featured WFIRM and Dr. Atala's in work in urethra regeneration in its list of Top 10 Medical Breakthroughs of 2011. http://www.time.com/time/specials/top10/0,33058,sci,00.html
  - A lecture by Dr. Atala at the prestigious TED conference on early experimental work to print human organs has been named "one of 18 great ideas" of 2011 by the Huffington Post.
    http:// www.huffingtonpost.com/anthony-atala/printing-organs_b_1160350.html
  - Geekwire, an independent technology news site, includes the Wake Forest Institute for Regenerative Medicine's bioprinting project as one of the top technology advances of 2011.
    http://www.geekwire.com/2011/important-technology-2011-geeks-weigh/

- George Christ, Ph.D., professor of regenerative medicine, and biomedical engineering graduate student Hannah Baker were interviewed by News 14 about research on the role of exercise in improving tissue engineered muscle implants.
  http://triangle.news14.com/content/local_news/660902/lab-engineered-muscle-implants-show-promise-to-help-repair-muscle-tissue?ap=1&MP4

- The hemophilia research of Professor Christopher Porada Ph.D. and Graca Almeida-Porada M.D. Ph.D. was reported on several science news websites. A single injection of genetically-modified adult stem cells in two sheep converted the severe disorder to a milder form, opening the door to the development of new therapies for human patients.

http://www.sciencedaily.com/releases/2011/11/111103081434.htm
http://www.medicalnewstoday.com/releases/237119.php

- The work of WFIRM researchers Bryon Peterson Ph.D., Seh-Hoon Oh, Ph.D., Thomas Shupe, Ph.D., and colleagues was in the headlines for discovery of a new protein that may play a critical role in how the human body regulates blood sugar levels. Reporting in the medical journal Pancreas, the research team says the protein may represent a new target for treating Type 1 diabetes.
http://www.sciencedaily.com/releases/2012/01/120104115051.htm

- The work of Khali Bitar Ph.D., professor of regenerative medicine, was the subject of several reports on new solutions to digestive diseases. Dr. Bitar's group has engineered a functional anal sphincter in the lab using human muscle cells.
http://www.news-medical.net/news/20111117/New-possibilities-for-relief-from-digestive-diseases.aspx

Future Work

Moving forward, the resources from the State of North Carolina will provide key support to ensure that the infrastructure for projects remains strong so that technologies can be translated to patients. The support of the infrastructure is continually being leveraged to attract additional federal and private funding to create and advance regenerative medicine technologies. For more information, please see our website, www.wfirm.org

Wake Forest Institute for Regenerative Medicine
Statement of Revenues and Expenses
Fiscal Year Ending June 30, 2012

Revenues: Less Deferrals	
Unrestricted Revenues:	
Institutional Support	2,813,549
Gift Income	403,052
Other Income	72,192
Total Unrestricted Revenues	3,288,792
Restricted Revenues:	
State of North Carolina	4,583,146
Federal Government	20,020,258
Foundation	740,899
Industry	890,073
Individual	800,844
Total Restricted Revenues	27,035,219
Total Revenues	**30,324,011**
Expenditures:	
Salaries/Wages	8,677,906
Fringe Benefits	1,958,814
Student and trainee expenses	193,607
Purchased Services	11,320,863
Laboratory Supplies	2,062,937
Service Dept Charges	1,203,638
General Operating	556,704
Facilities & Adminstration	3,831,770
Total Operating Expense	29,806,239
Capital (renovations, equipment, & software)	250,545
Total Expenditures	**30,056,785**