Wake Forest Institute for Regenerative Medicine

Legislative Report

July 1, 2010 to June 30, 2011

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)

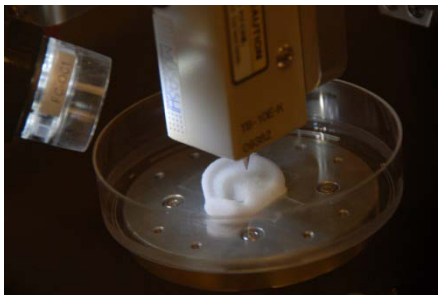
Introduction

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." 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. The global market for regenerative medicine products in 2008 was $1.5 billion, is expected to reach $4.5 billion by 2014, and has the potential to exceed $500 billion in the next 20 years.[2]

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 a new 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 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.

[1] *2020—A New Vision: A Future for Regenerative Medicine"*, U.S. DHHS (2007).
[2] *Worldwide Markets and Emerging Technologies for Tissue Engineering and Regenerative Medicine*, Life Science Intelligence (2009); *Regenerative Medicine Markets*, TriMark Publications (2010); *2020—A New Vision: A Future for Regenerative Medicine"*, U.S. DHHS (2007).

A common misconception about regenerative medicine is that only stem cells that come from human embryos can be used. 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 non-controversial 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 is developing a first-of-its-kind regenerative medicine "accelerator" 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. When complete, the Piedmont Triad Research Park will be 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

HHS in its report on regenerative medicine recommends a government/academic model to fund the growth of regenerative medicine, citing a similar model helped grow the nation's semiconductor industry from $8 billion to $170 billion in a 10-year period. State initiatives to capture shares of the regenerative medicine market are multiplying

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.

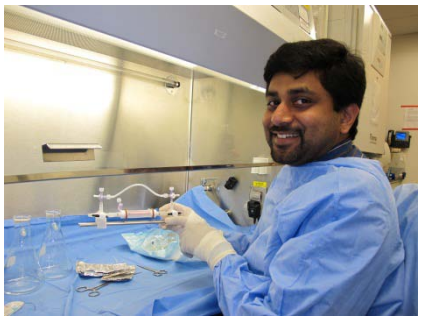
New York State Stem Cell Science (NYSTEM)
NYSTEM is $600 million, 11-year initiative of the State of New York to provide funding stem cell biology research and development. The fund was created through legislation authorizing the Empire State Stem Cell Trust Fund and is administered by the New York State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

across the country. California, for example, has committed $3 billion to the field of regenerative medicine. State funding can help accelerate the translation of scientific discoveries through pre-clinical and clinical trials, manufacturing and commercialization strategies. State support is also vital to help leverage additional funds.

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. 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.

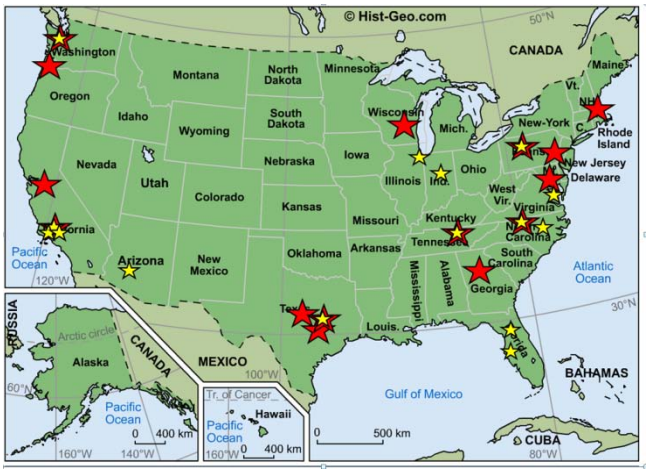
- ***GMP manufacturing facility***. Through WFIRM, regenerative medicine researchers have access to a current good manufacturing practices production facility that allows for the preparation of tissues and cell therapies under U.S. Food and Drug Administration guidelines. This facility helps accelerate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

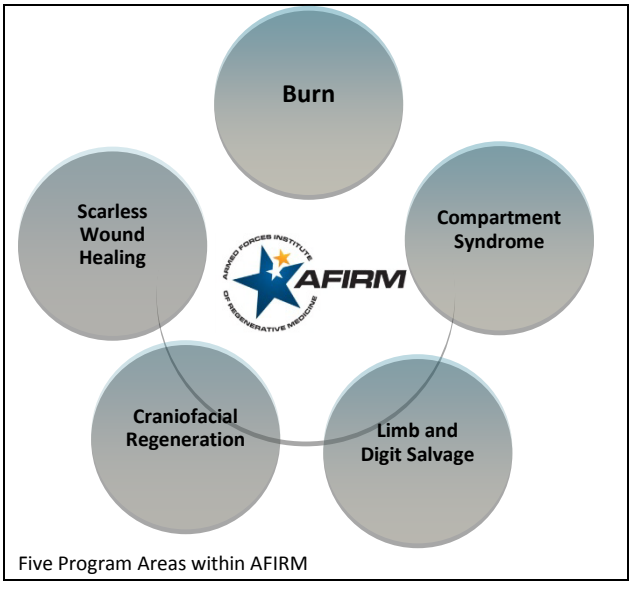
Armed Forces Institute of Regenerative Medicine

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 6,200 U.S. military fatalities and more than 46,000 injuries have been reported.[3] 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.



Five Major Program Areas within AFIRM



Five 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

[3] http://www.defense.gov/news/casualty.pdf (June 2011)

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. Over the next two years of AFIRM funding, at least six clinical trials can either be completed or initiated by the Burn Program.

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%) with good results.
- 100 patient FDA-approved clinical trial is ongoing

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.

Administrative Restructuring

Over the past year, it became apparent that while the mission is straightforward, research and development of innovative technologies is not. In an effort to balance mission expectations with the methodical pace of research, a reorganization of the research efforts within AFIRM was performed. Because the limb and digit program and the compartment syndrome program had many similarities, the two programs became administratively merged into the extremities injuries program. Both programs are thematically focused on injuries to the extremities and thus synergistically benefit from being combined.

Clinical Trials Begin

During the third year of operation, WFPC has continued to advance technologies to clinical trials. The effect of accelerating technology develop has resulted in some significant changes with the AFIRM-WFPC over the past year. Most notable is the shift from a project emphasis to a product emphasis in our research. Also of note is that the number of clinical trials is steadily increasing. The following table shows the number of Department of Defense 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); PI J. Holmes MD
Human Upper Extremity Allotransplantation; PI A. Lee, MD
Autologous Adipose Derived Stem Cell Therapy For Soft Tissue Reconstruction After Facial Trauma; PI P. Rubin, MD
A Novel Device to Mitigate Cutaneous Scar Formation Following Surgery; PI G. Lee, MD
Clinical Evaluation of the Neodyne Dressing for Diminished Scarring; PI 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.

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 have 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 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 described in the AFIRM proposal.

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. Four clinically relevant projects have begun utilizing the facility.

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 100 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 and technology transfer staff, all of which contribute to higher quality protection and better prospects for faster, more effective commercialization.

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

North Carolina State University Center for Comparative Medicine and Translational Research and WFIRM are collaborating to find safe and effective ways to use cells to regenerate damaged organs in people and pets. The new partnership will make regenerative medical treatments more quickly available to both human and animal patients.

North Carolina State University Edward P. Fitts Department of Industrial and Systems Engineering and WFIRM have teamed up bringing together advances in regenerative medicine and advances in manufacturing processes. The goal of this collaboration is to reduce the cost of regenerative medicine and improve its effectiveness by translating the biological and medical requirements into engineering terms that are needed for developing a full scale manufacturing process.

Virginia-Maryland Regional College of Veterinary Medicine joined with WFIRM to form a Center for Veterinary Regenerative Medicine. Researchers from both organizations will work collaboratively to develop new regenerative medicine treatments for animals and human patients.

Piedmont Triad Industry Collaborations

Ocular Systems Inc., a Piedmont Triad Research Park company, and WFIRM are collaborating 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. The collaboration was recently awarded a Collaborative Funding Grant from the North Carolina Biotechnology Center.

Creative Bioreactor Designs Inc., a Piedmont Triad Research Park company, and WFIRM are collaborating to improve laboratory equipment needed to efficiently grow new tissues. The collaboration was recently awarded a Collaborative Funding Grant from the North Carolina Biotechnology Center.

Applied Cather Technologies, a startup company located in the Piedmont Triad Research Park, is developing specially treated catheters and surgical products that prevent strictures and adhesions for better patient outcomes. The devices use collagen inhibition techniques developed at WFIRM.

KeraNetics LLC, located in the Piedmont Triad Research Park, was started in 2008 to commercialize keratin-based products for use in areas of regenerative medicine and trauma care based on technology from WFIRM. KeraNetics and WFIRM have collaborated on numerous research programs including SBIR awards from both NIH and the Department of Defense.

Tengion Inc. is a clinical stage company focused on developing, manufacturing and commercializing human neo-organs and neo-tissues for regenerative medicine based on advances pioneered by the WFIRM team. Tengion, whose research facility is located in Winston-Salem, and WFIRM maintain active research collaborations in regenerative medicine.

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, Shanghai Jiao Tong University School of Medicine, Shanghai, China
	Beihang University, Beijing, China
Egypt	Kasr Al Ainy Teaching Hospital, Cairo University, El Manial
Germany	European Center for Medical Technologies and Applications, Cologne
	Institute for Tissue Engineering and Regenerative Medicine ITERM, Lukas Hospital, Neuss
Ireland	National University of Ireland at Galway and The Regenerative Medicine Institute of Ireland at Galway
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, Korea
Russia	Kulakov Research Center of Obstetrics and Gynecology and Neurovita Clinic of Restorative Interventional Neurology and Therapy, Moscow, Russia
	Moscow University, Moscow, Russia
Switzerland	University Hospital Basel, ICFS, Basel
Taiwan	Taipei Medical University, Taipei, Taiwan

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 efforts 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
- Featured in the NC Association for Biomedical Research film to educate students about biotechnology

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 35 pre-doctoral (PhD) students and 56 postdoctoral fellows.

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 onto 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 over 70 research proposals to 15 different agencies, foundations, and companies during fiscal year 2011. New and continuing awards provided over $30 million in grant funding.

Notable Recruits

Support from the State of North Carolina has also been leveraged to attract top scientists in the field to advance the WFIRM mission. These top scientists along with their teams include:

Khalil N. Bitar, PhD Professor. Recruited from the University of Michigan where he spent 22 years directing the GI molecular motors laboratory at the medical school, Dr. Bitar has received several awards, including the Research Scientist Achievement Award and the League of Research Excellence from the University of Michigan, and was inducted as a Fellow of the American Gastroenterological Association. Bitar and his team made national headlines shortly after arriving at WFIRM for building the first functional anal sphincters

in the laboratory, suggesting a potential future treatment for both fecal and urinary incontinence. Made from muscle and nerve cells, the sphincters developed a blood supply and maintained function when implanted in mice. The results were reported in the medical journal *Gastroenterology*.

Bryon E. Petersen, PhD Professor. Dr. Petersen, recognized worldwide as a foremost authority in hepatic stem cells and their role in liver pathobiology, was recruited with his team of researchers from the University of Florida. He is currently conducting research in stem cell biology and how it relates to liver growth, development and regeneration under normal and carcinogeneic conditions. Petersen's group was in the headlines recently 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.

Graca Almeida-Porada, MD, PhD, Professor and ***Christopher Porada, PhD***, Associate Professor were recruited as a team from University of Nevada, Reno. Their work recently led to the first report of combined gene therapy and stem cell transplantation to successfully reverse the severe, crippling bleeding disorder hemophilia A in large animals.

Dr. Almeida-Porada was as professor and the director of graduate studies in animal biotechnology at the University of Nevada, Reno. Dr. Almeida-Porada's research focuses on the biological properties and regenerative capabilities of adult stem cells, with the goal of understanding disease processes and developing novel approaches to cell therapy and tissue repair. Dr. Porada's research is focused on developing novel gene delivery systems that precisely target individual cell types within the body and, is exploring the use of adult stem cells as vehicles for delivering therapeutic genes to specific sites of disease or injury.

Frank C. Marini, PhD, Professor
Dr. Marini, a national expert in cancer biology, was recruited from the University of Texas MD Anderson Cancer Center. Dr. Marini's research Interests lie in stem cells, mesenchymal stem cells, gene therapy, tumor microenvironment, and genetic vectors.

K.C. Balaji, MD, Professor
Dr. Balaji, a urological oncologist, a prostate cancer basic science researcher and a pioneer in field of robotic cancer surgery, was jointly recruited by WFIRM, the Department of Urology and the Comprehensive Cancer Center at Wake Forest Baptist Medical Center. Dr. Balaji's research efforts focus on cell signaling and role of stem cells in prostate cancer development and progression. His laboratory identified a novel tumor and metastasis suppressor role in prostate cancer.

News and Publications

Scientific Publications

WFIRM authors published 119 peer-reviewed papers in 72 different scientific journals during fiscal year 2011. Notable reports include:

- First demonstration of the use of engineered urethras in patients. A six year follow-up study showing that tissue-engineered urethras function normally without narrowing was published. Cells derived from the patients' own urethral tissue were separated into muscle and epithelial cells, grown up in culture, and then seeded on the interior and exterior, respectively, of a biodegradable mesh tube to act as a scaffold.

  Tissue-engineered autologous urethras for patients who need reconstruction: an observational study. Raya-Rivera A, Esquiliano DR, Yoo JJ, Lopez-Bayghen E, Soker S, Atala A. Lancet. 2011; 377(9772):1175-1182.

- First demonstration of a lab-grown three-dimensional liver using human cells with an intact and functional vascular tree, an early milestone on the way to creating a new source of livers for transplant.

  The use of whole organ decellularization for the generation of a vascularized liver organoid. Baptista PM, Siddiqui MM, Lozier G, Rodriguez SR, Atala A, Soker S. Hepatology 2011; 52 (2): 604-617.

- First demonstration of lab-grown functional bioengineered anal sphincters. The sphincters, tested in mice and made of human muscle and nerve cells, were able to develop blood supply and maintain their fecal function.

  Successful implantation of bioengineered, intrinsically innervated, human internal anal sphincter. Raghavan S, Gilmont RR, Miyasaka EA, Somara S, Srinivasan S, Teitelbaum DH, Bitar KN. Gastroenterology, 2011, 141(1):310-319

Popular Media Reports

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

60 Minutes	TED Conference	CBS Evening News
National Geographic	Smithsonian magazine	Discovery Channel
Nature Medicine	Discover magazine	Popular Science
National Public Radio	New Scientist	BBC
Science Channel	Washington Post	CNN International

Selected News Coverage

- Anthony Atala, MD, was an invited lecturer at the prestigious TED conference in Long Beach, California. He spoke on early experimental work to print human organs.
  http://www.ted.com/talks/anthony_atala_printing_a_human_kidney.html

- The March 2011 issue of *National Geographic* magazine featured the work of WFIRM in its "The Big Idea" section. National Geographic or http://ngm.nationalgeographic.com/2011/03/big-idea/organ-regeneration-text

- Anthony Atala, MD, was interviewed in this Scientific American.com blog, "Too Hard for Science?" about the challenges of developing off-the-shelf organs.
  http://www.scientificamerican.com/blog/post.cfm?id=too-hard-for-science-off-the-shelf-2011-07-01

- The work of Kahil Bitar, PhD, professor of regenerative medicine, whose team recently joined WFIRM, was reported in a *USA Today* science blog and other media outlets. The group has engineered a functional anal sphincter in the lab using human muscle cells.
  USA Today Biologists grow replacement sphincters in mice (http://ngm.nationalgeographic.com/2011/03/big-idea/organ-regeneration-text)

U.S. News & World Report Human Cells Used to Make Replacement Anal Sphincters in Mice (http://health.usnews.com/health-news/diet-fitness/bones-joints-and-muscles/articles/2011/08/10/human-cells-used-to-make-replacement-anal-sphincters-in-mice)

- The work of Shay Soker, PhD, and colleagues, to engineer miniature human livers in the lab was reported by a variety of media outlets including *Ivanhoe Broadcast*, which provides news to more than 100 partner television stations.
  http://www.ivanhoe.com/channels/p_printStory.cfm?storyid=26817
  http://www.ivanhoe.com/channels/p_channelstory.cfm?storyid=26867

- The work of WFIRM was included in an *AARP Magazine a*rticle, "Amazing Medical Discoveries that will Change Your Life." AARP is one of the world's largest-circulation magazines, with more than 47 million readers. AARP Article
  (http://www.wakehealth.edu/uploadedFiles/User_Content/Research/Institutes_and_Centers/WF_Institute_for_Regenerative_Medicine/Assets/Assets_Images/AARP%20-%2009-11.pdf)

- Other media reports featuring WFIRM work
  Video news report by *Reuters* http://www.reuters.com/video/2011/08/31/need-a-new-liver-get-one-printed?videoId=218887411&videoChannel=2602
  New York City's CBS affiliate http://newyork.cbslocal.com/2011/09/28/seen-on-cbs-2-growing-body-parts/
  CBS Evening News: CBS Liver Coverage
  (http://www.wfubmc.edu/uploadedFiles/User_Content/AboutUs/News_Media_Resources/Assets_2010/video/WFIRM/WFIRM-Liver_CBSEveningNews-102910.wmv)

Future Work

Moving forward, the resources from the State of North Carolina will provide key support for the GMP 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.

Revenues and Expenses Year End June 30, 2011

Wake Forest Institute of Regenerative Medicine
Statement of Revenues and Expenses
Fiscal year Ending June 30, 2011

	FY 2011	
Unrestricted Revenues:		
Institutional Support	$	3,030,985
Gift Income		140,504
Other income		290,479
Total Unrestricted Revenues		3,461,968
Restricted Revenues:		
State of North Carolina		8,234,226
Federal Government		19,043,221
Foundation		451,547
Industry		2,228,396
Individual		515,633
Total Restricted Revenues		30,473,023
Total Revenues	**$**	**33,934,991**
Expenditures:		
Salaries/Wages	$	7,942,747
Fringe Benefits		1,965,876
Student and trainee expenses		160,728
Purchased Services		9,406,006
Laboratory Supplies		2,125,091
Service Dept Charges		1,233,412
General Operating		800,130
Facilities & Administration		4,809,543
Total Operating Expense	$	28,443,533
Capital (renovations, equipment & software)		5,275,809
Total Expenditures	**$**	**33,719,342**