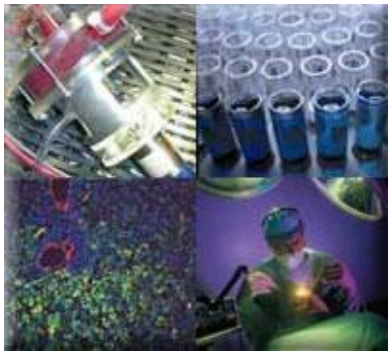
McGowan Institute for Regenerative Medicine
A program of the University of Pittsburgh and UPMC

Snapshot of Funded Research: Highlights for 2014



McGowan Institute faculty lead many studies that focus on the development of technologies to address tissue and organ insufficiency. Annually, funding for the research programs of the McGowan Institute comes from various sources. In 2014, McGowan Institute faculty received financial support from the Department of Defense, the National Institutes of Health, the National Science Foundation, and private industry. The following are a few select examples that highlight the depth and diversity of programs awarded to McGowan Institute affiliated faculty:

- ***Novel Strategies for Optic Neuroregeneration and Retinal Projection Reintegration after Ocular Trauma***. (PI: Vijay Gorantla; Co-I: Joel Schuman, Kia Washington) The proposed work will investigate, via a disruptive cross-disciplinary approach, the opportunities and challenges to vision restoration using translational strategies for optic nerve neuroregeneration, retinal ganglion cell neuroprotection and optic nerve reintegration into the brain, evaluated in a robust experimental model of a whole eyeball transplant. (Department of Defense Vision Research Program)

- ***3D Video Augmented High-Resolution Ultrasound Imaging for Monitoring Nerve Regeneration and Chronic Rejection after Composite Tissue Allotransplantation***. (PI: Vijay Gorantla, John Galeotti, George Stetten; Co-I: Michael Davis) A newly developed technology called ProbeSight determines and records the location of an ultrasound probe in terms of the particular anatomical structures being scanned. ProbeSight compares what its camera sees with its own internal "memory" of a patient's overall appearance. The ProbeSight system provides a valuable record of location information along with the ultrasound data, so that changes to nerves and arteries at a given place in a patient can be monitored from 1 day, week, or month to the next. (Department of Defense Peer Reviewed Medical Research Program)

- ***In Situ Influence of Cell Fate for Functional Soft Tissue Reconstruction.*** (PI: Stephen Badylak) ***Novel Strategies for Repair and Restoration of Calvarial Bone Defects in Wounds Compromised by Infection and Scarring.*** (PI: Joseph Losee; Co-I: Phil Campbell) ***Biodegradable Conduits for Large Extremity Nerve Injuries.*** (PI: Kacey Marra) The goals of the AFIRM-II program are to fund basic through translational regenerative medicine research, and to bring promising technologies and restorative practices into human clinical trials. This effort is coordinated through the U.S. Army Medical Research and Materiel Command and includes three projects within the

Pittsburgh-based program. (Department of Defense Armed Forces Institute of Regenerative Medicine Warrior Restoration Consortium, AFIRM-II)

- ***Myofibroblast Inhibition to Prevent Post-traumatic Joint Contracture***. (PI: Sandeep Kathju; Co-I: Latha Satish) The central idea for this proposal is to administer agents, specifically small interfering RNAs (siRNAs) or nonviral vectors expressing siRNAs that will inhibit myofibroblast function, and thereby prevent the development of post-traumatic joint contracture. (Department of Defense Congressionally Directed Medical Research Program)

- ***Mechanisms of Polyploidy and Aneuploidy in the Liver***. (PI: Andrew Duncan) The goals of this project are to identify mechanisms regulating hepatic aneuploidy/ polyploidy and to unravel how aneuploidy affects liver function. These studies will define the extent to which aneuploidy affects liver repair/regeneration as well as the molecular mechanisms that control this process. Understanding how aneuploid hepatocytes arise and function will provide new and crucial insights into liver homeostasis, diseases, and treatments. (National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases)

- ***Mini-Livers Derived from Human IPS Cells for Modeling Steatosis and Therapy***. (PI: Alejandro Soto-Gutierrez) The objectives of this study are to develop an organ culture system for liver engineering with induced pluripotent stem (iPS) cell-derived liver cells, and to investigate its employment to understand pathogenesis, natural history, and development of early detection tools and treatments for fatty liver diseases. The central hypothesis to be tested is that the decellularized natural liver scaffold can be extensively repopulated, will provide a stable organ-like environment for the metabolic maturation of iPS derived liver cells, and may be used as an approach to induce formation of functional mini-livers. (National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases)

- ***Non-Invasive Imaging of the In Situ Restoration of Brain Tissue***. (PI: Michel Modo; Co-I: Stephen Badylak, Tao Jin) This project aims to develop chemical exchange saturation transfer (CEST), a non-invasive MRI technique, as a core platform to visualize multiple cell types, as well as biomaterials, while maintaining the ability to characterize newly forming tissue with other MRI techniques, such as MRS, as well as diffusion and perfusion MRI. The studies aim to address challenges and provide a framework within which we can eventually explore the therapeutic potential of this approach. If a newly functional tissue can be generated to replace that which is lost due to the stroke, this approach could indeed dramatically change the long-term

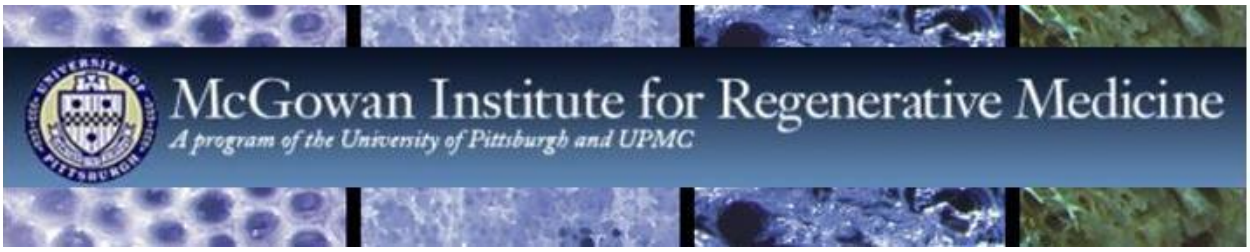
outcome after stroke. (National Institutes of Health, National Institute of Neurological Disorders and Stroke)

- ***Model-Based Decisions in Sepsis (MODS)***. (PI: Gilles Clermont; Co-I: Derek Angus, Robert Parker, Francis Pike, David Swigon) The overarching goal of this program is to validate computational models of human sepsis using data from the ProCESS study through advanced mathematical and computational methods. Leveraging data and preliminary analyses from the ProCESS trial on the one hand and an extensive existing transdisciplinary effort at expanding existing computational models of the acute inflammatory response on the other will provide an unprecedented opportunity to gain mechanistic understanding of the processes leading to organ failure and death, systemic recovery, and unexpected failure. (National Institutes of Health, National Institute of General Medical Sciences)

- ***NSF Engineering Research Center for Revolutionizing Metallic Biomaterials***. (PI: William Wagner) This effort will pursue revolutionary advances in metallic biomaterials and the underlying sciences and technologies, leading to engineered systems that will interface with the human body to prolong and improve quality of life. This research effort is coupled with the development of a vibrant, diverse workforce well-prepared for the global challenges and opportunities of the 21st century. (National Science Foundation Engineering Research Center)

- ***Small Blood Pumps for Small Patients***. (PI: Trevor Snyder; PI/Sub: Peter Wearden; Co-I/Sub: William Wagner, Marina Kameneva, Timothy Maul) The purpose of this project is to re-purpose the Revolution RVAD as a pediatric left heart assist device, the Revolution MINI, for children ages 1 and up. Then researchers will revise the design to create the Revolution NEO for neonates and infants, aged 0-1, who represent the largest clinical need for pediatric heart support. Throughout the program, considerable efforts will be focused on anatomic fit modeling and studies to devise approaches so that these devices can be implanted in the smaller bodies of children to avoid pumps protruding from the body, as occurs with the paracorporeal Excor. (VADovations, Inc., Oklahoma City, OK)

The McGowan Institute is one of the most ambitious regenerative medicine programs in the nation, coupling together biology, clinical science, and engineering. Success in its mission will impact patients' lives, bring economic benefit, serve to train the next generation of researchers, and advance the expertise of its faculty in the basic sciences, engineering, and clinical sciences. Projects awarded funding in 2014 may support the future commercialization of technologies in regenerative medicine and thereby accelerate the translation of research discoveries to clinical implementation and patient benefit.



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McGowan Institute for Regenerative Medicine Grant of the Month

Back to Home Page