

## FACILITIES AND OTHER RESOURCES

The environment at the University of Pittsburgh and specifically the Deiters, Wang, and Weber laboratories provide an ideal environment for the proposed research on developing a new treatment approach for myocardial ischemia/reperfusion injury using hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>)-responsive Nox2 inhibitors.

All equipment required for the synthesis and characterization of the H<sub>2</sub>O<sub>2</sub>-responsive Nox2 inhibitors is available in the Deiters lab and the Department of Chemistry at Pitt: several shared and staff-supervised facilities exist in the department and provide services at no cost, including a Mass Spectrometry Facility, an NMR Facility, and a Biological Core Instrumentation Facility. The University's Center for Biological Imaging and Cytometry Facility augment these services.

The department provides administrative support for facilities, IT, purchasing, payroll, grant administration, and clerical tasks. The chemistry department is home to three independent shops (electronics, machine, and glass) and design, fabricate, and repair equipment and instrumentation. Eight full-time technical personnel (an electrical engineer, three electronics technicians, three machinists, and a glassblower) staff the shops. The department's stockroom supplies commonly-used chemicals, gasses, glassware, office supplies, and general lab consumables.

**Deiters Laboratory.** Dr. Deiters has a combined total of 3,500 sq. ft. of lab space in the Chevron Science Center in the Department of Chemistry at Pitt, including two laboratories specifically designated for biochemical work with radioisotopes and a tissue culture laboratory (BSL2). The BSL2 lab is equipped with two Type A2 (Class II) biological safety cabinets. The synthetic laboratories are equipped with eight 2-person fume hoods, including individual nitrogen/vacuum lines, and the instrumentation necessary for all chemistry (solution, solid-phase, and microwave) experiments. Josh has a 2-person fume hood to himself, in addition to a 6-foot bench on both the chemistry and biology sides of the laboratory.

**Wang Laboratory.** Dr. Wang has over 2,000 sq. ft. of lab space in the Department of Bioengineering at Pitt, with dedicated labs for chemistry, materials characterization, animal procedures, microscopy, and cell culture. The cell culture lab is equipped with two 5' and two 6' BSL2 laminar flow hoods.

**Weber Laboratory.** The Weber lab consists of 3,150 sq. ft. of modern lab space, including a darkroom in which the group has constructed a microfluidic system dedicated to the quantification of thiols to study redox biology. The superfusion system for the near-instantaneous manipulation of oxygen levels in cultured tissue is set up in Langley Hall, which is 2 blocks away from Chevron. The apparatus is set up with the tissue chamber on the stage of a Leica TCS SP5 II Broadband Confocal microscope.

**Clinical.** Not applicable.

**Animal.** Dr. Wang and Dr. Weber have access to shared animal facilities through the Division of Laboratory Animal Resources (DLAR) at the University of Pittsburgh. Rats will be maintained at this facility, which has been fully accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC) since 1971 (Unit Number 000496). The University of Pittsburgh is registered with the USDA (23-R-0016) and OLAW, NIH (#A3187-01). All animal facilities are under the direction of full-time veterinarians. The University of Pittsburgh complies with all provisions of the Animal Welfare Act in addition to all other applicable federal, state, and local laws. Rats are housed in pairs and monitored daily by a member of the veterinary staff and/or animal care staff and by the PI. Veterinary services are available twenty-four hours a day, seven days a week for animal care issues. The facility has procedure rooms available for all treatments in this proposal.

**Computer.** Dr. Deiters' laboratories and offices are equipped with 6 networked computers, 3 printers, and 2 scanners. The computers include software for graphics, word, and data processing, chemical drawings, gel imaging, DNA analysis, and statistical analysis. Through Pitt, LAN access is provided to the electronic versions of all major scientific journals and important databases (including Reaxys and SciFinder). All computer equipment is networked and supported by a trained systems administrator. All data is backed up locally on a RAID array and remotely via LabArchives. Drs. Wang and Weber also have several computers with all necessary software to support the proposed research, in addition to scanners, printers, and digital cameras.

**Office.** Dr. Deiters' office (~150 sq. ft.) is about 25 ft. from the laboratories and is equipped with a networked computer and a printer. Josh has his own desk among the 18 desks in the lab that are available for technicians, post-docs, graduate, and undergraduate students. Dr. Deiters shares an administrative assistant with four other faculty members. Dr. Weber's office is located 7 floors below in the same building, and Dr. Wang's is 2 blocks away in Benedum Hall.

**Other.** The Deiters lab routinely uses instrumentation in shared facilities within the department (Biological Instrumentation Cluster, Mass Spectrometry Facility, NMR Facility) and the Pitt campus (Biomedical Mass Spectrometry Center at the University of Pittsburgh: <http://www.bioms.pitt.edu>; Genomics and Proteomics Core Laboratories (GPCL) at the University of Pittsburgh: [www.genetics.pitt.edu](http://www.genetics.pitt.edu); the University of Pittsburgh Cancer Institute Cytometry Facility: <https://upci.upmc.edu/cytometry/>). See Major Equipment section for more details.

Proposed imaging experiments may be completed through the Center for Biologic Imaging (CBI: <http://www.cbi.pitt.edu>), which is housed in the University of Pittsburgh Medical School South BST with approximately 5,500 sq. ft. of space. The CBI is a leading center for applying cellular imaging methods with a particular specialization in live cell fluorescence applications. Dr. Wang maintains an active collaboration with Donna Stolz, PhD, the associate director of the CBI. This dedicated, state-of-the-science imaging center has fully-equipped microscopy suites, computer labs, and wet and dry bench space for light and electron microscopy preparations. Apart from the office space for the director and faculty, desk areas are provided for the 12 full-time research specialists, post-doctoral fellows, and students who work in the facility. Importantly, there is sufficient undedicated bench space within the facility for users to conduct several concurrent projects. Most of the light microscopy suites can be reserved online and are available to trained users twenty-four hours a day, seven days a week.

The shared animal facility has common procedure rooms with three surgical areas equipped with thermoregulated surgical tables, isoflurane vaporizers, dissection microscopes, ventilators, all necessary instrumentation.

**Contribution of the Scientific Environment to Success.** The University of Pittsburgh consistently ranks among the top 10 recipients of NIH funding and has recently risen to the fifth-highest recipient. The Department of Chemistry is one of the nation's largest and most well-funded, and has awarded of 1,000 PhDs, including one to Nobel laureate Paul Lauterbur. The department is located in the Chevron Science Center (236,768 sq. ft.) and Eberly Hall (56,051 sq. ft.).

The research carried out in the Vascular Medicine Institute (VMI) will take place in the Thomas E. Starzl Biomedical Science Tower adjacent to UPMC Presbyterian, the flagship hospital of our academic medical center where Dr. Crock (Josh's cardiology mentor) practices. The VMI is amidst 4.2 million sq. ft. of research, academic, and administrative space in several connected buildings. The VMI works to determine the molecular mechanisms underlying cardiovascular disease and develops novel therapeutic interventions for diseases such as pulmonary hypertension, sickle cell disease, atherosclerosis, hypertension, and reperfusion injury. In addition to six core laboratories (nitric oxide metabolomics, reactive oxygen species measurement, animal phenotyping, human translational vascular biology, genomics, and confocal microscopy), the VMI offers numerous seminars, grand rounds, and research conferences. The Department of Chemistry and the VMI provide an exceptional research and training environment for the proposed studies.