Department of Plastic and Oral Surgery Research Laboratory

The Research Laboratory was established in 2007 and is directed by Arin Greene, MD. The Laboratory is located on the 10th floor of the Enders Research Building at Boston Children's Hospital. Our research has been funded by: (1) *Boston Children's Hospital* (Faculty Career Development, Translational Neuroscience Program, Translational Research Program, Translational Investigator Service, Technology Development Fund), (2) *Foundations/Societies* (Ambler Foundation, Educational Records Bureau Foundation, American Cleft Palate Association, American Society of Plastic Surgeons/Plastic Surgery Foundation, American Association of Plastic Surgeons, American Society of Maxillofacial Surgeons), (3) *Donors* (Taylor/McDonald Family, Gustafson Family, Rossi Family), and the *National Institutes of Health* [NICHD (R21, R21, K23, F32, T32, R01), NHLBI (R01, R01), NIAMS (R01 Co-I)].

Approximately 36 students, technicians, fellows, and faculty have trained in the Laboratory, including 14 fellows who have spent at least one year full-time (10 postdoctoral, 4 predoctoral). Three individuals completed formal research training programs at Harvard Medical School (Master's in Medical Sciences Degree or Executive Certificate), 2 received training grants (F32, K23), and 3 earned NIH loan repayment awards. Trainees have matriculated into extremely competitive medical schools, residencies, and graduate programs and include individuals who have their own laboratories and independent government funding.

The Laboratory has been focused on developing drugs to treat vascular malformations and on a cranioplasty method we termed "particulate bone graft". Between 2007-2013 the laboratory showed that particulate graft is different than bone dust, proved it will heal inlay cranial defects by osteogenesis, and helped popularize its use clinically. Since 2013 the laboratory has only been focused on vascular malformations which are congenital lesions that enlarge over time. These disorders cause disfigurement, pain, bleeding, ulceration, damage to organs, and occasionally death. Treatment consists of laser, sclerotherapy, embolization, and/or excision. Unfortunately, lesions have a high recurrence rate after these interventions and cure is rare. Historically, drugs have not been available to treat vascular malformations. The Laboratory has discovered the mutation responsible for 9 types of vascular anomalies and collaborated on the identification of 2 others. Currently, the Laboratory is focused on 2 types of vascular malformations: arteriovenous malformation (AVM) and capillary malformation (CM). We are determining how their causative mutations cause these lesions to form and enlarge. We are creating animal models of AVM and CM in order to develop drugs that will prevent their growth. Our work on AVM

already has been translated to patients. After we discovered the cause of extracranial AVM (*MAP2K1* mutation) our Vascular Anomalies Center and others began treating patients off-label with the FDA-approved *MAP2K1* inhibitor trametinib. Our experience and others has shown that the drug is efficacious for AVM and it is now routinely used to treat patients with severe AVMs. We currently are developing further medications to treat AVM and are attempting to create drugs to treat CM for the first time.

The Laboratory currently is funded by a NICHD R01, NICHD F32, NICHD T32, NHLBI R01, and the Taylor/McDonald, Gustafson, and Rossi families. The lead scientist in the Laboratory is Patrick Smits, PhD (Assistant Professor of Surgery, Harvard Medical School) who is a recognized expert in molecular biology/genetics and the creation of genetic animal models of disease. The laboratory also consists of a research technician and 2 post-doctoral research fellows who are spending 3 years in the laboratory during their general surgery residencies.

Research Laboratory Contact

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