

# Hemangiomas & Vascular Malformations Research Update 2013

## National Leadership

The CBDI's Hemangioma and Vascular Malformation Center is a leader within the International Society for the Study of Vascular Anomalies and a consistent presenter at ISSVA conferences. Adrienne Hammill's recent oral presentation, *Clinical Update: Six patients treated with sirolimus for complicated vascular anomalies* received the award for the best clinical paper. Denise Adams, the HVMC medical director was elected to the scientific committee of ISSVA.

Dr. Adams also leads the newly organized Vascular Anomalies Special Interest Group at the American Society of Pediatric Hematology Oncology, whose mission will be to educate physicians and provide an infrastructure for the start of a collaborative group to study vascular anomalies.

## Research Highlights

The Hemangioma and Vascular Malformations Center (HVMC) provides excellent multidisciplinary care for infants, children and young adults. The center's approach to research continues to do the same combining clinical research and new drug investigation with breakthroughs in the basic science of vascular biology. Scientific study of hemangiomas, other rare vascular tumors and vascular malformations is an important and growing area of research. Breakthroughs in the laboratory will help the medical community better understand the conditions, develop new treatments and improve the quality of life for patients.

Laboratory research at Cincinnati Children's provides the foundation for innovative treatments. This has become a major goal for the Center. Once a month basic science researchers from all specialties gather with clinicians from different disciplines in the newly formed Vascular Biology Clinical and Basic Science Working Group to discuss the latest basic and clinical findings in vascular biology. In this group potential collaborative projects are discussed as well as ongoing projects.

### Greater understanding of vascular development:

Knowing how genes regulate normal development of the



*A thermal imaging camera being used to assess blood flow*

vascular system will help us to understand genetic causes and possible treatments for human vascular disorders. Researcher Saulius Sumanas uses zebrafish embryos as a model system to study how vascular systems develop. He is among few clinician scientists in the world studying this key process.

Similar genes control both human and zebrafish vascular development. Dr. Sumanas is investigating detailed mechanisms of blood vessel formation and identifying new genes participating in these processes. Ultimately, he hopes to find new genes that can be targeted for treatment of vascular disorders.

Jennifer Williams is a senior hematology/oncology fellow at CCHMC whose primary research is lymphatic development. Dr. Williams uses the zebrafish animal model to study proteins required for normal lymphatic development. The zebrafish animal model, whose vascular development is similar to mice and humans, allows for in vivo visualization of lymphatic development; whereas in mice and humans, visualization is difficult. Her results will provide potential gene and protein targets for drug therapies for patients with complex lymphatic malformations.

Dr. Williams has presented her work at the International Society for the Study of Vascular Anomalies, North American Vascular Biology Organization, and American Society of Hematology.

### **Skin imaging to measure treatment response for hemangiomas:**

Physicians evaluate hemangiomas by visual examination of size, color, growth stage, depth and by palpation of temperature and tactile characteristics. However, it has been difficult to objectively measure the response of hemangiomas and assess treatment effectiveness. Cincinnati Children's researcher Marty Visscher, PhD uses four skin imaging techniques to quantify coloration (red, blue, lightness), size, 3D shape and volume, temperature and biological elasticity. From the thermal, color and 3D "maps", she is extracting physiological information, determining lesion stage and quantifying response to therapies over time. Ultimately, these methods will facilitate the development of new treatments.

### **Fluid Analysis of Vascular Malformations:**

Many malformations form cysts or large spaces filled with fluid. There is little understanding of the biology and pathophysiology behind the development, persistence and proliferation of these cystic structures. Dr. Belinda Dickie a pediatric surgeon on the HVMC team with researchers at the University of Cincinnati will test this fluid for cytokines or markers that may give us more information about pathways involved and lead to future therapies.

### **Learning more about Lymphatic Anomalies:**

Dr. Dickie and her lab are also investigating the pathophysiologic Characteristics of lymphatic malformations. These malformations can cause significant destruction and involve the soft tissue, bone, lungs, liver, spleen and GI tract. Her team will be searching for a causative genetic abnormality for these malformations so again pathways for the disease processes can be identified leading to improved treatment regimens.

### **A team approach to rare vascular tumors:**

Dr. Adams and Hammill from oncology, Dr. Jessica Foster a pediatric resident, Dr. Anita Gupta from pathology and Doctors Patel and Merrow from the CCHMC Division of Radiology have been working together to study rare vascular tumors such as Kaposiform hemangioendotheliomas. The group has presented several posters on the clinical, pathological and radiologic aspects of these tumors. Dr. Foster has recently done a comprehensive literature search looking for epidemiological features of these tumors to develop a risk stratification. Doctors Hammill and Foster will improve a registry protocol but moving it to a web based system so that the clinical aspects of these tumors are studied prospectively. Dr. Adams has submitted a comparison study to determine the best treatment for patients with



*Dr. Denise Adams with patient*

KHE tumors.

### **Advancing Laser therapy for Capillary Malformations:**

Dr. Ravi Elluru from the CCHMC Division of Otolaryngology and Marty Visscher, PhD are working on ways to improve the standard of care for patients receiving laser therapy. They will be using Dr. Visscher's imaging techniques to set up standards of practice for laser treatment and improvement of patient outcomes.

### **First FDA funded Study for Lymphatic malformations and other complicated vascular anomalies:**

The Phase II study, Sirolimus for the treatment of complicated anomalies is near completion of study enrollment. This study lead by Dr. Adams with the help of team members Mary Sue Wentzel, RN, Lisa Campbell and Paula Mobberley-Schuman will provide some insight into the safety and efficacy of sirolimus in the treatment of these complicated disorders. The hope is to use this platform for other investigational drug studies.

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