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RESEARCH CORES NEWS

UNIVERSITY OF VIRGINIA SCHOOL OF MEDICINE

From Director of School of Medicine Research Infrastructure, Jay W. Fox

Fellow UVA School of Medicine Researchers: Happy New Year! I hope you enjoyed a restful holiday and are looking forward to a productive new year of outstanding science. As we start this year a few things come to mind. One is of the interdependent relationship between the cores and the research faculty. We all need to work together to ensure the great science for which the UVA SoM is known continues to flow from our laboratories. For this to happen the cores need your input and advice in terms of what is new in your fields that could be brought to UVA and supported in a core for everyone's benefit. On the other hand the closer you work with the core staff in terms of planning experiments and analyzing data the more likely you will have a better experience and outcome. All the core staff welcomes your partnership in science.

On the same note I would please ask that you always acknowledge the cores that have contributed to the data presented in manuscripts and seminars. This is proper scientific etiquette as well as becoming critical for us to secure NIH support for our instrumentation. If any of the data produced in a core has utilized an NIH-funded instrument we must have a formal acknowledgement (with the NIH award number) in the manuscript that then must reported to the NIH with future proposals. We recognize this is bothersome but we have no choice but to comply if we hope to continue our success securing NIH funds for instrumentation.

Finally, many of our cores provide educational opportunities for students and staff and we hope to continue to expand that area as well educated students and faculty who use core technologies have a clearer understanding of the capabilities (and limitations) of the technologies and how best to approach an experiment to optimize success and limit costs and waste. If you feel there is additional educational needs for your students and staff please let me know and I will work to help meet those needs for your laboratory. Best Wishes for the New Year. Jay

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Introduction

The featured core for this quarter is the W.M. Keck Biomedical Mass Spectrometry Core (see below).

New billing and instrument reservation system

The research cores are preparing to use the iLab billing system which has new feature compared to the CORES system. The first wave of cores are setting up their accounts in iLab. iLab incorporates technology from CORES in addition to new features which make it more versatile, easier to use.

A change to iLab will start in March 2015.

UPCOMING EVENTS IN RESEARCH CORES

Flow Cytometry training courses

- April 13th-17th, 2015

Anderson Distinguished Lecture
Dr. Eric Betzig
March 25, 2015 (Location TBA)

Dr. Betzig is the 2014 Nobel Prize winner for his ground-breaking work in nanoscopy that has brought the optical microscopy into the nano dimension. He works at the Janelia Farm Research Campus/Howard Hughes Medical Institute.
Contact Dr. Jay Fox if you wish to meet Dr. Betzig during his visit.

ACKNOWLEDGEMENT OF USE OF RESEARCH CORES

If you use data generated by a research core in a paper, please acknowledge the core and we would be delighted if you tell us that you have published data from our cores.

We in the cores are happy to see that what we do results in publications.

The School of Medicine supports the cores financially. Publications that use the cores show that support from the School advances research.

Featured Cores

W.M. Keck Biomedical Mass Spectrometry Core

Gilbert R. Upchurch, Jr., M.D., Professor of Surgery, Division of Vascular and Endovascular Surgery

While being a surgeon is a demanding occupation, Dr. Gilbert (Gib) Upchurch also has a research lab at UVA that examines aortic aneurysms, volume outcome effects on surgery, and gender differences in disease. The research laboratory was established in 1999. It is one of the few labs in the nation that is dedicated solely to the basic scientific research of aortic aneurysm. In September 2010, he moved his lab from the University of Michigan to UVA. The research lab itself is located on the third floor of the MR4 building and consists of a molecular biology unit, a histology unit, a small animal microsurgery unit, a cold storage room and research offices. Gib is affiliated with the Department of Surgery and is part of the Robert M. Berne Cardiovascular Research Center.

Vascular Surgery Research Laboratory, University of Virginia

Abdominal aortic aneurysms (AAAs) are a gender-related disease with no current known medical treatment therapy. Aneurysms are normally diagnosed secondary to another vascular condition and are not able to be identified using plasma biomarkers. The only current therapy for aortic aneurysms is endovascular repair; thereby necessitating the monitoring of an aneurysm until it reaches a critical diameter followed by surgical repair. Therefore, the discovery of novel biomarkers or medical therapies to treat aneurysm formation would represent a major

OUTSTANDING CORE OF THE YEAR

Molecular Imaging Core

Director: Stuart Berr.
Email: berr@virginia.edu

The Molecular Imaging Core images small animals, organs and cells by MRI, biolumineseance, fluorescence, positron emission tomography. The core also operates a cyclotron to produces isotopes for PET and synthesizes tracers for PET.

See news item later in this newsletter.

USE OF NIH FUNDED EQUIPMENT

NIH requires investigators who use instruments funded by NIH SIG and HEI grants to acknowledge the use in publications.

A list of equipment in the research cores funded by these grants is at:

http://www.medicine.virginia.edu/research/cores/orca/nih-funded-equipment-list.html

advancement to the field. Interestingly, aneurysms have shown a bias for development within males with a current ratio of 4:1 male to female susceptibility for aneurysm formation.

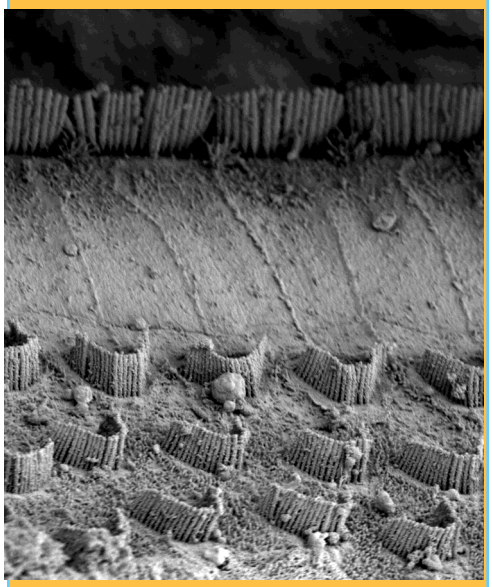
Recently, it has been demonstrated that estrogens and their derivatives play a protective role in the development of vascular diseases, such as atherosclerosis and aortic aneurysm formation. Recent research in the Upchurch Laboratory in the Department of Surgery has demonstrated that phytoestrogens, which are plant-derived chemicals that are strikingly similar to estrogens both in structure and function, may play a role in the inhibition of aortic aneurysm formation. Major sources of phytoestrogens include soybeans, alfalfa, and flaxseed and these compounds are selective estrogen receptor (ER) modulators that have anti-inflammatory, antioxidant, and anti-proliferative properties. Previous animal experiments have demonstrated that phytoestrogens can reduce plasma cholesterol and attenuate atherosclerosis; however, little is known regarding the effects of phytoestrogens on aortic aneurysm formation.

Thermo Scientific TSQ which identified and quantitated phytoestrogens from mouse serum

Drs. Guanyi Lu and Gang Su proposed a study to examine the levels of serum phytoestrogens in male and female mice on different diets in relation to AAA formation. The MS Core used a triple quadruple mass spectrometer (TSQ) to absolutely quantify the amount of the four most common phytoestrogens [Coumestrol, Daidzein, Genistein, Equol] in blinded sets of serum samples. The TSQ mass spectrometer is commonly used to perform an experiment termed Multiple Reaction Monitoring (MRM) that produces a signal only when a parent mass specific to the compound of interest and several fragments specific to the compound are produced in unison. By obtaining a standard curve of signal area versus concentration over several orders of magnitude, the exact concentration of compound can be determined in each sample. The extremely high specificity of the signal means that interferences are eliminated and sensitivity is enhanced. The Mass Spectrometry Core and the Upchurch Laboratory were able to demonstrate that feeding with a phytoestrogen-rich diet increased total phytoestrogen levels in both male and female mice as well as Daidzein, Genistein and Equol levels while estradiol levels remained unchanged in both

ADVANCED MICROSCOPY FACILITY IMAGE OF THE QUARTER

AMF invites users to submit images taken in the facility for consideration as Image of the Quarter. The user submitting the image selected will be awarded a $50 gift card. The facility will post the image on the AMF website and in a gallery in the AMF hallway. Images can be submitted anytime and will be considered for the corresponding quarter depending on the time of submission. See a larger version and description on the AMF website.



Scanning electron micrograph of mouse inner ear hair cells *By Jung-Bum Shin*

The judges were: Dr. Teng-Leong Chew,Director of the Advanced Imaging Center , HHMI, Janelia Campus; Dr. Douglas Murphy, Former Director of the Facilities for Light Microscopy, Histology and Cell Culture: Jan Redick, former director of AMF.

Send your images to Yalin Wang
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male and female mice. When aneurysms were surgically induced within the phytoestrogen-rich mice, the aneurysms were significantly smaller and contained less inflammation than the control, non-treated aneurysms. The Upchurch laboratory went on to demonstrate through protein cytokine arrays that the inflammatory cytokines IL-1, IL-6, MCP-1, RANTES and TIMP-1 were decreased following feeding of male mice with a phytoestrogen rich diet. The full set of results was published in the Journal of Surgical Research (1).

Work Published this Year Using MRM Technology:

Lu G, Su G, Zhao Y, Johnston WF, Rissman EF, Sherman NE, Lau CL, Ailawadi G, Upchurch G. Dietary Phytoestrogens Inhibit Experimental Aneurysm Formation in Male Mice. Journal of Surgical Research. 2014. 188:326-338.

Paige M, Burdick M, Kim S, Cha J, Jeffery E, Sherman NE, Wang K, Shim YM. Role of LTA4 Hydrolase Aminopeptidase in the Pathogenesis of Emphysema. Journal of Immunology. 2014. 192:5059-5068.

Biomolecular Interactions service

The Shared Instrumentation Core will provide a molecular interactions service early in 2015 with a fortéBIO Octet 96 instrument, which was funded by the Equipment Trust Fund.

The fortéBIO instrument generates data similar to that from surface plasmon resonance instruments like Biacore, but uses BioLayer Interferometry technology. Proteins are immobilized on probes which are dipped into a solution of analyte, and then the instrument takes interferometry measurements to determine the amount of analyte binding to the target protein. Only a small portion of analyte binds so that most can be recovered after the experiment.

The most common method for immobilizing proteins is biotinylation which causes the proteins to bind to a streptavidin surface. There are probes designed to couple antibodies. Other binding chemistries, such as amine coupling to carboxymethyl surfaces, are available. The common probes are relatively cheap so that instead of looking for regeneration conditions as done with SPR machine, the probes can be discarded after a measurement, which can greatly simplify some experiments. The use of disposable probes dipped into analyte solutions in 96 well plates avoids problems from contamination of the instrument.

After the instrument is installed and operational, further information will be posted on the Shared Instrumentation website.

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Services in research cores
http://www.medicine.virginia.edu/research/cores/orca/services-in-research-cores

Equipment in research cores
http://www.medicine.virginia.edu/research/cores/list-of-equipment-in-research-cores.html

Training in research cores
http://www.medicine.virginia.edu/research/cores/orca/training-opportunities-in-research-cores.html

OUTSTANDING CORE OF THE YEAR

The outstanding core of 2014 is the Molecular Imaging Core. Director Stuart Berr has been an early user of the Bruker/Siemens ClinScan 7 Tesla MRI and the Siemens Eclipse Cyclotron. In addition, the core has a 4.7 Tesla MRI, bioluminescence and fluorescence scanner, PET scanner and radiochemistry laboratory associated with the cyclotron.

Dr. Berr and staff member Jack Roy train researchers to use the instruments or perform scans for investigators.

Presentation of the Oustanding Core Award, December 2014. Brent French, Faculty Director; Jay Fox, Director SOM Infrastructure; Stuart Berr, Director, Molecular Imaging Core.