Summer 2012

AAB CARDIOVASCULAR RESEARCH INSTITUTE

Department of Medicine

CVRI Beat

UNIVERSITY of ROCHESTER MEDICAL CENTER

MEDICINE of THE HIGHEST ORDER

Upcoming Scientific Events:

High Blood Pressure Research 2012 Scientific Sessions in Washington, DC on Sept. 19-22 2012 (http://my.americanheart.org/professional/Sessions/HBPR/HBPR_UCM_316905_SubHomePage.jsp)

13th Biennial Midwest Platelet Conference in Chapel Hill, NC on Oct. 13-15, 2012 (http://www.med.unc.edu/biochem/mwpc2010)

Scientific Sessions of the American Heart Association in Los Angeles, CA on Nov 03-07 2012 (http://my.americanheart.org/professional/Sessions/ScientificSessions/Scientific-Sessions_UCM_316900_SubHomePage.jsp)

American Society of Hematology (ASH) annual meeting in Atlanta, GA on Dec. 08-11, 2012 (http://www.hematology.org/Meetings/Annual-Meeting/)

International MADS Box Conference (IMBC) in Canandaigua, NY on July 10-13, 2013

Director's Column

Summer's Almost Gone

The musical group The Doors wrote a song in the late 1960s entitled, "Summer's Almost Gone" and queried "Where will we be?" One of our long time faculty members (Dr. Burns Blaxall) would likely answer this question with his new and exciting position at the University of Cincinnati. Several people may answer with life-changing news of a baby boy or baby girl and all of the joy inherent in new life. Whatever one might speak to, we all can agree this was a great summer with an unusual abundance of sun. Interestingly, the same musical group penned a lovely waltz called "Wintertime Love" -- though one living in this part of the country might find little to love over wintertime in Rochester NY! Nevertheless, we do hope to have some ice on our pond for some wintertime skating and early morning hockey (you know who you are!).

The CVRI continues to thrive despite the economic challenges. Several new grants have been awarded (see below) and many investigators have obtained very close scores that may ultimately be funded. We have also seen a big increase in the number of publications, particularly from our junior faculty (see below). Our staff continues to provide incredible support and enthusiasm that make the Aab CVRI an awesome work environment.

After several power blackouts during severe storms a few years back, we bought a system to ensure uninterrupted power until our backup generator kicks in. We did sustain a prolonged power outage related to an electrical storm several weeks ago. Happily, the Flywheel UPS System worked like a charm and no "in-progress" experiments were lost! We very much appreciate and thank the University and Alberti & Associates for safe-guarding our research!

Eric Small and Joe Miano are organizing an international scientific meeting for July 2013 in scenic Canandaigua. The meeting is entitled: The International MADS Box Conference (or IMBC). This historic meeting will focus solely on the all-important SRF and MEF2 transcription factors, which each have critical roles in cardiac and vascular pathobiology. Many world-renowned investigators have agreed to speak, including Eric Olson, Jeff Molkentin, Brian Black, and Mike Parmacek, to name a few. A website will be launched near the end of this year. We have had some success in raising money from various sources. To further enhance our fund-raising efforts, we will hold raffles for Rochester Americans ("Amerks") ice hockey games over the course of the season (we might even offer a raffle to a Buffalo Sabres game, assuming there is an NHL season!). Look for signage around the CVRI and Cardiology and get ready for an exciting break from work! The Amerks raffles are part of a broader effort to forge a close working relationship with the Rochester Americans in order to raise public awareness of the great benefits of research for cardiovascular diseases. We will announce events related to this partnership as they emerge.

We would like to remind everyone of the upcoming Scientific Advisory Board (SAB) meeting to be held on September 14th here in the Aab CVRI. This year we welcome back SAB members Ed Fisher, José Jalife, Jake Lusis, and Alain Tedgui. Dr. Jalife will deliver a seminar entitled "The Cardiac

Myofibroblast and the Mechanism of Persistent Atrial Fibrillation" at 2:30 PM in the main conference room. We are pleased to announce a change in format of the SAB Meeting to better suit the needs of our trainees. On the morning of 14 September, faculty and trainees will have the opportunity to meet one-on-one with each SAB Member to discuss specific scientific issues or to obtain career advice. Each session will last 15 minutes and there may be opportunities for individuals to meet with more than one SAB Member. More information will be available in the next week.

Finally, we wish everyone a successful Fall semester. Please stop by our office so we can answer any questions you may have or to pass along advice concerning your present needs or future plans.

-- Charlie Lowenstein, MD
-- Joseph Miano, PhD

"In Focus"

Understanding mechanisms that regulate the structure of blood vessels (a process called "vascular remodeling") could prevent cardiovascular morbidity and mortality in humans. One of the major projects in my laboratory is focused on investigation of the immune mechanisms and vascular dysfunction in hypertension. In particular, we study the role of Axl, a receptor tyrosine kinase, in vascular diseases. We previously found that Axl-dependent pathways contribute to increases in blood pressure in a mouse model of hypertension. We showed that Axl-mediated survival of smooth muscle cells is responsible for arterial remodeling. However, we recently published a paper that describes novel cellular and molecular mechanisms by which Axl affects arterial remodeling (*American Journal of Pathology* 2012; 180(5):2134-43. Using bone-marrow transplant, we found that Axl controls arterial remodeling not only by inhibition of apoptosis but also via regulation of immune heterogeneity of vascular cells and extracellular matrix remodeling. It is now recognized that immune cells are critical in hypertension. In collaboration with URMC immunologist, Dr. Deborah Fowell, we are examining the role of Axl in subsets of immune cells in the development of hypertension. Our studies will refine the current concept of the immune response in hypertension and will lead to new therapeutic approaches. Studies in my laboratory are funded through an R01 grant from NHLBI.

Vyacheslav Korshunov, PhD

Recent Publications

Long, Z., Miano, J.M. Transforming Growth Factor-β1 (TGF- β1) Utilizes Distinct Pathways for the Transcriptional Activation of MicroRNA 143/145 in Human Coronary Artery Smooth Muscle Cells. JBC. 286(34): 30119-30129. 2011

Morrell, C.N., Maggiwar, S.B. Recently recognized platelet agonists. Curr Opin Hematol. 18:309-314. 2011

Ram, R., Mickelsen, D.M., Theodoropoulos, C., Blaxall, B.C. New approaches in small animal echocardiography: imaging the sounds of silence. Am J Physiol Heart Circ. 301(5):H1765-1780. 2011

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Miano, J.M., Small., E.M. MicroRNA133a: A New Variable in Vascular Smooth Muscle Cell Phenotypic Switching. Circulation. 109:825-827. 2011.

Belmonte, S.L., Margulies, K.B., Blaxall, B.C. S100A1: Another Step Toward Therapeutic Development for Heart Failure. J Am Coll Cardiol. 58(9):974-976. 2011.

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Spindel, O.N., Berk, B.C. Redox redux: protecting the ischemic myocardium. Journal of Clinical Investigation. 122(1):30-32. 2012.

Spindel, O.N., World, C., Berk, B.C. Thioredoxin Interacting Protein: Redox Dependent and Independent Regulatory Mechanisms. Antioxid Redox Signal. 16(6):587-596. 2012.

Nanda, V., Miano, J.M. *Leiomodin 1,* a New Serum Response Factor-dependent Target Gene Expressed Preferentially in Differentiated Smooth Muscle Cells. JBC. 287(4):2459-2467. 2012.

Korshunov, V.A. Axl-dependent signaling: a clinical update. Clinical Science. 122:361-368. 2012.

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Batchu, S.N., Korshunov, V.A. Novel Tyrosine kinase signaling pathways: implications in vascular remodeling. Curr Opin Nephrol Hypertens. 21:122-127. 2012.

Spindel, O.N., Yan, C., Berk, B.C. Thioredoxin-Interacting Protein (TXNIP) Mediates Nuclear-to-Plasma Membrane Communication: Role in Vascular Endothelial Growth Factor 2 (VEGFR2) Signaling. ATVB. 32(5):1264-1270. 2012.

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Heo, K.S., Fujiwara, K., Abe, J. Glucagon-like peptide-1 and Its Cardiovascular Effects. Current Atherosclerosis Reports. *In Press.* 2012.

Kuo, H.H., Morrell, C.N., Baldwin, W.M.3rd. Alloantibody induced platelet responses in transplants: Potent mediators in small packages. Hum Immunol. *In Press*. 2012.

Small, E.M. The actin-MRTF-SRF gene regulatory axis and myofibroblast differentiation. Journal of Cardiovascular Translational Research. *In press.* 2012.

Cai, Y., Knight, W.E., Guo, S., Li, J.D., Knight, P.A., Yan, C. Vinpocetine suppresses pathological vascular remodeling through inhibiting vascular smooth muscle cell proliferation and migration. Journal of Pharmacology and Experimental Therapy. *In press*. 2012

New Grants/Awards

Dr. Jane Sottile received funding for an RO1 entitled: Extracellular matrix remodeling and fibrosis. Burns Blaxall is a co-investigator on the grant.

Angela Aggrey received funding for an NIH F31 pre-doctoral grant

Angela Aggrey gave oral presentation and won an award for outstanding presentation voted on by conference attendees, at Gordon Research Conference on Hemostasis.

Dr. Craig Morrell received the CTSI Laboratory Support Award

Melissa Martin received a predoctoral fellowship from the American Heart Association

Dr. Kyung-Sun Heo is a finalist in The Melvin L. Marcus Young Investigator Award in Cardiovascular Sciences at the AHA Scientific Sessions, for the abstract 'Sumo Protease Senp2 Regulates Endothelial Dysfunction and Subsequent Atherosclerosis Formation' by: Heo KS, Chang E, Le NT, Cushman H, Yeh ET, Fujiwara K, and Abe J. 2012.

Walter Knight, a student in the Yan Lab received funding for a predoctoral AHA fellowship.

Dr. Robert Bell, a post-doctoral fellow in the Miano Lab received an AHA fellowship.

Dr. Chen Yan received funding for her AHA Grant-In-Aid (GIA).

Presentations

Dr. Craig Morrell will present at Mid-West Platelet Conference in Cleveland in Oct. and at Platelet and Megakaryocyte Gordon Conference in Galveston TX in March

Dr. Craig Morrell and Kristina Modjeski attended and presented posters at Gordon Research Conference on Hemostasis.

Dr. Slava Korshunov will be presenting two posters with his lab at the HBPR 2012 (high blood pressure research 2012 scientific sessions)

Dr. Jun-Ichi Abe presented 'PKCζ mediates disturbed flow-induced endothelial apoptosis via p53 SUMOylation.' By: Abe J. Invited lecture, The 7th International Symposium on Biomechanics in Vascular Biology and Cardiovascular Disease, April 26-27, 2012, Atlanta, GA.

Dr. Nhat Tu Le presented 'Statins directly activate ERK5 activation and improve endothelial dysfunction and subsequent acute allograft rejection' by: Takei Y, Le NT, Lee H, Heo KS, Hurley C, Smrcka AV, Miller B, Ko KA, Morrell C, Fujiwara K, Akaike M, and Abe J. At the BCVS, July 23-26, 2012, New Orleans, LA

Dr. Robert Bell presented "Discovery and Characterization of Long Intergenic Non-Coding RNA in Human Vascular Cells" at the Cold Spring Harbor Laboratory Meeting on Regulatory and Non-Coding RNAs held August 28-September 1, 2012

Comings and Goings

Welcome to our newly hired Aab CVRI Personnel:

Lissette Velasquez
Lab Technician
Small Lab

Sara Hillman
Lab Technician
Abe Lab

Takeki Hata
Postdoctoral Research Associate
Berk Lab

Yeonghwan Kim
Postdoctoral Research Associate
Berk Lab

Kang Tang
Senior Associate
Berk Lab

Martha Zettel
Tech Associate
Berk Lab

Sri Batchu
Postdoctoral Research Associate
Korshunov Lab

Eder DeMoraes
Postdoctoral Research Associate
Lopes Lab

Maria Garcia-Hernandez
Senior Associate
Lowenstein Lab

Robert Bell
Postdoctoral Research Associate
Miano Lab

Leisha Machin
Shared Tech

Il-Sun Kwon
Postdoctoral Research Associate
Jin Lab

Best Wishes and a Fond Farewell to:

Mike Getman (Berk Lab) has transferred to the Medical Center and is working in the Center for Pediatric Biomed Research as a Lab Tech.

Jin Man Cho (Berk Lab) his yearlong assignment ended.

Lindsay Marchetti (Berk Lab) has transferred to the Medical Center and is working in the Endo-Metab Division as a Lab Tech. Lindsay will be attending graduate school, for Physical Therapy, in the fall.

Emily Lambert (Lopes Lab) will be attending Med School in Arizona.

Christine Miller (Taubman Lab) has transferred to the Medical Center and is working in the Histopathology unit as a medical technologist.

Laurie Koek (Yan Lab) has transferred to the Medical Center and is working in the Ophthalmology unit as a Health Project Coordinator.

April Brooks (Shared Lab) is enjoying being a stay at home mom with her son.

Carolyn McClain (Abe Lab) has retired and is enjoying taking care of her garden and her cats.

Lian Wang (Berk Lab) her yearlong assignment ended.
Yuichiro Takei (Abe Lab) completed his postdoc fellowship.

Xiaoqun Wang (Berk Lab) his two year student appointment ended

Shusuke Yagi (Lowenstein Lab)

Dr. Burns Blaxall has moved to Cincinnati where he works for the Cincinnati Children's Hospital Medical Center, as a Professor, Director of Translational Science, for the Heart Institute, Molecular Cardiovascular Biology

Dr. Fadia Kamal is joining Dr. Blaxall at the Cincinnati Children's Hospital Medical Center.

Dr. Rashmi Ram is joining Dr. Blaxall at the Cincinnati Children's Hospital Medical Center.

Babies of the CVRI:

- Slava Korshunov-daughter; Maria Korshunov, 11/14/11, 7lbs 9oz
- Nhat Tu Le-son; Thanh-Phuoc Le, 12/7/11, 6lbs 10oz
- Shannon Pollock-daughter; Harper Grace Pollock, 12/11/11, 8lbs 12.5oz
- Orazio Slivano-son; Julien Luca Slivano, 4/19/12, 7lb 4oz
- Eric Small-son; Connor Thomas Small, 5/7/12, 6lbs 15.5oz
- Shin-Young Park-daughter; Jessica Eum, 6/26/12, 8lb 1oz
- Takeki Hata-daughter; Manami Hata, 7/23/12, 6lbs 7.7oz
- Allison Hobbins-son; Colin Thomas Hobbins, 7/25/12, 8lbs 10oz
- Oded Spindel-son; Ilan Maier Spindel, 9/6/12, 6lbs

Congratulations!

A team of 12 CVRI employees, friends, and family put together a team for the AHA heart walk held on April 28, 2012 through the Corn Hill Neighborhood. Together, they raised almost $2,000 in donations for this amazing cause. Pictures have been added to the Aab CVRI Server. Next year we hope to recruit more members and raise more in donations; remember, every dollar counts!

CVRI Partners with Amerks Hockey

Each month, beginning in October, we will hold a raffle for 4 premium seats to two Rochester ("Amerks") Americans Hockey games (combined value of $80/game). The cost per raffle ticket is only $5 (or 3 for $10). All proceeds will support the International MADS Box Conference held next summer in Canandaigua. We will announce the raffle each month through Amerks signs placed on the first and second floors in CVRI as well as in Cardiology at Strong and Highland. We look forward to wide participation in this important and fun event!

CVRI Christmas Donations

For the 3rd year in a row, the CVRI donated gifts and money to the Child & Adolescent Psychiatry Inpatient Service, at SMH. We collected toys, gift cards, music, money, and games for the kids whose range in ages is 2-18 years old. The Nurse Leader on the unit said this to us: "Your gifts mean so much to the patients of 4-9000. It is so sad that some of our children need to be hospitalized over the holidays away from family, friends, and familiar traditions. Your kindness and good wishes will certainly make their holidays much brighter! I wish you could be here to see the kids smiling faces when they receive their gifts. There are no words that can adequately express my personal gratitude. Happy Holidays!"

Thank you to all who donated. We look forward to participating again during the 2012 Holiday Season

Friendly Reminders

Fire alarms and Drills:

The NYS Fire Marshall requires that all building tenants evacuate the building when a fire alarm goes off, regardless if it's a drill or not.
Please remember to follow these steps when evacuating the building for a fire alarm:

- Leave by using the nearest exit
- When you get outside, report to the main parking lot, and take attendance with your lab members.

- Report your lab attendance to the admin staff. Please notify admin staff if anyone is missing.
- In the event of a real emergency, the admin staff will report missing people to the Fire Department Command Post.

If you are working in the vivarium, with **LIVE** mice, when an alarm goes off, you must follow these directives: mice with any **open incision,** at the time of the fire alarm, must be euthanized by employee, and employee to leave building by nearest emergency exit. Mice undergoing any **non-surgical** anesthetized procedure (e.g. Doppler, echo) must be returned to cage, and employee to leave building by nearest emergency exit. If gas anesthesia is being used at the time of the fire alarm, turn off vaporizer and shut off O2, and employee to leave building by nearest emergency exit.

PPE (personal protective equipment):

The Institutional BioSafety Committee requires lab coats to be worn when working in TC rooms Lab coats are available to all CVRI employees. They are located in C260-help yourself.

Vivarium Security:

Please help us maintain compliance with UR Security by locking all vivarium procedure and housing room doors when you exit.