

AAB CARDIOVASCULAR RESEARCH INSTITUTE

Department of Medicine


 UNIVERSITY of
ROCHESTER
 MEDICAL CENTER

MEDICINE of THE HIGHEST ORDER

CVRI



Beat

In This Issue

- ♥ Director's Column
by Dr. Joe Miano
- ♥ Welcome New Aab CVRI Personnel
- ♥ Upcoming Events
- ♥ "In Focus" *by Dr. Burns C. Blaxall*
- ♥ Recent Publications
- ♥ Promotions
- ♥ Awards

Directors' Column

Most Aab CVRI members will recall October 22, 2007 as the day we moved from the Medical Center to the current building in which we spend much of our waking hours. It has been nearly one year now and while the transition was difficult at times, the cooperative help of faculty and staff, as well as the dedicated crew of Alberti & Associates, have been instrumental in minimizing our "growing pains." Three important developments occurred over the last year. First, Mr. Richard Aab formed an Administrative Advisory Board with Mr. Tansukh Ganatra (Director, Paetec Holding Corporation) and Dr. Louis G. Lange (Founder/CEO of CV Therapeutics). Second, we have reached out to several renowned scientists who have agreed to serve on our Scientific Advisory Board (SAB). The names of SAB members are: Dr. Edward Fisher, Dr. David Ginsburg, Dr. Jose "Pepe" Jalife, Dr. Douglas Losordo, Dr. Aldon "Jake" Lusic, Dr. Eric Olson, and Dr. Alain Tedgui. Several SAB members will be visiting the Aab CVRI for a scientific retreat to be held here on June 10th (details to follow). A third important development was the recruitment of our new Director and Chief of Cardiology, Dr. Charles ("Charlie") Lowenstein who arrives on May 1, 2009. Dr. Lowenstein is an internationally recognized leader in vascular biology with projects related to nitric oxide, endothelial cell exocytosis, microRNAs, and inflammation. Dr. Lowenstein's first recruit is Dr. Craig Morrell, who studies platelet biology. For the next year or so, I will assist Dr. Lowenstein as an Associate Director. As we continue to grow into our new workplace, it is important that we have a means of communicating ideas to further enhance our work place. We already have had several "Town Hall" meetings and these will continue in the months ahead. In the meantime, if you have any suggestions for ways to improve the Aab CVRI workplace, please place them in the "suggestion box" located on Shannon Mawhinney's desk.

Welcome New Aab CVRI Personnel

Abha Sahni (Alexis Lab); Kyung-Sun (Abe lab); Jennifer Findeis-Hosey (Xu lab); Steve Belmonte (Blaxall lab); Heidi Michaloski (Berk lab); Dmitriy Migdalovich (White lab); Nhat Tu Le (Abe lab); Jin Ouchi (Lopes lab); Kyung-Sun Heo (Abe lab); Jinjing Zhao (Jin lab); Hakjoo Lee (Abe lab); Ji Young Kim (Jin lab); Heather Martin (Blaxall lab); Dietrich Machleder (Berk Lab); Masayoshi Oikawa (Yan Lab); Eiichiro Yamamoto (Berk Lab); Sandeep Chadha (Taubman Lab)

Upcoming Events

ATVB Annual Conference in Washington, DC; April 29-May 1, 2009.

“In Focus”

Heart failure (HF) is a debilitating disease with poor prognosis, and our laboratory has three main projects that aim to understand and treat HF. One project focuses on adrenaline receptors (β -ARs) on the surface of cardiac cells, which are normally responsible for regulating rate and force of contraction of the heart. However, these receptors are chronically desensitized in heart failure patients by elevated levels of an enzyme (GRK2) that is recruited to the β -ARs by the G-protein $G\beta\gamma$. In collaboration with URMCI investigator Alan V. Smrcka, we recently developed a novel strategy to selectively inhibit recruitment of GRK2 to $G\beta\gamma$. Our preliminary results demonstrate that compounds we have identified reduce β -AR desensitization and increase contractility in isolated cardiac cells. Further, the drug normalized cardiac function, morphology and GRK2 expression in an acute pharmacologic mouse model of HF. Importantly, we found that a daily dose of the drug for four weeks completely halts progression of HF in mice with established HF, without obvious side effects. Current pharmacologic therapies at best halt progression of HF, suggesting that our novel $G\beta\gamma$ inhibitor drugs are on par, and may synergize with, current best-practice HF therapy. Intense efforts are now being focused on further academic research as well as formation of a corporate entity to commercialize this promising technology.



Recent Publications

Bell, RD. et al, (Streb, JW, Long, X, Miano, JM). *SRF and myocardin regulate LRP-,mediated amyloid- β clearance in brain vascular cells.* Nat. Cell Biol. 11(2). 2009

Wang, L. et al, (Taubman, MB). *Vascular smooth muscle derived tissue factor is critical for arterial thrombosis after ferric chloride induced injury.* Blood. 113; 705-713. 2009

Ishinaga, H., et al, (Yan. C). *Synergistic induction of nuclear factor- κ B by transforming growth factor- β and tumor necrosis factor- α is mediated by protein kinase A-dependent RelA acetylation.* Biochem. J. 417; 583-591. 2009

Yamakuchi, M., Lowenstein, CJ. *MiR-34, SIRT1 and p53.* Cell Cycle. 8(5); 712-715. 2009

Korshunov, VA., Berk BC. *Genetic Modifier Loci Linked to Intima Formation Induced by Low Flow in the Mouse Carotid.* ATVB. 29; 47-53. 2009

Jaffre, F., et al, Blaxall BC. *Serotonin and Angiotensin Receptors in Cardiac Fibroblasts Coregulate Adrenergic-Dependent Cardiac Hypertrophy.* Circ. Res. 104; 113-123. 2009

Kirk, AD. et al, (Morrell, CN). Platelets Influence Vascularized Organ Transplants from Start to Finish. *AM. J. Transpl.* 2009 by Gq-coupled receptors. *J. Mol. Cell. Cardiol.* 2009

Matavel, A., Lopes, CMB. PKC activation and PIP2 depletion underlie biphasic regulation of IKs by Gq-coupled receptors. *J. Mol. Cell. Cardiol.* 2009

Ibrahim, J., Berk, BC. Flow-Mediated Vascular Remodeling in Hypertension: Relation to Hemodynamics. *Stroke.* 40; 582-590. 2009

Alexis, JD. et al, (Abe, J). Bcr Kinase Activation by Angiotensin II Inhibits Peroxisome Proliferator-Activated Receptor γ Transcriptional Activity in Vascular Smooth Muscle Cells. *Circ. Res.* 104; 69-78. 2009

Wang, J. et al, (Berk, BC). GIT1 Mediates VEGF-Induced Podosome formation in Endothelial Cells. Critical Role for PLC γ . *ATVB.* 29; 202-208. 2009

Jeong, Y. et al, (Lowenstein). Aldosterone activated endothelial exocytosis. *PNAS.* 2009

Awards

Jinjiang Pang, GIT1 Mediates Beta-Adrenergic Receptor Phosphorylation and Traffic in GRK2-Src-ARF6 Pathway in Cardiomyocyte, (AHA SDG)

Chang Hoon Ha, Role of HDAC5 in VEGF Signaling and Function, (AHA SDG)

Weiyue Wang, A Novel Role of HDAC5 in Flow-induced Atheroprotective Gene Expression, (AHA Post-Doc)

Clint Miller, Role Of PDE1A And Cyclic GMP Signaling In Regulating Cardiac Hypertrophy, (AHA Post-Doc)

Joe Miano, SRF/MYOCD: New Targets in Alzheimer's Neurovasculature, (NIH, STTR Phase II)

Jun-ichi Abe, Kinase-Mediated Sumoylation In Diabetic Cardiomyopathy, (NIH, RO-1)

Chen Yan, Regulation and Function of Phosphodiesterase in the Heart, (NIH, RO-1)

Burns Blaxall, A Role for Mena in the Heart, (NIH, RO-1)

Chang-Hoon Woo, ERK5-Sumoylation, CHIP And ICER Stability In Diabetes: Involvement In Apoptosis After MI, (AHA, SDG)

Elaine Smolock, Role of Ribosomal Proteins in Vascular Smooth Muscle Cell Proliferation, (NRSA Post-Doc)

Promotions

Staff Promotions:

Elena Fujiwara to Tech Associate II
Amy Mohan to Sr. Tech Associate, Operations Mgr
Mike O'Dell to Tech Associate IV
Debra Polizzi to Sr. Accountant
Ora Slivano to Tech III

Faculty Promotions:

TO-Research Assistant Professor

Jian Fu
Yan Lu
Xiaochun Long
Jinjiang Pang
Feng Shi
Chang Hoon Woo

TO- Assistant Professor

Shi Pan

TO-Associate Professor with Tenure

Jun-ichi Abe
Joe Miano