
THE NEWSLETTER OF THE DAVIS HEART AND LUNG RESEARCH INSTITUTE

WHITNEY WORKS, EDITOR; COLETTE TORNIK, ASSOCIATE EDITOR

WINTER 2009

Trading Places- Clinical Research Nurse Brings Innovative Care to Patients

Featured in the December 2008 Insight issue, **Mahmood Khan, PhD**, works with laboratory models aimed at developing a therapy to improve heart function following a heart attack. Khan recently “traded places” with a clinical research nurse, Beth Fisher, in order to get a better understanding of how laboratory research such as his is translated into clinical trials for evaluation among patients. Khan learned about the many facets of clinical research such as, the clinical trials unit at The James Cancer Hospital, patient details about cytic leukemia (a cancer that affects B cells), Phase I drugs, the informed consent process, and most of all the overall impact of the translational research process. Khan recognizes that it is both his and Beth’s contributions to academic research today that impact the lives of those affected by heart disease and cancer tomorrow.

DHLRI New Employees



Please join us in welcoming these new employees to the DHLRI. Contact Whitney.Works@osumc.edu to announce a new employee in the next issue.

Michelle Applegate- Account Clerk (Finance Coordinator)

Debra Cannon- Clinical Research Specialist

Melinda Freed-Administrative Assistant

Catherine Frentz- Clinical Research Coordinator

Michael Nkrumah-Clinical Research Coordinator

Chandra Shrestha- Research Associate, PI: Frederick Villamena

Guru Meenakshisundaram- Post Doctoral Researcher, PI: Periannan Kuppusamy

Roopa Subramanian- Research Assistant 1, PI: Edward Eteshola

Lin Xie- Post Doctoral Researcher, PI: Jay Zweier

Yuanjing Li- Post Doctoral Researcher, PI: Guanglong He

Whitney Works- Office Associate

Kudos



Rishi Patel, an undergraduate student, was selected for the Deans’ Undergraduate Research Fund award for autumn quarter 2008.

The OSU Cardiac MRI Research Team was well represented with four oral presentations and four poster presentations at the recent meeting of the Society for Cardiovascular Magnetic Resonance in Orlando. These included talks by BME students **Harris Lin** and **Shivraman Giri**, who was also a finalist for the Young Investigator Award.



2008 DHLRI Distinguished Award Winners

Distinguished Post-Doc Award: Binata Joddar, PhD

Binata is a highly resourceful and talented scientist who expertly bridges the fields of biomedical engineering and vascular biology. She has been instrumental in the design and implementation of a clinically relevant project involving ex plant cultures of human saphenous veins, which are commonly used as vascular grafts to replace coronary arteries. Her mastery of the tenets of her project, which involve aspects of molecular and cellular biology, cell signaling, pathophysiology, histology, and vascular tissue engineering, positively reflects her intense work-ethic and intellectual aptitude to integrate information into a workable systems-based model.

Distinguished Research Staff: Brian Rivera

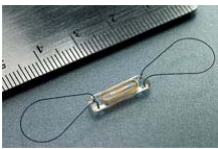
Brian has contributed to our research program in a myriad of significant ways for achieving excellence and recognition in extramural research funding, manuscripts and reputation in science, service, and leadership. He is a scientist full of enthusiasm and willingness to share his vast knowledge with all around him. At the same time, he is capable of providing very open and honest critiques of all aspects of our scientific goals. His contribution of knowledge in bioengineering and cell biology was essential in solving many problems that we have faced conducting our research. He is genuine and respectful in his communication and mediates problems with the finesse of an arbitrator.

Distinguished Mentor: Narisimham Parinandi, PhD

Dr. Parinandi is one of the brightest scientists in the field. He has trained numerous undergraduate and graduate students. These students have won several awards and they have achieved their goals because of his guidance. He is a passionate teacher/mentor to many including senior investigators. He makes himself available any time of the day, everyday. You will always find him working on someone else's manuscripts, grant proposals or research protocols, often sacrificing his own work.

Alpha-1 Antitrypsin Deficiency

Rumors have been surfacing that the King of Pop, Michael Jackson, may be suffering from a rare genetic condition called alpha-1 antitrypsin deficiency. **Dr. Mark Wewers**, professor, Pulmonary, Allergy, Critical Care, and Sleep Medicine, started working with this disorder twenty-five years ago and now runs a specialty clinic for affected patients. Alpha-1 antitrypsin deficiency leads to a low level of alpha-1 antitrypsin, a protein in the blood that acts as a protective shield and blocks the activity of destructive enzymes. Symptoms usually include shortness of breathe or wheezing upon exertion. This condition has a huge effect on a patient's wind power, which is really important for professional singers. It affects anything requiring voice effort. As far as treatment, there is augmentation therapy, which is giving intravenous infusions of the alpha-1 protein itself. Because lung damage is permanent, the most severe cases are left with little options. While a lung transplant is the ultimate therapeutic approach; the most important issue is getting patients to quit smoking, which increases the onset of symptoms.



Wireless Heart Failure Monitoring System

With millions of Americans hospitalized each year due to heart failure, **Dr. William Abraham**, Director of the Division of Cardiovascular Medicine and co-principal investigator, is testing the safety and effectiveness of an implanted, wireless pressure sensor that may allow for more rapid intervention by cardiologists in treating these patients. The device is implanted in the patient's pulmonary artery using a simple, catheter-based procedure. Dr. Abraham explains that "the device provides real time access to critical information at any time". The data can be available to the physician on a handheld computer, such as a PDA, around the clock. This pivotal "study will help determine if physicians can use this data the device provides to assist in identifying the appropriate medical treatment for heart failure patients." This remarkable heart monitoring system could decrease the millions of Americans hospitalized each year due to heart failure.

Blueberries May Inhibit Growth of Blood-Vessel Tumor

Principal investigator, **Dr. Gayle Gordillo** has shown that feeding blueberry extract to mice with tumors that are primarily found in infants and children will decrease tumor size and increase survival. Gordillo explains that “this work provides the first evidence demonstrating that blueberry extract can limit tumor formation by inhibiting the formation of blood vessels and inhibiting certain signaling pathways.” Usually ninety percent of these vascular tumors will resolve on their own within nine years, so they are not treated. However, they can often occur on the head or neck, resulting in an obvious deformity, and can be life-threatening if they obstruct the airway. Dr. Gordillo explains that her hope is that if blueberry juice is fed to a child with the tumor, scientists can intervene, and shrink the tumor before it becomes a big problem. The study also showed that the blueberry extract inhibited two important biochemical signaling pathways needed by tumor cells to grow.

New Awards: Federal, State, and Foundations

PI: Christopher Baran

Co-I: Gerard Nuovo, Charles Hitchcock, Gary Phillips

Sponsor: NIH/NHLBI, Award No. 1 R03 HL095431-01

Title: *The human correlation: studies of data obtained from a mouse model of IPF*

Start date: 09/19/2008 End date: 07/31/2010

PI: Melissa Hunter

Co-I: Clay Marsh

Sponsor: American Thoracic Society

Title: *MicroRNA regulation in idiopathic pulmonary fibrosis (IPF)*

Start date: 01/01/2009 End date: 12/31/2010

PI: Mahmood Khan

Sponsor: American Heart Association-National Center

Title: *Role of hyperbaric oxygen therapy in survival and engraftment of stem cells in the ischemic heart*

Start date: 01/01/2009 End date: 06/30/2012

PI: Rami Khayat

Co-I: William Abraham, David Jarjoura, Min Pu

Sponsor: NIH/NHLBI, Award No. 1 R21 HL092480-01

Title: *The role of obstructive sleep apnea in the acutely decompensated heart failure*

Start date: 09/17/2008 End date: 05/31/2010

PI: Stephen Kirkby

Sponsor: Cystic Fibrosis Foundation

Title: *Fourth year clinical fellowship award*

Start date: 07/01/2008 End date: 06/30/2009

PI: Narasimham Parinandi

Sponsor: International Academy of Oral Medicine & Toxicology

Title: *Mercury-induced lipid signaling and barrier dysfunction in vascular endothelial cells: Implications in mercury-mediated cardiovascular diseases*

Start date: 11/15/2008 End date: 11/15/2009

PI: Sam Parthasarathy

Sponsor: Emory University (NICHD subcontract, R21)

Title: *Development of nuclear antioxidants for the treatment of endometriosis*

Start date: 09/01/2008 End date: 08/31/2010

PI: Jonathan Parsons

Sponsor: American College of Sports Medicine Foundation

Title: *Prevalence of exercise-induced asthma in college athletes*

Start date: 07/01/2008 End date: 06/30/2009

PI: Mark Wewers
Co-I: Mikhail Gavrilin, Anasuya Sarkar
Sponsor: NIH/NHLBI, Award No. 1 R01 HL089440-01A2
Title: *RIP2 caspase-1 signaling in macrophages*
Start date: 01/12/2009 End date: 12/31/2013

New Industry Support

PI: Ralph Augostini
Sponsor: Cardiac Pacemakers
Title: *SMARTDELAY determined AV optimization: A comparison to other AV delay methods used in cardiac resynchronization therapy (SMART-AV)*
Start date: 11/03/2008

PI: Quinn Capers
Sponsor: University of Toledo
Title: *CORAL*
Start date: 12/19/2008

PI: Quinn Capers
Sponsor: Abiomed
Title: *RECOVER II*
Start date: 12/05/2008

PI: Curt Daniels
Sponsor: Actelion Pharmaceuticals US, Inc.
Title: *INHALE-15*
Start date: 10/01/2008

PI: Phil Diaz
Sponsor: MPEX pharmaceuticals
Title: *MPEX 302*
Start date: 12/15/2008

PI: Rami Khayat
Sponsor: Respironics
Title: *Evaluation of software enhancements to the Respironics BiPAP AutoSV device*
Start date: 11/03/2008

PI: Rami Khayat
Sponsor: Respironics, Inc.
Title: *The role of sleep apnea in the exacerbation of heart failure*
Start date: 09/30/2008

PI: Ernest Mazzaferri
Sponsor: Ardian, Inc.
Title: *Renal denervation in end stage renal disease patients with refractory hypertension (TP-041)*
Start date: 11/06/2008

PI: Ernest Mazzaferri
Sponsor: Ardian, Inc.
Title: *Renal denervation in patients with refractory hypertension (TP-040)*
Start date: 11/06/2008

PI: Ernest Mazzaferri
Sponsor: Carolinas Healthcare System
Title: *Assessment of dual antiplatelet therapy with drug-eluting stents (ADAPT-DES)*
Start date: 08/01/2007

PI: Laxmi Mehta
Sponsor: Yale University
Title: *Young women with acute myocardial infarction (VIRGO)*
Start date: 01/01/2009

PI: Vincent Pompili
Sponsor: Arteriocyte, Inc.
Title: *Therapeutic potential of ex vivo expanded human cord blood derived CD133+ cells*
Start date: 09/18/2008

PI: Subha Raman
Sponsor: Edwards Lifesciences
Title: *EVOLUTION II CT analysis*
Start date: 10/15/2008

PI: Namita Sood
Sponsor: Gilead Sciences, Inc.
Title: *ATHENA*
Start date: 10/10/2008

PI: Raul Weiss
Sponsor: St. Jude Medical Co.
Title: *Persistent atrial fibrillation feasibility study using the Gen2 cardiac ablation system*
Start date: 08/12/2008

PI: Mani Vannan
Sponsor: Siemens
Title: *Cardiovascular ultrasound of 2D imaging and volumetric imaging*
Start date: 03/03/2008



Recent Publications

Amin A, Davis M, Auseon A.

Isolated cleft posterior mitral valve leaflet: an uncommon cause of mitral regurgitation.

Eur J Echocardiogr. 2009 Jan;10(1):173-4. Epub 2008 Jul 29.

Blissett AR, Garbellini D, Calomeni EP, Mihai C, Elton TS, Agarwal G.

Regulation of collagen fibrillogenesis by cell-surface expression of kinase dead DDR2.

J Mol Biol. 2009 Jan 23;385(3):902-11. Epub 2008 Oct 30.

Chen CA, Druhan LJ, Varadharaj S, Chen YR, Zweier JL.

Phosphorylation of endothelial nitric-oxide synthase regulates superoxide generation from the enzyme.

J Biol Chem. 2008 Oct 3;283(40):27038-47. Epub 2008 Jul 13.

Chen CL, Chen J, Rawale S, Varadharaj S, Kaumaya PP, Zweier JL, Chen YR.

Protein tyrosine nitration of the flavin subunit is associated with oxidative modification of mitochondrial complex II in the post-ischemic myocardium.

J Biol Chem. 2008 Oct 10;283(41):27991-8003. Epub 2008 Aug 5.

Curry JM, Eubank TD, Roberts RD, Wang Y, Pore N, Maity A, Marsh CB.

M-CSF signals through the MAPK/ERK pathway via Sp1 to induce VEGF production and induces angiogenesis in vivo.

PLoS ONE. 2008;3(10):e3405. Epub 2008 Oct 14.

Dzwonczyk R, Fujji J, Simonetti L, Nieves-Ramos R, Bergese S. Electrical noise in the intraoperative magnetic resonance imaging setting. *Anesth Analg* 2009;108:181-186.

Field SM, Villamena FA.

Theoretical and experimental studies of tyrosyl hydroperoxide formation in the presence of H-bond donors.

Chem Res Toxicol. 2008 Oct;21(10):1923-32. Epub 2008 Sep 25.

Gordillo G, Fang H, Khanna S, Harper J, Phillips G, Sen CK.
Oral administration of blueberry inhibits angiogenic tumor growth and enhances survival of mice with endothelial cell neoplasm. *Antioxid Redox Signal*. 2009 Jan;11(1):47-58.

Lai JP, Bao S, Davis IC, Knoell DL.
Inhibition of the phosphatase PTEN protects mice against oleic acid-induced acute lung injury. *Br J Pharmacol*. 2009 Jan;156(1):189-200.

Liu B, Tewari AK, Zhang L, Green-Church KB, Zweier JL, Chen YR, He G.
Proteomic analysis of protein tyrosine nitration after ischemia reperfusion injury: Mitochondria as the major target. *Biochim Biophys Acta*. 2009 Mar;1794(3):476-85. Epub 2008 Dec 25.

Mihai C, Chotani M, Elton TS, Agarwal G.
Mapping of DDR1 distribution and oligomerization on the cell surface by FRET microscopy. *J Mol Biol*. 2009 Jan 16;385(2):432-45. Epub 2008 Nov 5.

Mohan IK, Khan M, Wisel S, Selvendiran K, Sridhar A, Carnes CA, Bogner B, Kálai T, Hideg K, Kuppusamy P.
Cardioprotection by HO-4038, a novel verapamil derivative, targeted against ischemia and reperfusion-mediated acute myocardial infarction. *Am J Physiol Heart Circ Physiol*. 2009 Jan;296(1):H140-51. Epub 2008 Oct 31.

Raices RM, Kannan Y, Sarkar A, Bellamkonda-Athmaram V, Wewers MD.
A synergistic role for IL-1beta and TNFalpha in monocyte-derived IFNgamma inducing activity. *Cytokine*. 2008 Nov;44(2):234-41. Epub 2008 Sep 19.

Sen CK.
Wound healing essentials: let there be oxygen. *Wound Repair Regen*. 2009 Jan-Feb;17(1):1-18.

Sun Q, Yue P, Ying Z, Cardounel AJ, Brook RD, Devlin R, Hwang JS, Zweier JL, Chen LC, Rajagopalan S.
Air pollution exposure potentiates hypertension through reactive oxygen species-mediated activation of Rho/ROCK. *Arterioscler Thromb Vasc Biol*. 2008 Oct;28(10):1760-6. Epub 2008 Jul 3.

Sun Q, Yue P, DeLuca JA, Lumeng CN, Kampfrath T, Mikolaj MB, Cai Y, Ostrowski MC, Lu B, Parthasarathy S, Brook RD, Moffatt-Bruce SD, Chen LC, Rajagopalan S.
Ambient air pollution exaggerates adipose inflammation and insulin resistance in a mouse model of diet-induced obesity. *Circulation*. 2009 Feb 3;119(4):538-46. Epub 2009 Jan 19.

Talukder MA, Yang F, Nishijima Y, Chen CA, Kalyanasundaram A, Periasamy M, Zweier JL.
Reduced SERCA2a converts sub-lethal myocardial injury to infarction and affects postischemic functional recovery. *J Mol Cell Cardiol*. 2009 Feb;46(2):285-7. Epub 2008 Nov 12.

Xu Y, Liu B, Zweier JL, He G.
Formation of hydrogen peroxide and reduction of peroxynitrite via dismutation of superoxide at reperfusion enhances myocardial blood flow and oxygen consumption in postischemic mouse heart. *J Pharmacol Exp Ther*. 2008 Nov;327(2):402-10. Epub 2008 Aug 6.

Yang, E.V., Kim, S.J., Donovan, E.L., Chin, M., Gross, A.C. Webster Marketon, J.I. Barsky, S.H. & Glaser, R. (2009)
Norepinephrine upregulates VEGF, IL-8 and IL-6 expression in human melanoma tumor cell lines: Implications for stress-related enhancement of tumor progression. *Brain, Behavior and Immunity*, 23, 267-275.

Ziolo MT, Kohr MJ, Wang H.
Nitric oxide signaling and the regulation of myocardial function. *J Mol Cell Cardiol*. 2008 Nov;45(5):625-32. Epub 2008 Aug 3. Review.

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