

BENCH NOTES



Volume 7, Issue 1
Winter 2009

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Department Notes

The Department of Molecular Cardiology was well-represented in awards at the annual LRI Retreat in Geneva-on-the-Lake which took place in September 2008. Riku Das, Ph.D. (Plow lab) was a 2008 Semi-Finalist of the F. Merlin Bumpus, Ph.D. Junior Investigator Award in Basic Science for the abstract entitled, "A new mechanism of action of calcium channel blockers: Inhibition of inflammatory macrophage recruitment via suppression of plasminogen receptors". Poster Award winners included Rick Page, Ph.D. (Misra lab) and Linda Yan, a Solon High School summer student (Qin lab).

On January 2, 2009, **Dr. Arie Horowitz, D.Sc.** joined our department as Assistant Staff. Dr. Horowitz studies mechanisms of blood vessel sprouting and guidance. These processes are part of angiogenesis – the growth of new vessels from preexisting ones. The ultimate translational objective of research on angiogenesis is to develop new therapies that can either entice or suppress this process. Blood vessel sprouting is being studied by endothelial cell culture assays and with animal models. The lab is using mice missing a single gene which codes for a guanine exchange factor intercellular adhesion and cell migration. These mice bear an angiogenesis-specific defect. A second project in the lab is focused on neuropilin, a receptor of both attractant and repellent guidance cues, which determine the spatial pattern of vessel growth. Dr. Horowitz worked previously at the Dartmouth Medical School in New Hampshire.

Congratulations To.....

Rajani Tendulkar on the birth of her daughter, Parisa Leela, on October 17, 2008.

Priya Raman (Stenina lab), **Mark Rishavy** (Berkner lab), **Gong-Qing Shen** (Wang lab), **Ting Shi** (Perez lab), **Somanath Shenoy** (Byzova lab), **Yan-Qing Ma** (Plow lab) on their promotion to Project Staff.

Yanqing Gong (Hoover-Plow lab) and **Shenghan Chen** (Wu lab) on their promotion to Research Associate.

Laurie Castel (Van Wagoner lab) on the adoption of her daughter, Ana, who is 4 years old and from the Ukraine.

Rashmi Ram (Van Wagoner lab) on defending her Ph.D. thesis. Rashmi graduated from the Kent State-Cleveland Clinic Biomedical Sciences Ph.D. program.

Carla Drumm (Plow lab) on her recent marriage. Carla and her new husband, Mike, were married in Key West in December.

Sandro Yong, Ph.D. (Wang lab) on the birth of his son, Aiden Michael, on December 7, 2008.



Department Publications

Misra Lab

- Structural Basis of Nucleotide Exchange and Client Binding by the Hsp70 Cochaperone Bag2. Xu, Z, Page, RC, Gomes MM, Kohli E, Nix JC, Herr AB, Patterson C, Misra S. *Nat Struct Mol Biol.* 2008 Dec;15(12):1309-17.
- Stabilization and Characterization of a Heme-Oxy Reaction Intermediate in Inducible Nitric-oxide Synthase. Tejero J, Biswas A, Wang ZQ, Page RC, Haque MM, Hemann C, Zweier JL, Misra S, Stuehr DJ. *J Biol Chem.* 2008 Nov 28;283(48):334-98-507.

Wu Lab

- Corin variant associated with hypertension and cardiac hypertrophy exhibits impaired zymogen activation and natriuretic peptide processing activity. Wang W, Liao X, Fukuda K, Knappe S, Wu F, Dries DL, Qin J, Wu Q. *Circulation Res.* 2008;103:502-508.
- Corin: New insights into the natriuretic peptide system. Wu Q, Xu-Cai YO, Chen S, Wang W. *Kidney Int.* 2009;75:142-146.

Qin Lab

- Migfilin—A molecular switch for regulation of integrin activation. Ithychanda S, Das M, Ma YQ, Ding K, Wang X, Gupta S, Wu C, Plow EF, and Qin J. *J Biol Chem* 2008 [Epub ahead of print].
- Structural basis of focal adhesion localization of LIM-only adaptor PINCH by integrin-linked kinase. Yang Y, Wang X, Hawkins CA, Chen K, Vaynberg J, Mao X, Tu Y, Zuo X, Wang YX, Wu C, Tjandra N and Qin J. *J Biol Chem* 2008 [Epub ahead of print].

Byzova Lab

- 14-3-3beta– Rac1 - p21 activated kinase signaling regulates Akt1 mediated cytoskeletal organization, lamellipodia formation and fibronectin matrix assembly. Somanath PR and Byzova T. *J Cell. Physiol.* 2009 218(2):394-404.
- Integrin and growth factor receptor alliance in angiogenesis. Somanath PR, Ciocea A and Byzova T. *Cell Biochem. Biophys.* 2008 (in press).
- The angiogenic response is dictated by beta3 integrin on bone marrow-derived cells. Feng W, McCabe NP, Mahabeleshwar GH, Somanath PR, Phillips DR and Byzova TV. *J Cell Biol.* 2008 183(6) (in press).

Podrez Lab

- Oxidized phospholipids: Biomarker for cardiovascular diseases. Ashraf MZ, Kar NS, and Podrez EA. *Int J Biochem Cell Biol.* 2008 Nov 17 [Epub ahead of print].

Sen Lab

- Blockade of NF- κ B using I κ B dominant negative mice ameliorates cardiac hypertrophy in myotrophin overexpressed transgenic mice. Young D, Popovic ZB, Jones K and Gupta S. *J Mol Biol* 2008;381:559-568.
- Prevention of Cardiac Hypertrophy and Heart Failure by Silencing of NF- κ B. Gupta S, Young D, Maitra RK, Gupta A, Popovic ZB, Yong SL, Mahajan A, Wang Q, and Sen S. *J Mol Biol.* 2008;375(3):637-649.
- Nuclear Co-translocation of Myotrophin and p65 Stimulates Myocyte Growth. Regulation by Myotrophin Hairpin Loops. Das B, Gupta S, Vasanthi A, Xu Z, Misra S, Sen S. *J Biol Chem.* 2008 Oct 10;283(41):27947-56.

Wang Lab

- Liu P, Yang Q, Wang X, Feng A, Yang T, Yang R, Wang P, Yuan M, Liu M, Liu J, and Wang QK. (2008) Identification of a Novel Genetic Locus for Ichthyosis Vulgaris on Chromosome 10q22.3-q24.2. *J of Invest Derm* 128; 1418-1422.
- Ren X, Liu J, Zhai L, Yao Q, Dai X, Cai Z, Liu P, Sun K, Huang C, Wang QK*, and Liu M*. (2008) A splicing mutation in the COL7A1 gene causes autosomal dominant dystrophic epidermolysis bullosa pruriginosa. *Br J of Derm* 158(3):618-20.
- Shen G, Rao S, Martinelli N, Olivieri O, Corrocher R, Abdullah KG, Hazen SL, Smith J, Barnard J, Plow EF, Girelli D, and Wang QK. (2008) Association between four SNPs on chromosome 9p21 and myocardial infarction is replicated in an Italian population. *J Human Genetics* 53(2):144-50.
- Shen G, Li L, Rao S, Abdullah, Ban JM, L BS, Park JE, and Wang QK. (2008) Four SNPs on Chromosome 9p21 in a South Korean Population Implicate a Genetic Locus that Confers High Cross-Race Risk for Development of Coronary Artery Disease. *ATVB* 28:360-365.
- Dai X, Wang X, Cui J, Sheng J, Jiang X, Tu X, Tang Z, Bai Y, Liu M, and Wang QK (2008) Identification and functional characterization of a novel splicing mutation in RP gene PRPF31. *Biochem Biophys Res Comm.* 367(2):420-426.
- Li H, Li C, Lu Q, Ting S, Ke T, Li CW, M Yuang, J Liu, Ren X, Zhang Z, Zeng S, Wang QK*, and Liu M*. (2008) Cataract mutation P20S of α B-crystallin impairs chaperone activity of α A-crystallin and induces apoptosis of human lens epithelial cells. *BBA - Molecular Basis of Disease* 1782(5):303-9.
- Seidelmann SB, Li L, Shen GQ, Topol EJ, and Wang QK. (2008) Identification of a novel locus for triglyceride on chromosome 1p31-32 in families with premature CAD and MI. *J Lipid Res.* 49, 1034-1038.
- Zhang S, Wang, L, Hao Y, Wang P, Hap P, Yin K, Wang QK*, and Liu M*. (2008) T14484C and T14502C in the mitochondrial ND6 gene are associated with Leber's hereditary optic neuropathy in a Chinese family. *Mitochondrion* 8(3):205-10.
- Zhang S, Yin K, Ren X, Wang P, Zhang S, Cheng L, Yang J, Liu J, Liu M, and Wang QK. (2008) Identification of a novel KCNQ1 mutation associated with both Jervell and Lange-Nielsen and Romano-Ward forms of long QT syndrome in a Chi-

Department Publications (cont'd)

nese family. *BMC Medical Genetics* 9:24.

- Liu P, Zhang S, Yao Q, Liu X, Wang X, Xiong K, Liu J, Huang C, Huang X, Wang P, Yuang M, Liu J, Wang QK*, Liu M*. (2008) Identification of a genetic locus for autosomal dominant disseminated superficial actinic porokeratosis on chromosome 1p31.3-p31.1. *Human Genetics* 123(5):507-13.
- Abdullah KG, Li L, Shen G, Hu Y, Yang Y, MacKinlay KG, Topol EJ, and Wang QK. (2008) Four SNPS on chromosome 9p21 confer risk to premature, familial CAD and MI in an American Caucasian population (GeneQuest). *Ann Human Genetics*. 72:654-657.
- Hu Y, Li L, Seidemann SB, Timur AA, Shen PH, Driscoll, DJ, and Wang QK. (2008) Identification of association of common AGGF1 variants with susceptibility for Klippel-Trenaunay syndrome using the structure association program. *Ann Human Genetics*. 72:636-643.
- Zhang X, Chen S, Zhang L, Liu M, Redfearn, Bryant, RM, Oberti C, Vincent GM, and Wang QK. (2008) Protective effect of KCNH2 single nucleotide polymorphism K897T in an LQTS family and identification of novel KCNQ1 and KCNH2 mutations. *BMC Medical Genetics* 9:87.
- Dai XH, Chen WW, Wang X, Zhu QH, Li C, Li L, Liu M, Wang QK*, and Liu JY*. (2008) A novel genetic locus for familial febrile seizures and epilepsy on chromosome 3q26.2-q26.33. *Human Genetics* 124(4):423-9.
- Zhang X, Chen S, Yoo S, Chakravarti S, Zhang T, Ke T, Oberti C, Yong SL, Fang F, Li L, de la Fuente R, Wang L, Chen Q, and Wang QK. (2008) Mutation in nuclear pore component NUP155 leads to atrial fibrillation and early sudden cardiac death. *Cell* 135:1017-1027.
- Zhang S, Liu M, Dong JM, Yin K, Wang P, BU J, Li J, Hao YS, Hao P, Wang QK*, and Wang L*. (2008) Identification of a genetic locus for autosomal dominant infantile cataract on chromosome 20p12.1-p11.23 in a Chinese family. *Mol Vis*. 2008;14:1893-7.

Plow Lab

- Plow EF, Ma Y-Q, Byzova, TV, Qin J. Platelet aggregation: a brief historical and molecular perspective. *Thrombosis and Thrombolysis*, 2009, In Press.
- Ithychanda S, Das M, Ma YQ, Ding K, Wang X, Gupta S, Wu C, Plow EF, Qin J. Migfilin: a molecular switch in regulation of integrin activation. *J Biol Chem*. 2008 Dec 13. [Epub ahead of print]
- Larjava H, Plow EF, Wu C. Kindlins: essential regulators of integrin signaling and cell-matrix adhesion. *EMBO Rep*. 2008 Dec;9(12):1203-8. Epub 2008 Nov 7.
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- Stenina O and Plow, EF. Counterbalancing forces: what is thrombospondin-1 doing in atherosclerotic lesions? *Circ. Res.* 103 (10): 1053-1055, 2008.
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- Pluskota E, Soloviev DA, Szpak D, Weber C, Plow EF. Neutrophil apoptosis: selective regulation by different ligands of integrin $\alpha\text{M}\beta\text{2}$. *J Immun*. 181: 3609-3619, 2008.
- Pluskota E, Woody NM, Szpak D, Ballantyne CM, Soloviev DA, Simon DI, Plow EF. Expression, activation and function of integrin $\alpha\text{M}\beta\text{2}$ (Mac-1) on neutrophil derived particles. *Blood*, 112:2327-2335, 2008.
- Book Chapter: Plow EF, Kelly P. Platelets in arterial thrombosis. In: Antithrombotic Drug Therapy in Cardiology, Askari, A.A., et al. eds., Human Press, Totowa, NJ. In press, 2009.

Hoover-Plow Lab

- Hoover-Plow J, Hart E, Gong Y, Shchurin A, Schneeman T. A Physiological Function for Apolipoprotein(a): A Natural Regulator of the Inflammatory Response. *Exp Biol Med*, 2009 Jan;234(1):28-34. Epub 2008 Nov 7.
- Sa Q, Hart E, Hill AE, Nadeau JH, Hoover-Plow JL. Quantitative trait locus analysis for hemostasis and thrombosis. *Mamm Genome*. 2009 Jun;19(6):406-12. Epub 2008 Sep 12.
- Gong Y, Hart E, Shchurin A, Hoover-Plow J. Inflammatory macrophage migration requires MMP-9 activation by plasminogen in mice. *J Clin Invest*. 2008 Sep;118(9):3012-24.
- Hoover-Plow JL, Gong Y, Shchurin A, Busuttill SJ, Schneeman TA, Hart E. Strain and model dependent differences in inflammatory cell recruitment in mice. *Inflammation Research*. Oct. 2008, 57:457-463.

Karnik Lab

- Yue H, Li W, Desnoyer R, Karnik SS. Unphosphorylated STAT3 Mediates Pathological Gene Expression Associated with Angiotensin II Type 1 Receptor-induced Cardiac Hypertrophy. *Circulation*. 2008;118:S_431.

Invited Talks/Presentations

Qingyu Wu, M.D., Ph.D.

- ◇ Featured Speaker, “Corin: New discoveries of heart failure and disease”, Friends of the LRI, Cleveland, OH, June 17, 2008.
- ◇ Invited Lecture, “Transmembrane Serine Proteases in Cardiovascular and Hematological Diseases”, 2008 Suzhou Summit on Hematology, Suzhou, China, September 25-28, 2008.
- ◇ Invited Lecture, “The type II transmembrane serine protease corin”, Dept. of Pharmacology, Barbara Ann Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI, December 5, 2008.
- ◇ Invited Lecture, “The cardiac protease corin: discovery, function and disease”, Cardiovascular Biology Research, Oklahoma Medical Research Foundation, Oklahoma City, OK, January 8, 2009.

Somanath Shenoy, Ph.D.

- ◇ Oral Presentation: “Protein Kinase B alpha differentially regulates hypoxia– and tumor induced angiogenesis by Akt1”, 12th Biennial Midwest Platelet Conference, Lexington, JY, October 2008.

Wei Wang, Ph.D.

- ◇ Oral Presentation: “Corin variant associated with hypertension and cardiac hypertrophy exhibits impaired zymogen activation and natriuretic peptide processing activity”, 2008 AHA meeting, New Orleans, LA, November 8-12, 2008.

Biswajit Das, Ph.D.

- ◇ Oral Presentation: “Myotrophin and the p53 signaling cascade in cardiac hypertrophy/heart failure”, 2008 AHA meeting, New Orleans, LA, November 8-12, 2008.

Qing Wang, Ph.D.

- ◇ Session Chair, Genetics of Coronary Artery Disease and Nutrigenomics, 11th Cardiovascular Genomics and Atherosclerosis Symposium, Oct 31, 2008, Seoul, South Korea
- ◇ Session Chair, 11th Cardiovascular Genomics and Atherosclerosis Symposium Satellite Meeting, Nov. 1, 2008, Seoul, South Korea
- ◇ Session Chair, Genetics of Coronary Artery Disease and Risk Factors, Sunday Morning Programs, Nov. 9, 2008, AHA Scientific Sessions 2008, New Orleans, Louisiana.
- ◇ Invited Talk, December 5, 2008, Molecular Genetics of Key Cardiovascular Disease, Atrial Fibrillation. Invited Lecture, College of Pharmacology, The Second Army Medical University of China, Shanghai, China.
- ◇ Invited Talk, November 9, 2008, Linkage Mapping and Gene Identification for Coronary Heart Disease and Related Risk Factors by Family-based Approaches. AHA Scientific Sessions 2008, New Orleans, LA.
- ◇ Invited Speaker, Genetics of Coronary Artery Disease in the Post-Genomic Era, 11th Cardiovascular Genomics and Atherosclerosis Symposium, Oct 31, 2008, Seoul, South Korea
- ◇ Invited Speaker, Molecular Genetics of Atrial Fibrillation, 11th Cardiovascular Genomics and Atherosclerosis Symposium Satellite Meeting, Nov. 1, 2008, Seoul, South Korea
- ◇ Invited Talk, September 4-5, 2008, Key Overview Talk, Genetic Susceptibility Issues in Cardiovascular Diseases. NIH/NIEHS Workshop: Global Variability in Response to Air Pollution: Approaches to Translation of Cardiopulmonary Animal Disease Models, Chapel Hill, NC
- ◇ Invited Speaker, Molecular Genetics Advances in Atrial Fibrillation, The 6th China Atrial Fibrillation Symposium (CAFS), July 3-5, 2008, Dalian, China.

Invited Talks/Presentations (cont'd)

Edward F. Plow, Ph.D.

- ◇ Session Chair/Discussion Leader, Gordon Research Conference on Hemostasis, “Hot Topics in Hemostasis”, Waterville Valley, NH, July 2008.
- ◇ Invited Speaker, Midwest Platelet Conference, “Kindling the Flame of Integrin Activation with Kindlins”, Lexington, KY, October 2008.

Jane L. Hoover-Plow, Ph.D.

- ◇ Invited Speaker, Midwest Platelet Conference, “Genetic Modifiers of Thrombosis”, Lexington, KY, October 2008.

New Grants

- **Qingyu Wu, M.D., Ph.D.:** R01 (NHLBI) for the period 8/1/08—6/30/13 (\$1.93M), project entitled, “Role of corin in natriuretic peptide processing and hypertension”.

Awards

Recipients of Cleveland Clinic Service Awards in 2008 are:

20 Years David Van Wagoner

15 Years Xiaolun Zhang
Laurie Castel
Kathy Berkner

10 Years Ela Pluskota
Nadine Klimczak
Don Wallick

5 Years Lin Li
Miroslava Tischenko
Beth Bunnell
Somanath Shenoy



Departmental Recognition Awards were given out at the Employee Appreciation Party on December 19, 2008 to: **Mille Branch** (glassware rep), **Beth Bunnell** (Van Wagoner lab), **Tim Burke** (Plow lab), **Russ Desnoyer** (Karnik Lab), **Sue De Stefano**, and **Dianne Perez**.

Somanath Shenoy (Byzova lab) received the Young Investigator Award at the 12th Biennial Midwest Platelet Conference held at the University of Kentucky in Lexington in October 2008.

Qingyu Wu, M.D., Ph.D. and **Zahid Ashraf, Ph.D.** received a Cleveland Clinic 2008 Innovator Award.

Sue De Stefano received an Award of Excellence from the World Class Ideas Program for her idea “Routing of Patients to the Genomics Medicine Institute”.

Who's New in Molecular Cardiology



Sudesh Agrawal, Ph.D. is a Research Associate in the new laboratory of Dr. Arie Horowitz. Sudesh comes to our department from the Department of Cell Biology. His expertise is in vascular, cell and molecular biology. Sudesh is friendly, a team worker and a meticulous scientist who cares about society and science. In his free time, Sudesh is an All-Star Baseball Coach in Shaker Heights and a yoga instructor.

Lisa Plungas is a Department Coordinator working with Dr. Tatiana Byzova. She is a full-time student at CWRU studying nutrition. In her free time, Lisa likes to go running, read a good book and spend time with her friends and family.



Sara Whitson, P.D. is a Postdoctoral Fellow in the laboratory of Dr. Kathy Berkner. Sara completed her MS in biological mass spectrometry at The Ohio State University and her PhD in polymer mass spectrometry at The University of Akron. She and her husband had their first baby, Jacob, in July.



Happy Birthday to you.....



January

1—Tim Burke, Riku Das
3—Sue De Stefano
4—Rajani Tendulkar
12—Ekta Kohli
14—Rong Yang
17—Lining Ma
19—Didier Allexandre, Ella Frolova
 Sujoy Ithychanda
24—Valentin Ustinov
25—Qing Wang
27—Maria Madajka
28—Olga Stenina
30—Michele Barnard

February

1—Stephen Archacki
2—Zahid Ashraf, Dmitry Solovjov
9—Christa Harry
13—Sanghamitra Bhattacharyya
18—Fang Fang
20—Susmita Chakrabarti
24—Yi Ma

March

13—Kalil Abdullah
14—Yiqing Jiang, Eugene Podrez
16—Kasia Bialkowska
18—Saurav Misra
19—Vinay Pasupuleti
22—Yanqing Gong

April

1—Sadashiva Karnik
8—Niladri Kar
10—Manveen Gupta
12—Nadine Klimczak
18—Robin Lewis, Dhanuja Perera
19—Brian McCue
21—Tie Ke
23—Fadia Mayyas, Julie Rennison
30—Somanath Shenoy

May

1—Kathy Berkner
9—Tatiana Byzova
22—Dorota Szpak
25—Xianqin Zhang
29—Julia Vaynberg

June

1—Carla Drumm
2—Ed Plow
7—Andrew Provost
8—Hong Yue
13—Wei Wang
15—Michelle Pesho
16—Rajaganapathi Jagannathan
18—Valentina Verbovetskaya
19—Russ Desnoyer
20—Kamila Bledzka, Wei Du
24—Nikolai Malinin
26—Hamiyet Unal
27—Biswajit Das
30—Malory Weber

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2009 Holiday Schedule

New Year's Day
January 1, 2009
(Thursday)

Memorial Day
May 25, 2009

Independence Day
July 4, 2009
(CC holiday July 3)

Labor Day
September 7, 2009

Thanksgiving
November 26, 2009

Christmas
December 25, 2009
(Friday)

Welcome.....New Employees

Podrez lab

Detao Gao, Visiting Grad Student

Fox lab

Quinn Tian, Research Student
Maryam Soliman, Research Student
Kristina Sul, Research Student
Cindy Cheng, Research Student
Amir Babar, Research Student
Catie Chillemi, Volunteer
Caitlin Wong, Volunteer
Michael Dzuricky, Work Study Student
Vikram Santhanam, Work Study Student

Byzova lab

Mircea Pavkov, Fellow
Lining Ma, Research Associate

Berkner lab

Aisulu Usubalieva, Graduate Student
Sara Whitson, Fellow

Plow lab

Khalid Sossey-Alaoui, Project Staff

Wu lab

Xiaofei Qi, Fellow

Misra lab

Anna Neyman, Research Technician

Karnik lab

Zhong-Hui Duan, Visiting Scientist
Afshan Hussain, Research Technologist
Jacqueline Kemp, Rotating Graduate Student

Horowitz lab

Arie Horowitz, Ph.D., Assistant Staff
Sudesh Agrawal, Research Associate

Administration

Lisa Plungas, Dept. Coordinator II

WELCOME

Good-bye and Best Wishes!

Yi Zhang Eui-Seock Hwang
Joe Roshetsky Don Wallick
Patrick McCabe Tie Ke
Sonia Sharma
Yang Yang
Anna Fiskin
Ying Hu
Erika Hart
Sang-Uk Nham
John Phan

