CCRAM Newsletter

December 2013

Center for Cardiovascular Research and Alternative Medicine, University of Wyoming

2013 CCRAM Award for Xihui (Alex) Xu

CCRAM presents an annual research award for the outstanding CCRAM researcher based on a points system taking into account the publications, journal impact factor, presentations, awards etc. This year's recipient of the award Xihui (Alex) Xu has to his credit 11 papers published/accepted in top-tier journals including *Cardiovasc. Res., Hypertension, Autophagy, J. Mol. Cell Cardiol.* and *J Am. Heart Assoc.* He had presented three posters at the 2013 AHA Scientific Sessions (Dallas) and an oral presentation in the Third Biennial Western Regional IDEA Conference (Hawaii). He is also the recipient of this years ACRE-CnAHA Symposium award (second prize) and the BCVS-AHA Travel grant. Alex also successfully defended his PhD thesis in 2013 and has the distinction of the fist graduate student form the Biomedical Sciences Graduate Program.

The C-CRAM award was established in 2004 and the past recipients are: Sreejayan Nair and Feng Dong (2005), Xiaoping Yang (2006), Min Du (2007), Ji Li (2008), Heng Ma and Meijun Zhu (2009); Tuerdi Subati and Yingmei (Megan) Zhang (2010), Yinan Hua (2011); Yingmei (Megan) Zhang (2012).

Photo: Alex with his dissertation committee members Drs. Bruce Culver, Jun Ren (Alex's advisor), Sreejayan Nair, and Enette Larson Meyer .

Inside this issue:

Research Papers Published in 2013

Twenty six of the 51 research papers published in 2013 appeared in journals with impact factor 5 or above

1. Barcelo-Coblijn G, Wold LE, Ren J, Murphy EJ: Prenatal ethanol exposure increases brain cholesterol content in adult rats. *Lipids* 48:1059-1068, 2013
2. Ceylan-Isik AF, Dong M, Zhang Y, Dong F, Turdi S, Nair S, Yanagisawa M, Ren J: Cardiomyocyte-specific deletion of endothelin receptor A rescues aging-associated cardiac hypertrophy and contractile dysfunction: role of autophagy. *Basic Res Cardiol* 108:335, 2013
3. Ceylan-Isik AF, Kandadi MR, Xu X, Hua Y, Chicco AJ, Ren J, Nair S: Apelin administration ameliorates high fat diet-induced cardiac hypertrophy and contractile dysfunction. *J Mol Cell Cardiol* 63:4-13, 2013
4. Dong M, Hu N, Hua Y, Xu X, Kandadi MR, Guo R, Jiang S, Nair S, Hu D, Ren J: Chronic Akt activation attenuated lipopolysaccharide-induced cardiac dysfunction via Akt/GSK3beta-dependent inhibition of apoptosis and ER stress. *Biochim Biophys Acta* 1832:848-863, 2013
5. Dong M, Ren J: What Fans the Fire: Insights Into Mechanisms of Leptin in Metabolic Syndrome-Associated Heart Diseases. *Curr Pharm Des*, 2013
6. Dong M, Zheng Q, Ford SP, Nathanielsz PW, Ren J: Maternal obesity, lipotoxicity and cardiovascular diseases in offspring. *J Mol Cell Cardiol* 55:111-116, 2013
7. Fan W, Li C, Qin X, Wang S, Da H, Cheng K, Zhou R, Tong C, Li X, Bu Q, Li C, Han Y, Ren J, Cao F: Adipose stromal cell and sarpogrelate orchestrate the recovery of inflammation-induced angiogenesis in aged hindlimb ischemic mice. *Aging Cell* 12:32-41, 2013
8. Ge W, Hu N, George LA, Ford SP, Nathanielsz PW, Wang XM, Ren J: Maternal nutrient restriction predisposes ventricular remodeling in adult sheep offspring. *J Nutr Biochem* 24:1258-1265, 2013
9. Guo R, Zhang Y, Turdi S, Ren J: Adiponectin knockout accentuates high fat diet-induced obesity and cardiac dysfunction: role of autophagy. *Biochim Biophys Acta* 1832:1136-1148, 2013
10. Hu N, Han X, Lane EK, Gao F, Zhang Y, Ren J: Cardiac-specific overexpression of metallothionein rescues against cigarette smoking exposure-induced myocardial contractile and mitochondrial damage. *PLoS One* 8:e57151, 2013
11. Hua Y, Dolence J, Ramanan S, Ren J, Nair S: Bisdemethoxycurcumin inhibits PDGF-induced vascular smooth muscle cell motility and proliferation. *Mol Nutr Food Res* 57:1611-1618, 2013
12. Hua Y, Xu X, Shi GP, Chicco AJ, Ren J, Nair S: Cathepsin K knockout alleviates pressure overload-induced cardiac hypertrophy. *Hypertension* 61:1184-1192, 2013
13. Hua Y, Zhang Y, Dolence J, Shi GP, Ren J, Nair S: Cathepsin K knockout mitigates high-fat diet-induced cardiac hypertrophy and contractile dysfunction. *Diabetes* 62:498-509, 2013
14. Jiang S, Guo R, Zhang Y, Zou Y, Ren J: Heavy metal scavenger metallothionein mitigates deep hypothermia-induced myocardial contractile anomalies: role of autophagy. *Am J Physiol Endocrinol Metab* 304:E74-86, 2013
15. Johnson DH, Ahmad R, He G, Samouilov A, Zweier JL: Compressed sensing of spatial electron paramagnetic resonance imaging. *Magn Reson Med*, 2013
16. Kandadi MR, Hu N, Ren J: ULK1 plays a critical role in AMPK-mediated myocardial autophagy and contractile dysfunction following acute alcohol challenge. *Curr Pharm Des* 19:4874-4887, 2013
17. Kandadi MR, Hua Y, Zhu M, Turdi S, Nathanielsz PW, Ford SP, Nair S, Ren J: Influence of gestational overfeeding on myocardial proinflammatory mediators in fetal sheep heart. *J Nutr Biochem* 24:1982-1990, 2013
18. Kandadi MR, Roe ND, Ren J: Autophagy Inhibition Rescues against Leptin-Induced Cardiac Contractile Dysfunction. *Curr Pharm Des*, 2013
19. Li XY, Zheng ZH, Li XY, Guo J, Zhang Y, Li H, Wang YW, Ren J, Wu ZB: Treatment of foot disease in patients with type 2 diabetes mellitus using human umbilical cord blood mesenchymal stem cells: response and correction of immunological anomalies. *Curr Pharm Des* 19:4893-4899, 2013
20. Li Y, Cai M, Sun Q, Liu Z, Cardounel AJ, Swartz HM, He G: Hyperoxia and transforming growth factor beta1 signaling in the post-ischemic mouse heart. *Life Sci* 92:547-554, 2013
21. Liu Y, Wang B, Zhang WW, Liu JN, Shen MZ, Ding MG, Wang XM, Ren J: Modulation of staurosporine-activated volume-sensitive outwardly rectifying Cl- channel by PI3K/Akt in cardiomyocytes. *Curr Pharm Des* 19:4859-4864, 2013
22. Luo FL, Ren J: The role of autophagy in metabolic syndrome-related cardiovascular injury. *Chin. J. Hypertens.* 21:203-206, 2013

Research Papers Published in 2013

23. Panzhinskiy E, Culver B, Ren J, Nair S: Role of mammalian target of rapamycin (mTOR) in muscle growth. In *Nutrition and enhanced sports performance: Recommendations for muscle building.* Bagchi D, Nair S, Sen CK, Eds., Elsevier/Academic Press, 2013, p. 217-227
24. Panzhinskiy E, Hua Y, Culver B, Ren J, Nair S: Endoplasmic reticulum stress upregulates protein tyrosine phosphatase 1B and impairs glucose uptake in cultured myotubes. *Diabetologia* 56:598-607, 2013
25. Panzhinskiy E, Ren J, Nair S: Protein Tyrosine Phosphatase 1B and Insulin Resistance: Role of Endoplasmic Reticulum Stress/ Reactive Oxygen Species/Nuclear Factor Kappa B Axis. *PLoS One* 8:e77228, 2013
26. Panzhinskiy E, Ren J, Nair S: Pharmacological inhibition of protein tyrosine phosphatase 1B: a promising strategy for the treatment of obesity and type 2 diabetes mellitus. *Curr Med Chem* 20:2609-2625, 2013
27. Roe ND, He EY, Wu Z, Ren J: Folic acid reverses nitric oxide synthase uncoupling and prevents cardiac dysfunction in insulin resistance: Role of Ca(2+)/calmodulin-activated protein kinase II. *Free Radic Biol Med* 65:234-243, 2013
28. Roe ND, Ren J: Oxidative activation of Ca(2+)/calmodulin-activated kinase II mediates ER stress-induced cardiac dysfunction and apoptosis. *Am J Physiol Heart Circ Physiol* 304:H828-839, 2013
29. Roy S, Banerjee J, Gnyawali SC, Khanna S, He G, Pfeiffer D, Zweier JL, Sen CK: Suppression of Induced microRNA-15b Prevents Rapid Loss of Cardiac Function in a Dicer Depleted Model of Cardiac Dysfunction. *PLoS One* 8:e66789, 2013
30. Steiner JB, Wu Z, Ren J: Ticagrelor: positive, negative and misunderstood properties as a new antiplatelet agent. *Clin Exp Pharmacol Physiol* 40:398-403, 2013
31. Sun A, Ren J: ALDH2, a novel protector against stroke? *Cell Res* 23:874-875, 2013
32. Tong X, Peng H, Liu D, Ji L, Niu C, Ren J, Pan B, Hu J, Zheng L, Huang Y: High-density lipoprotein of patients with type 2 diabetes mellitus upregulates cyclooxgenase-2 expression and prostacyclin I-2 release in endothelial cells: relationship with HDL-associated sphingosine-1-phosphate. *Cardiovasc Diabetol* 12:27, 2013
33. Turdi S, Ge W, Hu N, Bradley KM, Wang X, Ren J: Interaction between maternal and postnatal high fat diet leads to a greater risk of myocardial dysfunction in offspring via enhanced lipotoxicity, IRS-1 serine phosphorylation and mitochondrial defects. *J Mol Cell Cardiol* 55:117-129, 2013
34. Turdi S, Hu N, Ren J: Tauroursodeoxycholic acid mitigates high fat diet-induced cardiomyocyte contractile and intracellular Ca2+ anomalies. *PLoS One* 8:e63615, 2013
35. Turdi S, Sun W, Tan Y, Yang X, Cai L, Ren J: Inhibition of DNA methylation attenuates low-dose cadmium-induced cardiac contractile and intracellular Ca(2+) anomalies. *Clin Exp Pharmacol Physiol* 40:706-712, 2013
36. Wang D, Luo P, Wang Y, Li W, Wang C, Sun D, Zhang R, Su T, Ma X, Zeng C, Wang H, Ren J, Cao F: Glucagon-like peptide-1 protects against cardiac microvascular injury in diabetes via a cAMP/PKA/Rho-dependent mechanism. *Diabetes* 62:1697-1708, 2013
37. Wang HT, Li ZL, Fan BY, Su FF, Zhao JB, Ren J, Zheng QS: The independent role of the aortic root ganglionated plexi in the initiation of atrial fibrillation: An experimental study. *J Thorac Cardiovasc Surg*, 2013
38. Wang L, Li L, Ran X, Long M, Zhang M, Tao Y, Luo X, Wang Y, Ma X, Halmurati U, Mao X, Ren J: Ellagic Acid Reduces Adipogenesis through Inhibition of Differentiation-Prevention of the Induction of Rb Phosphorylation in 3T3-L1 Adipocytes. *Evid Based Complement Alternat Med* 2013:287534, 2013
39. Wang Z, Zhang Y, Guo J, Jin K, Li J, Guo X, Scott GI, Zheng Q, Ren J: Inhibition of protein kinase C betaII isoform rescues glucose toxicity-induced cardiomyocyte contractile dysfunction: role of mitochondria. *Life Sci* 93:116-124, 2013
40. Wu Z, He EY, Scott GI, Ren J: alpha,beta-Unsaturated aldehyde pollutant acrolein suppresses cardiomyocyte contractile function: Role of TRPV1 and oxidative stress. *Environ Toxicol*, 2013
41. Xu X, Bucala R, Ren J: Macrophage migration inhibitory factor deficiency augments doxorubicin-induced cardiomyopathy. *J Am Heart Assoc* 2:e000439, 2013
42. Xu X, Hua Y, Nair S, Bucala R, Ren J: Macrophage Migration Inhibitory Factor Deletion Exacerbates Pressure Overload-Induced Cardiac Hypertrophy Through Mitigating Autophagy. *Hypertension*, 2013
43. Xu X, Hua Y, Nair S, Zhang Y, Ren J: Akt2 knockout preserves cardiac function in high-fat diet-induced obesity by rescuing cardiac autophagosome maturation. *J Mol Cell Biol* 5:61-63, 2013
44. Xu X, Hueckstaedt LK, Ren J: Deficiency of insulin-like growth factor 1 attenuates aging-induced changes in hepatic function: role of autophagy. *J Hepatol* 59:308-317, 2013
45. Xu X, Pacheco BD, Leng L, Bucala R, Ren J: Macrophage migration inhibitory factor plays a permissive role in the maintenance of cardiac contractile function under starvation through regulation of autophagy. *Cardiovasc Res* 99:412-421, 2013
46. Xu X, Ren J: Cardiac stem cell regeneration in metabolic syndrome. *Curr Pharm Des* 19:4888-4892, 2013

Research Papers Published in 2013

47. Zhang B, Zhang Y, La Cour KH, Richmond KL, Wang XM, Ren J: Mitochondrial aldehyde dehydrogenase obliterates endoplasmic reticulum stress-induced cardiac contractile dysfunction via correction of autophagy. *Biochim Biophys Acta* 1832:574-584, 2013
48. Zhang RH, Gao JY, Guo HT, Scott GI, Eason AR, Wang XM, Ren J: Inhibition of CYP2E1 attenuates chronic alcohol intake-induced myocardial contractile dysfunction and apoptosis. *Biochim Biophys Acta* 1832:128-141, 2013
49. Zhang Y, Han X, Hu N, Huff AF, Gao F, Ren J: Akt2 knockout alleviates prolonged caloric restriction-induced change in cardiac contractile function through regulation of autophagy. *J Mol Cell Cardiol*, 2013
50. Zhang Y, Ren J: Pathophysiology and therapeutics of cardiovascular health in metabolic syndrome. *Curr Pharm Des*, 2013
51. Zhang Y, Xu X, Ren J: MTOR over activation and interrupted autophagy flux in obese hearts: a dicey assembly? *Autophagy* 9:939-941, 2013

Manuscripts Under Revision/Accepted/in Press

1. Guo R, Xu X, Zhang Y, Ren J. Aldehyde dehydrogenase-2 (ALDH2) ameliorates chronic alcohol ingestion-induced hepatic steatosis and inflammation: Role of autophagy. *J. Hepatol.* under revision
2. Yang J,* Yang L,* Yu S, Liu J, Zuo J, Chen W, Duan W, Zheng Q, Xu X, Li J, Zhang J, Xu J, Sun L, Yang X, Xiong L, Yi D, Wang L, Liu Q, Ge S, Ren J. Transcatheter versus surgical closure of perimembranous ventricular septal defects in children: A randomized controlled trial. *J. Am. Coll. Cardiol.* in press (*Equal first authorship).
3. Zhang Y, Ren J Targeting autophagy for the therapeutic application of histone deacetylase (HDAC) inhibitors in ischemic reperfusion heart injury. *Circulation* accepted.
4. Ren J, Taegtemeyer H. Too much or not enough of a good thing – the paradox of autophagy in heart disease. *J. Mol. Cell Cardiol.* invited review. (accepted)
5. Sun A*, Cheng Y*, Zhang Y*, Zhang Q, Wang S, Hu K, Ren J, Ge J. Aldehyde dehydrogenase-2 ameliorates doxorubicin-induced cardiomyopathy via attenuating autophagy. J. *Mol. Cell. Cardiol.* in press (Equal 1st).
6. Xu X, Hua Y, Nair S, Bucala R, Ren J. Macrophage migration inhibitory factor (MIF) activates mitophagy to ameliorate pressure overload-induced cardiac hypertrophy. *Hypertension,* in press.
7. Xu X, Roe ND, Weiser-Evans MCM, Ren J. Inhibition of mTOR with rapamycin reverses hypertrophic cardiomyopathy in mice with cardiomyocyte-specific knockout of PTEN. *Hypertension*, in press.
8. Zhang Y*, Xu X*, Ceylan-Isik AF, Dong M, Ren J. Ablation of Akt2 protects against lipopolysaccharide-induced cardiac dysfunction: Role of Akt ubiquitination E3 ligase TRAF6. *J. Mol. Cell. Cardiol.* under revision
9. Zhang Y*, Han X*, Hu N, Huff AF, Gao F, Ren J. Akt2 knockout alleviates caloric restriction-induced change in cardiac contractile function through regulation of autophagy. *J. Mol. Cell. Cardiol.* in press.
10. Hu N, Dong M, Ren J. Hydrogen sulfide alleviates cardiac contractile dysfunction in an Akt2 knockout murine model of insulin resistance: Role of mitochondrial injury and apoptosis. *Am. J. Physiol. Regul. Integr. Comp. Physiol.,* under revision
11. Hu N, Ren J. Nicotine, cigarette smoking and cardiac function: an Update. *Toxicol. Res.* 3: 7-10, 2014.
12. Panzhinskiy E, Lapchak PA, Ren J, Nair S. A novel neurotrophic compound augments insulin signaling and alleviates insulin resistance in high-fat diet-fed mice. *J. Pharm. Exp. Therap.* Under revision
13. Wang L, Li LL, Ran XJ, Zhang MF, Tao Y, Luo X, Wang Y, Mao XM, Ren J. Lipopolysaccharides reduce adipogenesis in 3T3-L1 adipocytes through downregulation of PPARγ and AMPK expression. *Cardiovasc. Toxicol*. in press
14. Yuan M*, Wang Q*, Li C, Tao L, Zhang H, Wang H, Zhang Y, Ren J. Adrenomedullin in vascular endothelial injury and combination therapy: Time for a new paradigm. *Curr. Vasc. Pharmacol.* in press.
15. Yang L*, Hu N*, Jiang S, Zou Y, Yang J, XiongL, Ren J. Heavy Metal Scavenger Metallothionein Attenuates ER Stress-Induced Myocardial Contractile Anomalies: Role of Autophagy. *Toxicol Lett.,* accepted (*Equal first)

EPSCoR INBRE Undergraduate Fellowship

Sidney Ren (Pre-pharmacy; Mentor: Alex Xu), Benjamin Pacheco (Pharm D, Mentor: Jun Ren), Ellen Sloan (Sophomore; Mentor: Jun Ren); Songlin Cai (PharmD, Mentor: Sree Nair), Dawn Davison (PharmD: Mentor: Sree Nair).

Meetings and Presentations

Dr. Jun Ren served as a session chair at the AHA Scientific Sessions 2013 in Dallas.

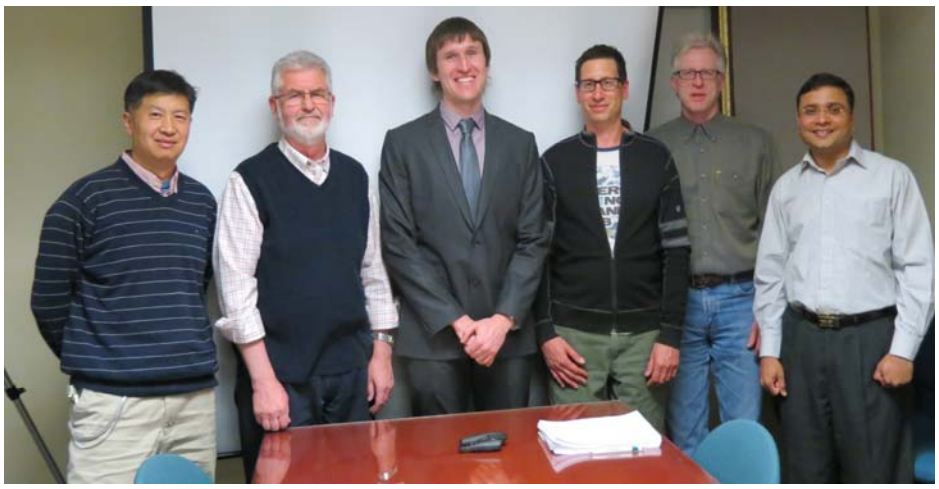
Dr. Nair was an invited speaker at the IFT 2013 Meeting in Chicago

1. He EY, Wu Z, Scott GI, Ren J. Cigarette smoke-induced myocardial inflammation and contractile dysfunction is mediated by unsaturated aldehydes and TRPV1. FASEB J. 27:1086.15, 2013. Poster.
2. Hu N, Zhang Y, Nunn JM, Ren J. Aldehyde dehydrogenase 2 (ALDH2) obliterates insulin resistance-induced myocardial contractile dysfunction through regulation of mitochondrial function. Diabetes 62:A7, 2013. Oral.
3. Hua Y, Shi GP, Ren J, Nair S. Cathepsin K deficiency attenuates starvation-induced cardiac autophagy and apoptosis. Circulation 128:A14091, 2013, Oral,
4. Kandadi MR, Hu N, Roe ND, Ren J. Genetic deletion of Akt2 protects against diet-induced adiposity and hepatic steatosis independent of AMPK. Diabetes 62:A525-A526 2013, Poster
5. Kandadi MR, Roe ND, Ren J. Knockout of the energy sensing AMP kinase disengages Akt deletion-conferred cardioprotection against obesity cardiomyopathy. Circulation 128:A15269, 2013, Poster
6. Luo F, Ren J. Deficiency of AMPK exacerbates lipopolysaccharide-induced cardiac contractile dysfunction: the Role of autophagy. Circulation 128:A15517, 2013, Poster
7. Yang J, Yang L. Randomized controlled trial of transcatheter versus surgical closure of perimembrane ventricular septal defects in children. 2013 American Heart Association Annual Meeting SS-A-10319.
8. Xu X, Ren J. Macrophage migration inhibitory factor deficiency exacerbates aging-induced cardiac dysfunction in mice: Role of autophagy. Circulation 128:A13868, 2013. Poster
9. Xu X, Ren J. Macrophage migration inhibitory factor knockout preserves cardiac function in high fat diet-induced metabolic syndrome. Circulation 128:A15144, 2013, Poster
10. Xu X, Roe ND, Weiser-Evans MC, Ren J. Inhibition of mTOR with rapamycin reverses cardiomyocyte-specific knockout of PTEN-induced hypertrophic cardiomyopathy. Circulation 128:A15113, 2013. Poster
11. Xu X, Roe ND, Ren J. Inhibition of mTOR with rapamycin reverses cardiomyocyte-specific knockout of PTEN-induced hypertrophic cardiomyopathy. 3rd Biennial Western Regional IDeA Conference, Hawaii, 10/2013. Oral.
12. Zhang Y, Ren J. ALDH2 alleviates high fat diet-induced cardiac contractile and mitochondrial dysfunction through regulation of AMPK/SIRT1 and PGC1alpha. Diabetes 62:A75, 2013. Oral.
13. Zhang Y. Tips on scientific writing and publication. Northern Cardiovascular Forum. Shenyang, China, Oral

AJP Podcast

July 18th, 2013. Together with Dr. William C. Stanley editor in chief of the *American Journal of Physiology—Heart and Circulation* and the lead author of a featured paper Thunder Jalili (University of Utah), Dr. Jun Ren featured as an expert in the Podcast discuss the role of dietary fats and carbohydrates in cardiovascular function in hypertension (available at *http://ajpheart. podbean.com/2013/07/18/low-carbohydrate-high-fat-diet-lowers-blood-pressure-in-spontaneously-hypertensive-rats/*).

Graduation



Evgeniy Panzhinskiy successfully defended his PhD thesis in May and graduated from the Molecular and Cellular Life Sciences Graduate Program. In the picture he is seen (third form right) with his committee members Drs. Jun Ren, Bruce Culver, David Fay, Mark Stayton, and Sree Nair (advisor). Evgeniy is currently a post-doctoral fellow in University of British Colombia, Vancouver.

Alex Xu is the first graduate student form the new Biomedical Sciences Graduate Program, seen here with his advisor Dr. Jun Ren.

Other News

Jun Ren received 2013 American Diabetes Association Research grant award on "Obesity and Autophagy".

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Alex Xu and **Yinan Hua** received research awards at the CHS Grand Rounds.

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Former CCRAM researchers **Maolong Dong**, Megan **Zhang**, **Fuling Luo** and **Henry Ma** each received major NFSC research grants based on continuation work from their training at the University of Wyoming.

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Yinan Hua received the overseas outstanding PhD graduate award from the Chinese Government. She also won the AAiPS (American Association of Indian Pharmacists Association) research award for 2013. Yinan defended her PhD thesis in December– she is the second student to graduate from the BMS program

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Alex Xu won AHA travel award and AHA/ACRE presentation award (2nd place).

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Megan Zhang and **Jun Ren** received provincial international collaborative grant to work on obesity.

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Journal editorships: BBA Mol Basis Dis (Jun Ren, Megan Zhang), Patent Endo Metab Imm Drug Disc (X Xu, Jun Ren), Curr Pharm. Design (Megan Zhang, Jun Ren).

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Elected to editorial boards: Cardiovascular Diagnosis Therapy (Megan Zhang, Jun Ren), Vasc Pharmacol (Jun Ren), World Journal of Cardiology (Jun Ren), Translational Med (Jun Ren).

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Book Editing: Nutrition and Enhanced Sports Performance: Recommendations for Muscle Building, Eds. Bagchi D, Nair S, Sen CK.(eds), Academic Press ISBN: 978-0123964540; 2013.

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Productive Year!

CCRAM researchers **Rui, Qiurong, Lifang** and **Yinan** with their newborns.

CCRAM Newsletter

Edited by Sreejayan Nair on behalf of the Center for Cardiovascular Research and Alternative Medicine
University of Wyoming, School of Pharmacy
1000 E. University Avenue, Laramie, WY 82072
Phone: (307)766-6138; Email: sreejay@uwyo.edu
Url: http://www.uwyo.edu/pharmacy/_files/documents/newsletters-ccram/2013/ccram_newsletter_2013.pdf