

CCRAM Newsletter

 Center for Cardiovascular Research and Alternative Medicine

COBRE/INBRE Meeting

Dear Colleagues,

Here is the second issue of the CCRAM newsletter. Dr. Ji Li, the former director of CCRAM, moved on to take up a faculty position at the University at Buffalo, State University of New York. We thank you very much Dr. Li for all that you have done for CCRAM and wish you well in your new endeavor.

The next issue of CCRAM is due in December. We would like to hear your stories and publish them in the newsletter - so please keep us informed!

- Sreejayan Nair



CCRAM members attended the INBRE-COBRE Meeting of the Western states (Hawaii, Alaska, WY, MT, ID, NV, NM) research conference for INBRE-COBRE program at Big Sky, Montana. Backdrop- Old Faithful Geyser at the Yellowstone National Park.

Manuscripts in Press or Print During the Second Quarter of 2009

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1. Alexander BM, Singh P, Austin KJ, Cockrum RR, Cammack KM, Hess BW, Moss GE, Nathanielsz PW, Ford SP. Effect of maternal fatness on fetal steroids and semi-quantitative real-time PCR expression of receptor genes in sheep. *Animal Reproduction Science*, in press
2. Ceylan-Isik AF, Erdogan-Tulmac OB, Ari N, Ozansoy G, Ren J. Impact of 17- β estradiol replacement on vascular responsiveness in ovariectomized rats under diabetes. *Clin. Exp. Pharm. Physiol.* in press.
3. Ceylan-Isik AF, Guo KK, Carlson EC, Privratsky JR, Liao SJ, Cai L, Chen AF, Ren J. Metallothionein abrogates GTP cyclohydrolase I inhibition-induced cardiac contractile and morphological defect: Role of mitochondrial biogenesis. *Hypertension* 53: 1023-1031, 2009

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Manuscripts in Press or Print During the Second Quarter of 2009

(...continued from page 1)

3. Dong F, Hua Y, Zhao P, Ren J, Du M, Sreejayan, N. Chromium supplement inhibits skeletal muscle atrophy in hindlimb suspended mice. *J. Nutr. Biochem.* in press.
4. Doser TA, Tuerdi S, Thomas DP, Epstein PN, Li SY, Ren J. Transgenic overexpression of aldehyde dehydrogenase-2 rescues chronic alcohol intake-induced myocardial hypertrophy and contractile dysfunction. *Circulation* 119: 1941-1949, 2009.
5. Ford SP, Zhang L, Zhu MJ, Miller MM, Smith DT, Hess BW, Moss GE, Nathanielsz PW. Maternal obesity accelerates fetal pancreatic β -cell but not α -cell development in the sheep: prenatal and postnatal consequences. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* (In Press)
6. Ge W, Ren J. Combined L-/T- type calcium channel blockers: Ready for prime time. *Hypertension* 53: 592-594, 2009.
7. Guo R, Ma H, Gao F, Zhong L, Ren J. Metallothionein alleviates oxidative stress-induced endoplasmic reticulum stress and myocardial dysfunction. *J. Mol. Cell. Cardiol.* 47:228-237, 2009.
8. Hu H, Li DL, Fan L, Ren J, Wang SP, Jia B, Liu BH, Sun L, Yu XJ, Zang WJ. Involvement of volume-sensitive chloride channels in the proliferation of human subcutaneous preadipocytes. *Clin. Exp. Pharm. Physiol.* in press.
9. Hua Y, Ma H, Samson WK, Ren J. Neuronostatin inhibits cardiac contractile function via a protein kinase A- and JNK-dependent mechanism in murine hearts. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* in press.
10. Li J, Wu F, Zhang H, Fu F, Ji L, Dong L, Li Q, Liu W, Zhang Y, Lv A, Wang H, Ren J, Gao F. Insulin inhibits leukocyte-endothelium adherence via an Akt-NO-dependent mechanism in myocardial ischemia/reperfusion. *J. Mol. Cell. Cardiol.* in press.
11. Li L, Li H, Chen D, Liu H, Tang F, Zhang Y, Ren J, Li Y. Preparation and characterization of quantum dots coated magnetic hollow spheres for magnetic fluorescent multimodal imaging and drug delivery. *J. Nanosci Nanotechnol.* 9: 2540-2545, 2009.
12. Li Q, Hueckstaedt LK, Ren J. UCF-101 ameliorates streptozotocin-induced cardiomyocyte contractile dysfunction in vitro: Role of AMP-activated protein kinase. *Exp. Physiol.* in press.
13. Li Q, Li J, Ren J. UCF-101 mitigates streptozotocin-induced cardiomyocyte dysfunction: Role of AMP-activated protein kinase *Am J Physiol Endocrinol Metab.* in press.
14. Li SY, Gilbert SAB, Li Q, Ren J. Aldehyde dehydrogenase-2 (ALDH2) ameliorates chronic alcohol-induced myocardial insulin resistance and endoplasmic reticulum stress. *J. Mol. Cell. Cardiol.* 47: 247-255, 2009.
15. Long NM, Vonnahme KA, Hess BW, Ford SP (2009) Effects of early gestational undernutrition on fetal growth, organ development, and placentomal composition in the bovine. *J. Anim. Sci.* 87:1950-1959.
16. Lu QL, Xie Zj, Zhang HW, Ren J. Evaluation of the appropriate diagnostic threshold of waist circumference for cardiometabolic syndrome in Chinese Uygur adults. *J. Cardiometab. Syndrome* 4:120-125, 2009.
17. Ma H, Li J, Gao F, Ren J. Aldehyde dehydrogenase 2 (ALDH2) ameliorates acute cardiac toxicity of ethanol: Role of protein phosphatase and forkhead transcription factor. *J. Am. Coll. Cardiol.* in press.
18. Ma H, Li SY, Xu PS, Babcock SA, Dolence EK, Brownlee M, Li J, Ren J. Advanced glycation endproduct (AGE) accumulation and AGE receptor (RAGE) upregulation contribute to the onset of diabetic cardiomyopathy. *J. Cell. Mol. Med.* in press.
19. Nair RP, Ren J. Pharmacotherapy of obesity - benefit, bias and hyperbole. *Curr. Med. Chem.* 16: 1888-1897, 2009.
20. Nathanielsz PW, Loehle M, Schwab M, Kadner S, Gilbert J, Brenna JT, Ford SP, Nijland MJ. Dose response effects of betamethasone on maturation of the fetal sheep lung. *Am. J. Obstet. Gynecol.* in press
21. Pei Z, Zhuang ZQ, Xiao PX, Chen J, Sang H, Ren J, Wu Z, Yan G. Influence of infrasound exposure on the whole L-type calcium currents in rat ventricular myocytes. *Cardiovasc. Toxicol.* 9:70-77, 2009.
22. Ren J, Babcock SA, Li Q, Huff AF, Li SY, Doser TA. Aldehyde dehydrogenase-2 transgene ameliorates chronic alcohol ingestion-induced apoptosis in cerebral cortex. *Toxicol. Lett.* 187: 149-156, 2009.
23. Ren J, Kelley RO. Cardiac health in women with metabolic syndrome – clinical aspects and pathophysiology. *Obesity* 17:1114-1123, 2009.
24. Sun JB, Wang ZL, Duan JH, Ren J, Yang XD, Dai SL, Li Y. Targeted distribution of bacterial magnetosomes isolated from *Magnetospirillum gryphiswaldense* MSR-1 in healthy Sprague-Dawley rats. *J. Nanosci. Nanotechnol.* 9:1881-1885, 2009.

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C-CRAM,
launched in
2004 and has
over **190** peer
reviewed
publications to
its credit

Manuscripts in Press or Print During the Second Quarter of 2009

25. Sun JB, Wang ZL, Duan JH, Ren J, Yang XD, Dai SL, Li Y. Targeted distribution of bacterial magnetosomes isolated from *Magnetospirillum gryphiswaldense* MSR-I in healthy Sprague-Dawley rats. *J. Nanosci. Nanotechnol.* 9:1881-1885, 2009.
26. Sun Y, Yi D, Wang Y, Zheng R, Sun G, Wang J, Liu Y, Ren J, Wang Y, Zhang S, Gu C, Pei J. Age-dependent mobilization of circulating endothelial progenitor cells in infants and young children undergoing cardiac surgery with cardiopulmonary bypass. *Cytokine* in press.
27. Tong JF, Yan X, Zhu MJ, Ford SP, Nathanielsz PW, Du M. Maternal obesity down-regulates myogenesis and beta-catenin signaling in fetal skeletal muscle. *Am. J. Physiol. Endocrinol Metab.* 296: E917-E924, 2009
28. Turdi S, Guo R, Huff AF, Wolf EM, Culver B, Ren J. Cardiomyocyte contractile dysfunction in the APP-swe/PS1E9 mouse model of Alzheimer's disease. *PLoS One* 4:e6033, 2009.
29. Turdi S, Schamber RM, Roe ND, Chew HG, Jr., Culver B, Ren J. Acute methamphetamine exposure inhibits cardiac contractile function. *Toxicol. Lett.* 189:152-158, 2009.
30. Wang GJ, Lin YL, Chen CH, Wu XC, Liao JF, Ren J. Cellular calcium regulatory machinery of vasorelaxation elicited by petasin. *Clin. Exp. Pharm. Physiol.* in press.
31. Wang J, Ma H, Zhang X, He L, Wu J, Gao X, Ren J, Li J. A novel AMPK activator from Chinese herb medicine and ischemia phosphorylate the cardiac transcription factor FOXO3. *Int. J. Physiol. Pathophysiol. Pharmacol.* in press.
32. Wang J, Li J. Activated protein C: a potential cardioprotective factor against ischemic injury during ischemia/reperfusion. *Am J Trans Res* 1: 381-392, 2009
33. Yang XP, Pei ZH, Ren J. Making up or breaking up - the Tortuous role of platelet-derived growth factor (PDGF) in vascular aging. *Clin. Exp. Pharm. Physiol.* 36: 739-747, 2009.
34. Zhao P, Turdi S, Dong F, Xiao X, Su G, Zhu X, Scott GI, Ren J. Cardiac-specific overexpression of insulin-like growth factor I (IGF-I) rescues lipopolysaccharide-induced cardiac dysfunction and activation of stress signaling in murine cardiomyocytes. *Shock* 32: 100-107, 2009.
35. Zhao P, Wang J, He L, Ma H, Zhang X, Zhu X, Dolence EK, Ren J, Li J. Deficiency in TLR4 signal transduction ameliorates cardiac injury and cardiomyocyte contractile dysfunction during ischemia. *J. Cell. Mol. Med.* in press.
36. Zhu MJ, Du M, Nathanielsz PW, Nijland MJ, Hess BW, Moss GE, Ford SP. Down-regulation of growth signaling pathways linked to reduced cotyledonary vascularity in placentomes of overnourished, obese pregnant ewes. *Placenta* 30: 405-410, 2009

Five abstracts from the CCRAM group have been accepted for presentation at the AHA Scientific Sessions

Abstracts and Presentations (Second Quarter, 2009)

1. Hua Y, Ren J. Insulin-like growth factor-I deficient mice exhibit resistance to abdominal aortic constriction-induced cardiac hypertrophy and contractile dysregulation: Role of microRNA-1, microRNA-133a and microRNA-208. *Circulation* 119:, 2009.
2. Li Q, Ma, H, Thomas DP, Kandadi M, Ren J. Forkhead transcription factor 3a (FOXO3a) is involved in the regulation of functional response to aging and stress in murine cardiomyocytes. *Circulation* 119:, 2009.
3. Heng Ma, Jingying Wang, Lin Leng, Richard Bucala, Jun Ren, Ji Li. Role for reduced MIF secretion in attenuated AMPK activation and ischemic recovery in the senescent heart. Scientific Sessions 2009 Resuscitation Science Symposium:
4. Heng Ma, Jingying Wang, Lin Leng, Richard Bucala, Jun Ren, Ji Li, Extracellular signal-regulated kinase (ERK) Mediates the Cardioprotective Effect of Macrophage Migration Inhibitory Factor (MIF) during Ischemia/Reperfusion. Scientific Sessions 2009 Resuscitation Science Symposium:
5. Wang J, Ma H, Zhang H, Zhao P, Ren J, Ford SP, Nathanielsz PW and Li J. Impairment of JNK-IRS-I signaling cascades and cardiac function in fetal heart during overnourished obese sheep pregnancy. *American Heart Association (AHA) 2009 Scientific Session*, Orlando, FL, Nov. 14-18, 2009

Abstracts and Presentations (Second Quarter, 2009)

6. Ma H, Wang J, Thomas DP, Leng L, Wang W, Merk M, Zierow S, Bernhagen J, Ren J, Bucala R and Li J. Role for reduced MIF secretion in attenuated AMPK activation and ischemic recovery in the senescent heart. *American Heart Association (AHA) 2009 Resuscitation Science Symposium (ReSS)*, Orlando, FL, Nov. 14-15, 2009
7. Zhang X, Wang J, Li W and Li J. Natural antioxidant-isoliquiritigenin protects heart against ischemia/reperfusion injury via activation of cardioprotective signaling pathways. *American Heart Association (AHA) 2009 Resuscitation Science Symposium (ReSS)*, Orlando, FL, Nov. 14-15, 2009
8. Wang J, Yang L, Rezaie AR and Li J. Activated protein C protects heart against ischemia-reperfusion injury via activating AMPK signaling pathway and decreasing inflammatory response. *American Heart Association (AHA) 2009 Resuscitation Science Symposium (ReSS)*, Orlando, FL, Nov. 14-15, 2009
9. Cerbulo Vazquez A., R. Romero, M.J. Nijland, M. Zhu, P.W. Nathanielsz, and S.P. Ford. 2009. Maternal obesity (MO) and nutritional excess (NE) two months prior and throughout sheep pregnancy produce a fetal inflammatory state in fetal (F) peripheral blood monocytes (PMBCs) and splenic immune cells. Proceedings, Society for Gynecologic Investigation, Glasgow, Scotland, UK.
10. Ford, S.P., D.T. Smith, N.M. Long, A. Uthlaut, L.A. George, P.W. Nathanielsz, and M.J. Nijland. 2009. Maternal obesity (MO) and nutritional excess (NE) results in delivery of lambs with increased body fat and impaired pancreatic function at birth. Proceedings, Society for Gynecologic Investigation, Glasgow, Scotland, UK.
11. Ford, S.P., B.E. Burt, L.A. George, M.J. Nijland, and P.W. Nathanielsz. 2009. Decreased nutrition in the first half of pregnancy impairs ovarian progesterone (P4) secretion and decreases fertility in offspring. Proceedings, Society for Gynecologic Investigation, Glasgow, Scotland, UK.
12. Nijland, M.J., M. Loehle, M.Schwab, S. Kadner, S.P. Ford, P. Lawrence, J.T. Brenna, and P.W. Nathanielsz. 2009. Dose response effects of betamethasone (BM) on maturation of the fetal sheep lung: is the clinically administered glucocorticoid (GC) dose supramaximal? Proceedings, Society for Gynecologic Investigation, Glasgow, Scotland, UK.
13. Nijland, M.J., B. Burt, L.A. George, P.W. Nathanielsz, and S. P. Ford. 2009. Maternal nutrient restriction (MNR) in sheep during early gestation depresses offspring hypothalamo-pituitary-adrenal axis (HPAA) stress responses but not pituitary responses to CRH/AVP or adrenal responses to an ACTH challenge. Proceedings, Society for Gynecologic Investigation, Glasgow, Scotland, UK.
14. Nijland, M.J., R. Wimmer, N. Zurcher, J. Ren, P.W. Nathanielsz, and S.P. Ford. 2009. Maternal obesity induces ovine fetal vascular endothelial dysfunction at 0.9 gestation. Proceedings, Society for Gynecologic Investigation, Glasgow, Scotland, UK.
15. Zhu, M.J., M. Du, B.W. Hess, P.W. Nathanielsz, and S.P. Ford. 2009. Maternal obesity (MO) induces an inflammatory response in ewe placentomes at 0.5 gestation (G). Proceedings, Society for Gynecologic Investigation, Glasgow, Scotland, UK.
16. Wang, J., H. Ma, H. Zhang, P. Zhao, J. Ren, S.P. Ford, P.W. Nathanielsz, and J. Li. 2009. Impairment of JNK-IRS-I signaling cascades in maternal and fetal heart tissue during overnourished obese sheep pregnancy. Proceedings, Society for Gynecologic Investigation, Glasgow, Scotland, UK (Abstract #139).
17. Zhou, Y., Mark Nijland, Myrna Miller, Stephen Ford, Peter Nathanielsz. 2009. The influence of maternal early to mid-gestation nutrient restriction on long chain polyunsaturated fatty acids in fetal sheep. The International Congress of Nutrition, Bangkok, Thailand.
18. Long, N.M., M. Zhu, M. Du, P.W. Nathanielsz, S.P. Ford. 2009. Effects of maternal obesity and high nutrient intake on fetal adiposity and associated fatty acid and glucose transporter expression. Proceedings, Society for the Study of Reproduction, Pittsburgh, PA
19. George, L.A., A.B. Uthlaut, N.M. Nathanielsz, S.P. Ford. 2009. Effects of diet-induced weight gain prior to and during pregnancy on body fat deposition and insulin sensitivity. Proceedings, Society for the Study of Reproduction, Pittsburgh, PA
20. Zhang, L., S.M. Hein, N.M. Long, P.W. Nathanielsz, S.P. Ford. 2009. Maternal obesity (MO) and Nutritional excess (NE) decrease pancreatic beta-cell numbers and function by late gestation. Proceedings, Society for the Study of Reproduction, Pittsburgh, PA
21. Ma, Y., P.W. Nathanielsz, S.P. Ford. 2009. Angiogenic factor expression is correlated with cotyledonary (COT) blood flow and fetal growth during gestation of overnourished, obese ewes. Proceedings, Society for the Study of Reproduction, Pittsburgh, PA

Seminars Presented (Second Quarter, 2009)

1. Ren J. *"Cardiac health in obesity and diabetes"*, The First Affiliated Hospital of Xinjiang Medical University, Urumqi, China, June 2009.
2. Ren J. *"NIH Millennium Promise Award for Non-communicable Chronic Diseases"*, the Fourth Military Medical University, Xi'an, China, July 2009.
3. Ren J. *"Mitochondrial aldehyde dehydrogenase (ALDH2) and alcoholic cardiomyopathy"* the 11th Chinese Conference on Cell Biology & Xi'an International Conference on Cell Biology, Xi'an, China, July 2009.
4. Ren J. *"Cardiac disease in cardiometabolic syndrome: Pathogenesis and Protection"*, the State Graduate Summer School, Xi'an, China, July 2009.
5. Ren J. *Alcoholic cardiomyopathy: pathogenesis and therapeutics"*, the State Graduate Summer School, Xi'an, China, July 2009.
6. Ren J. *"NIH Millennium Promise Award for Non-communicable Chronic Diseases"*, the Fourth Military Medical University, Xi'an, China, July 2009.
7. Ren J. *"Cardiomyopathy in Cardiometabolic Syndrome: Pathogenesis and Protection"*, Xi'an International Cardiovascular Forum 2009 & 14th Xijing Hospital – Mayo Clinic Cardiovascular Symposium, Xi'an, China, July 2009.
8. Ren J. *"Cardiac contractile function in critical care medicine: problem and hope"*, Department of Anesthesia, Xijing Hospital, Xi'an, China, August 2009.
9. Sreejayan N, *"Cell Cell Communication: Emerging Strategies in Drug Discovery"* Manipal College of Pharmaceutical Sciences, Manipal University, India, July 2009.
10. Ford, S.P. *Optimal Nutrition in the womb: Key to Reducing Offspring Obesity, Insulin Resistance and Type II Diabetes in Humans and Animals.* Presented at the West Virginia University Reproductive Physiology Reunion Symposium, Morgantown, WV, July 16th – 18th, 2009.

Training High School and Undergraduate Students

Several high school and undergraduate students received training in the labs of CCRAM investigators this summer. Kelsey J Haugh (Junior) from South Dakota Douglas High School, Gretchen K McCormick (Senior) from Mountain View High School, joined Dr. Li's lab supported by the Summer Research

Assistant Program (SARP). , 2009. Yuanda Li (Junior), Gavin Lawis (Biology), Malav K Patel (Biology) also received training in Dr. Li's lab. Other SARP students enrolled in various labs of CCRAM investigators include: Cecilai Soto (Denver, CO, Du Lab), Araolyn Mosby

(South Bend, IA., Zhu lab), Shantelle Fritz (Douglas, WY, Sree lab)

Since its inception in 2004, CCRAM has procured about 22 million dollars in research and infrastructure support (including InBRE)

Grants Awarded and Pending

1. NIH-INBRE Grant (5P20 RR016474) project entitled: "Impact of maternal obesity and dietary excess on fetal adiposity and offspring health" S.P. Ford Mentor: Funds for entire project \$703,450.20; 07/01/2009-06/30/2014.
2. Rezaie R and Li J. *Protease Activated Receptor-I Signaling by Coagulation Proteases.* NHLBI/NIH R01 (\$315,350 direct cost for LiLab, Score: 23, fundable score).

CCRAM

Center for Cardiovascular Research and Alternative Medicine

Address

University of Wyoming, School of Pharmacy
1000 E. University Ave, Department 3375
Laramie, WY 82072

Phone: (307)766-6138

Fax: (307)766-2953

E-mail: sreejay@uwyo.edu

We're on the Web

<http://www.uwyo.edu/pharmacy/info.asp?p=4057>

