

C-CRAM 2005 Annual Report (PI= Culver, Ren and Sreejayan)

- A. Research paper in print/in press in 2005 (alphabetically by last name of 1st author):**
1. Ceylan-Isik AF, LaCour KH, Ren J. Gender disparity of streptozotocin-induced intrinsic contractile dysfunction in murine ventricular myocytes: Role of chronic activation of Akt. *Clin Exp Pharm Physiol*. in press.
 2. Ceylan-Isik AF, LaCour KH, Ren J. Sex difference in cardiomyocyte function in normal and metallothionein transgenic mice: the effect of diabetes mellitus. *J. Appl. Physiol*. in press.
 3. Ceylan-Isik AF, Ren J. Gender difference in cardiac excitation-contraction coupling: Role of estrogen. *Cardiology* 1:1-7, 2005.
 4. Ceylan-Isik AF, Wu S, Li Q, Li SY, Ren J. High-dose benfotiamine rescues cardiomyocyte contractile dysfunction in streptozotocin-induced diabetes mellitus. *J. Appl Physiol*. in press.
 5. Dong F, Esberg LB, Roughead ZK, Ren J, Saari JT. Increased contractility of cardiomyocytes from copper-deficient rats is associated with up-regulation of the cardiac insulin-like growth factor-I receptor. *Am J Physiol: Heart Circ Physiol* 289:H78-H84, 2005.
 6. Dong F, Fang CX, Yang XP, Zhang X, Ren J. Cardiac over-expression of catalase rescues insulin resistance-induced cardiac contractile dysfunction: Role of oxidative stress, protein carbonyl formation and insulin sensitivity. *Diabetologia* acceptable pending minor revision.
 7. Dong F, Ford SP, Fang XC, Nijland MJ, Nathanielsz PW, Ren J. Intrauterine nutrition deficiency during early to mid gestation up-regulates cardiac insulin-like growth factor (IGF) receptors associated with ventricular hypertrophy in fetal sheep. *Growth Horm IGF Res* 15: 291-299, 2005.
 8. Dong F, Zhang X, Culver B, Chew, HG, Jr., Kelley RO, Ren J. Dietary iron deficiency induces ventricular dilation, mitochondrial ultra-structural aberrations and cytochrome C release: Involvement of nitric oxide synthase and protein tyrosine nitration. *Clin Science* 109: 277-286, 2005.
 9. Dong F*, Zhang X*, Li SY, Zhang Z, Ren Q, Culver B, Ren J. Involvement of NADPH oxidase and JNK in homocysteine-induced oxidative stress and apoptosis in human umbilical vein endothelial cells. *Cardiovasc. Toxicol.* 5: 9-20, 2005 (*: equal first authorship)..
 10. Dong F, Zhang X, Ren J. Leptin regulates cardiomyocyte contractile function through endothelin-1 receptor - NADPH Oxidase pathway. *Hypertension* in press.
 11. Dong F, Zhang X, Wold LE, Ren Q, Zhang Z, Ren J. Endothelin-1 enhances oxidative stress, cell proliferation and reduces apoptosis in human umbilical vein endothelial cells: Role of ET_B receptor, NADPH oxidase and caveolin-1. *Br. J. Pharmacol.* 145: 323-333, 2005.
 12. Dong F, Zhang X, Yang X, Yang H, Zhang Z, Culver B, Ren J. Impaired cardiac contractile function in ventricular myocytes from leptin deficient ob/ob obese mice. *J. Endocrinol* in press.
 13. Duan J, Dai S, Fang XC, Sun RY, Shavali S, Sharma SK, Ebadi M, Ren J. Phytoestrogen α -zearalanol antagonizes homocysteine-induced imbalance of nitric oxide/endothelin-1 and apoptosis in human umbilical vein endothelial cells (HUVEC). *Cell. Biochem. Biophys.* in press.
 14. Fang CX, Dong F, Ren BH, Epstein PN, Ren J. Metallothionein alleviates insulin resistance-induced cardiac contractile dysfunction: Role of Akt phosphorylation, PTB1B, PPAR γ and c-Jun. *Diabetologia* 48:2412-2421, 2005.
 15. Fang CX, Doser TA, Yang X, Sreejayan N, Ren J. Metallothionein antagonizes aging-induced cardiac contractile dysfunction: Role of PTP1B, insulin receptor tyrosine phosphorylation and Akt. *Aging Cell* in press.

16. Gupta A, Aberle II NS, Kapoor R, Ren J, Sharma A. Bigendothelin-1 via p38-MAPK dependent mechanism regulates adult rat ventricular myocyte contractility in sepsis. *Biochimica et Biophysica Acta* 1741:127-139, 2005.
17. Gupta A, Aberle II NS, Ren J, Sharma AC. Bigendothelin-1 modulates ventricular myocyte contractile function via a p38-MAPK-dependent mechanism in sepsis. *J. Mol. Cell. Cardiol.* 38: 527-537, 2005.
18. Li SY*, Fang CX*, Aberle NS II, Ren BH, Ceylan-Isik AF, Ren J. Inhibition of PI-3 kinase/Akt/mTOR but not calcineurin signaling reverses insulin-like growth factor I-induced protection against glucose toxicity in cardiomyocyte contractile function. *J. Endocrinol.* 186: 491 – 503, 2005 (*: equal first authorship).
19. Li SY, Du M, Dolence EK, Fang CX, Mayer GE, Ceylan-Isik AF, LaCour KH, Yang X, Wilbert CJ, Sreejayan N, Ren J. Aging induces cardiac diastolic dysfunction, oxidative stress, accumulation of advanced glycation endproducts and protein modification. *Aging Cell* 4: 57-64, 2005.
20. Li SY, Golden KL, Jiang Y, Wang GJ, Privratsky JR, Zhang X, Eason AR, Culver B, Ren J. Inhibition of sarco(endo)plasmic reticulum Ca^{2+} -ATPase (SERCA) differentially regulates contractile function in cardiac myocytes from normotensive and spontaneously hypertensive rats: role of Ca^{2+} regulatory proteins. *Cell. Biochem. Biophys.* 42: 1-12, 2005.
21. Li SY, Li Q, Shen J, Dong F, Sigmon VK, Liu Y, Ren J. Attenuation of acetaldehyde-induced cell injury by overexpression of aldehyde dehydrogenase-2 transgene in human cardiac myocytes: Role of MAP kinase signaling. *J. Mol. Cell. Cardiol.* in press.
22. Li SY, Liu Y, Sigmon VK, McCort A, Ren J. High fat diet enhances advanced glycation endproduct (AGE) and apoptosis: Role of nuclear O-GlcNAc modification and p38 MAP kinase activation. *Diabetes Obese. Metab.* 7: 448-454, 2005.
23. Li SY, Yang X, Ceylan-Isik AF, Du M, Sreejayan N, Ren J. Cardiac contractile dysfunction in ob/ob obesity is accompanied with NADPH Oxidase Activation, oxidative modification of sarco(endo)plasmic reticulum Ca^{2+} -ATPase and myosin heavy chain isozyme switch. *Diabetologia* in press.
24. McBride SM, Flynn FW, Ren J. Cardiovascular alteration and treatment of hypertension: Do men and women differ? *Endocrine* in press.
25. Muralikrishnan D, Ren J. The emerging role of coenzyme Q-10 in aging, neurodegeneration, cardiovascular disease, cancer and diabetes mellitus. *Curr. Neurovasc. Res.* in press.
26. Relling DP, Esberg LB, Fang CX, Johnson WT, Murphy EJ, Carlson EC, Saari JT, Ren J. High fat diet induced-juvenile obesity leads to cardiomyocyte dysfunction and upregulation of Foxo3a transcription factor independent of lipotoxicity and apoptosis. *J. Hypertension* in press.
27. Ren J, Fang CX. Small guanine nucleotide-binding protein Rho and myocardial function. *Acta Pharmacologica Sinica* 26:279-285, 2005.
28. Ren J, Relling DP. Interaction between tumor necrosis factor- α and leptin-induced inhibition of cardiac contractile function in isolated ventricular myocytes. *Cytokine* in press.
29. Ren J, Relling DP. Leptin-induced suppression of cardiomyocyte contraction is amplified by ceramide. *Peptide* in press.
30. Ren J, Wei CM. New sniper assignment for a celebrity – Role of endothelin-1 in diabetic cardiomyopathy. *J. Cardiothoracic Renal Res.* in press.
31. Ren J, Wu S. A burning issue: Do sepsis and systemic inflammatory response syndrome (SIRS) directly contribute to cardiac dysfunction? *Frontier Biosci* 11:15-22, 2006.
32. Ren J. Hope or hype: the obsession for tetrahydrobiopterin and GTP cyclohydrolase I (GTPCH I) in cardiovascular medicine. *J. Cardiothoracic Renal Res.* in press.
33. Ren J. Lessons from the leptin paradox in cardiac regulation - too much versus too little. *J. Physiol* 565: 347, 2005.

34. Shen Q, Du M, Ren J. Fitness or fatness: the debate continues for AMP-activated protein kinase (AMPK) in the heart. *Curr. Cardiol. Rev.* in press.
35. Wold LE, Aberle II NS, Ren J. Doxorubicin induces cardiomyocyte dysfunction via a p38 MAP kinase-dependent oxidative stress mechanism. *Cancer Detect. Prev.* 29: 294-299, 2005.
36. Wold LE, Ceylan-Isik AF, Fang CX, Yang X, Li SY, Sreejayan N, Privratsky JR, Ren J. Metallothionein alleviates cardiac dysfunction in streptozotocin-induced diabetes: Role of Ca²⁺ cycling proteins, NADPH oxidase, poly(ADP-Ribose) polymerase and myosin heavy chain isozyme. *Free Rad Biol Med.* in press.
37. Wold LE, Ceylan-Isik AF, Ren J. Oxidative stress and stress signaling: the menace of diabetic cardiomyopathy. *Acta Pharmacologica Sinica* 26:908-917, 2005.
38. Wold LE, Dutta K, Mason MM, Ren J, Cala SE, Schwanke ML, Davidoff AJ. Impaired SERCA function contributes to cardiomyocyte dysfunction in insulin resistant rats. *J. Mol. Cell. Cardiol.* 39:297-307, 2005.
39. Wu S, Fang CX, Kim J, Ren J. Enhanced pulmonary inflammation following experimental intracerebral hemorrhage. *Exp. Neurol.* acceptable pending minor revision.
40. Wu S, Ren J. Benfotiamine alleviates diabetes-induced cerebral oxidative damage independent of advanced glycation end-product, tissue factor and TNF- α . *Neurosci Lett* in press.
41. Yang X, Doser TA, Fang CX, Nunn JM, Janardhanan R, Zhu MJ, Sreejayan N, Quinn MT, Ren J. Metallothionein prolongs survival and antagonizes senescence-associated cardiomyocyte diastolic dysfunction: Role of oxidative stress. *FASEB J.* in press.
42. Yang X, Li SY, Dong F, Ren J, Sreejayan N. Insulin-sensitizing and cholesterol lowering effects of chromium (phenylalanine)₃. *J. Inorganic Biochem.* acceptable pending minor revision.
43. Yang X, Palanichamy K, Ontko AC, Rao MNA, Fang CX, Ren J, Sreejayan N. A newly synthetic chromium complex - chromium (phenylalanine)₃ improves insulin responsiveness and reduces whole body glucose tolerance. *FEBS Lett* 579: 1458-1464, 2005
44. Yang X, Sreejayan N, Ren J. Views from within and beyond: narratives of cardiac contractile dysfunction under senescence. *Endocrine* 26:127-138, 2005.
45. Yang X, Thomas DP, Zhang X, Culver BW, Alexander BM, Murdoch WJ, Rao MNA, Tulis DA, Ren J, Sreejayan N. Curcumin inhibits PDGF-stimulated vascular smooth muscle cell function and injury-induced neointima formation. *Arter. Thromb. Vasc. Biol.* in press.
46. Yang X, Zhu MJ, Sreejayan N, Ren J, Du M. Angiotensin II promotes smooth muscle cells proliferation and migration through EGF-receptor pathway. *Molecules Cells* 20:263-270, 2005.
47. Zhang X, Dong F, Li Q, Borgerding AJ, Klein AL, Ren J. Cardiac overexpression of catalase antagonizes ADH-associated exacerbation of contractile depression and stress signaling following acute ethanol exposure in murine myocytes. *J. Appl Physiol.* 99:2246-2254, 2005.
48. Zhang X, Dong F, Ren J, Driscoll MJ, Culver B. High dietary fat induces NADPH oxidase-associated oxidative stress and inflammation in rat cerebral cortex. *Exp. Neurol.* 191:318-325, 2005.

Statistics of paper by group members – congratulations to these big paper winners:

Asli Ceylan-Isik: 9 (4 being the first author);
Cindy X. Fang: 13 (3 being the first author);
Shan Wu: 4 (2 being the first author);
Xiaoping Yang: 12 (6 being the first author);
Tom Doser: 2;
Karissa LaCour: 3;

Feng Dong: 12 (8 being the first author)
Shi-Yan Li: 10 (6 being the first author)
Qun Li: 3
Xiaochun Zhang: 10 (3 – first author)
Jennifer Nunn: 1
Sreejayan: 10

B. Meeting presentation at the national or international levels - 2005

1. Experimental Biology 2005 - San Diego, CA, March 2005 (*indicates presenter)

1. Saari JT*, Dong F, Esberg LB, Ren J. Increased contractility is associated with increased cardiac IGF-I receptor protein in copper-deficient cardiomyocytes. *FASEB J.* 19: A1486, 2005.
2. Gupta A, Aberle NS, II, Ren J, Sharma AC*. Bioendothelin-1 via p38-MAPK dependent mechanism regulates adult rat ventricular myocytes (ARVM) contractility in sepsis. *FASEB J.* 19: A1550, 2005.
3. Wu S*, Li Q, Li SY, Du M, Ren BH, Aberle NS, II, Epstein PN, Ren J. Cardiac overexpression of antioxidant catalase prevents aging-induced cardiac diastolic contractile dysfunction, protein damage and proteomic alterations. *FASEB J.* 19: A701, 2005.
4. Fang CX*, Dong F, Ren BH, Epstein PN, Ren J. Metallothionein alleviates insulin resistance-induced cardiac contractile dysfunction: Role of Akt, PTB1B and PPAR γ . *FASEB J.* 19: A1686, 2005.

2. 2nd Annual Symposium of the AHA Council on Basic Cardiovascular Sciences - Targeting Heart Failure: New Science, New Tools, New Strategies, July 24-27, 2005, Keystone, CO

5. Sreejayan N*, Yang X, Thomas DP, Zhang X, Culver B, Ren J. Curcumin attenuates neointimal development and collagen content following arterial injury in rats.

3. 12th World Congress for Heart Diseases - Vancouver, BC, Canada, July 2005

6. Dong F, Fang CX, Ren BH, Ren J*. Cardiac over-expression of catalase ablates insulin resistance-induced cardiac contractile dysfunction independent of insulin receptor signaling. *J. Heart Disease* 4: 57, 2005.

4. Society for Neuroscience Meeting: Washington D.C. November 2005

7. Culver B*, Zhang X, Dong F, Mayer G, Gardner K, Ren J. Cyclooxygenase-2 is a target during the acute stage of methamphetamine-induced neurotoxicity and its selective inhibition exacerbates the dopamine depletion in striatum. Society for Neuroscience Meeting 2005.
8. Li Q*, Ren J, Zhang XC. Chronic alcohol consumption reduces activation of mammalian target of rapamycin (mTOR) and ribosomal p70s6 kinase in cerebral cortex associated with glucose intolerance. Society for Neuroscience, Washington, DC, November 2005.

5. Other National Meeting Presentation from our collaborators:

9. Xu, P, Li SY, Li Q, Ren J, Shen Y, Radosz M. Modified polymers as safe and efficient gene delivery carriers. 230th ACS National Meeting, Washington, DC, 8/28, 2005, POLY-335.
10. Shen Y, Xu P, Li SY, Li Q, Ren J, Kirk EV, Murdoch WJ, Radosz M. Biodegradable cationic polymers as efficient gene delivery carriers. 229th ACS National Meeting, San Diego, CA, March 13-17, 2005, PMSE-362

C. Proposal submitted or grant dollars awarded for the year of 2005:

Total \$\$ awarded (direct + indirect) for fiscal year 2005: \$139,000 to Sreejayan and \$305,331 to Ren.

A C-CRAM center project grant (PI: Ren, project leaders: Sreejayan and Li SY) was submitted to NIH/NCCAM "Treatment of Diabetes and Vascular Injury with Natural Products"

D. Patent: Sreejayan N, Yang X, Ren J. UW 05-094 "Application of chromium-D-phenylalanine complexes in the treatment of diabetes, obesity and related diseases" (US provisional application 60/694,543).

E. Awards & etc:

- (1). Dr. Sreejayan received the inaugural C-CRAM Research Award (7/05) and the American Diabetes Association Junior Investigator Research Award to work on chromium complexes in diabetes.
- (2). Graduate students Cindy Fang and Olalekan Ajayi (mentor: Ren and Culver, respectively) were chosen as graduate students by Dean Roth of UW graduate school to participate in National Institute of Health Biomedical Science Awareness Project.

Merry Christmas and Happy New Year!!!