



## Lisa Stehno-Bittel

### Department Chair & Professor

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## EDUCATION

- Post-Doctoral fellowship, Pharmacology, Mayo School of Medicine, Rochester, MN, 1995.
- Ph.D., Physiology, University of Missouri, Columbia, MO, 1992.
- B.S., Physical Therapy, University of Kansas, Kansas City, KS, 1983.

## ACADEMIC / CLINICAL APPOINTMENTS

Professor, Department of Physical Therapy and Rehabilitation Sciences  
Professor, Department of Anatomy and Cell Biology (adjunct appointment)  
Scientific Director, Great Plains Diabetes Institute

## TEACHING RESPONSIBILITIES

- PTRS 810 - Case Studies in Pathophysiology (post-professional course)
- PTRS 815 - Case Studies in Differential Diagnosis (post-professional course)
- PTRS 855 – Pharmacology
- PTRS 880 - Differential Diagnosis of the General Medical Condition

## RESEARCH INTERESTS

The complications of diabetes along with methods for curing type 1 diabetes. The laboratory is involved in basic benchtop research aimed at curing diabetes along with community-based studies on the ability to prevent type 2 diabetes or improve the quality of life for those already diagnosed with type 2 diabetes.

## RECENT PUBLICATIONS

- Stehno-Bittel L**, Laughlin M, Sturek M. Exercise training alters Ca<sup>2+</sup> release from coronary smooth muscle sarcoplasmic reticulum. *Am. J. Physiol.* 259:H643-647, 1990.
- **Stehno-Bittel L**, Laughlin M, Sturek M. Exercise training depletes sarcoplasmic reticulum Ca<sup>2+</sup> in coronary smooth muscle. *J. Appl. Physiol.* 71(5): 1764-1773, 1991.
  - **Stehno-Bittel L**, Luckhoff A, Clapham D. Calcium release from the nucleus by InsP<sub>3</sub> receptor

channels, *Neuron* 14:1-5, 1995.

- **Stehno-Bittel L**, Krapivinsky G, Krapivinsky L, Perez C, Clapham D. The G protein  $\beta\gamma$  subunit transduces the muscarinic receptor signal for  $\text{Ca}^{2+}$  release in *Xenopus* oocytes, *J. Biol. Chem.* 270:30068-30074, 1995.
- **Stehno-Bittel L**, Perez-Terzic C, and D. Clapham. Diffusion across the nuclear envelope inhibited by depletion of the nuclear  $\text{Ca}^{2+}$  store, *Science* 270:1835-1838, 1995.
- Perez-Terzic C, Pyle J, **Stehno-Bittel L**, Jaconi M, Clapham D. Conformational states of the nuclear pore complex induced by depletion of nuclear  $\text{Ca}^{2+}$  stores, *Science* 273: 1875-1877, 1996.
- **Stehno-Bittel L**, Perez-Terzic C, Luckhoff A, Clapham D. Nuclear ion channels and regulation of the nuclear pore. *Soc. Gen. Physiol. Ser.* 51:195-207, 1996.
- Perez-Terzic C, **Stehno-Bittel L**, Clapham D. Fluorescent dye behavior in the nuclear environment. *Cell Calcium* 21:275-282, 1997.
- Gum G, Reddy GK, **Stehno-Bittel L**, Enwemeka CS. Combined ultrasound, electrical stimulation, and laser promote collagen synthesis with moderate changes in tendon biomechanics. *Am. J. Phys. Med. Rehab.* 76:288-296, 1997.
- **Stehno-Bittel L**, Reddy GK, Gum S, Enwemeka CS. Biochemistry and Biomechanics of healing tendon: Prt 1. The effects of rigid plaster casts and functional polyurethane casts. *Med. Sci. Sports Exerc.* 30:788-793, 1998.
- Reddy GK, Gum S, **Stehno-Bittel L**, Enwemeka CS. Biochemistry and Biomechanics of healing tendon: Prt 2. Effects of combined laser therapy and electrical stimulation, *Med. Sci. Sports Exerc.* 30:794-800, 1998.
- Reddy GK, **Stehno-Bittel L**, Enwemeka CS, Laser photostimulation of collagen production in healing rabbit Achilles tendon. *Las. Surg. Med.* 22:281-287, 1998.
- Lee MA, Dunn R, Clapham D, **Stehno-Bittel L**, Calcium control of nuclear pore permeability. *Cell Calcium* 23:91-101, 1998.
- Reddy GK, Enwemeka CS, **Stehno-Bittel L**, Comparison of biomechanical and biochemical properties of the Achilles tendon, *Lasers Surg. Med.* 22:281-287, 1999.
- Reddy GK, **Stehno-Bittel L**, Enwemeka CS. Matrix remodeling in regenerating Achilles tendon, *Wound Repair and Regeneration.* 7:518-527, 1999.
- Chi L, Li Y, **Stehno-Bittel L**, Gao J, Morrison DC, Stechschulte DJ, Kilepan KN. Interleukin-6 production by endothelial cells via stimulation of protease-activated receptors is amplified by endotoxin and tumor necrosis factor- $\alpha$ . *Interferon & Cytokine Res.* 21:231-240, 2001.
- Reddy GK, **Stehno-Bittel L**, Enwemeka CS. Laser therapy accelerates wound healing. *Wound Repair and Reg.* 9:248-256, 2001.
- Reddy GK, **Stehno-Bittel L**, Hamade S, Enwemeka CS, Biomechanical integrity of bone in experimental diabetes. *Diabetes Res. and Clin. Pract.* 54:1-8, 2001.
- Timberlake GT, Reddy GK, **Stehno-Bittel L**, Weber JF, Amslinger S, Givens RS, Photoactivated coumaryl-diazopyruvate fluorescent label for amine functional groups of tissues containing type-1 collagen. *Photochem. Photobiol.* 76:473-479, 2002.
- Reddy GK, **Stehno-Bittel L**, Enwemeka CS. Glycation-induced matrix stability in the rabbit achilles tendon. *Arch Biochem Biophys.* 15;399(2):174-80, 2002.
- Chi L, **Stehno-Bittel L**, Smirnova IV, Stechschulte D, Dilepan KN, The effects of mast cell granules on calcium mobilization, MAP kinase activation and NF- $\kappa$ B translocation in endothelial cells. *Mediators of Inflammation.* 12:79-87, 2003.
- Burns, D, **Stehno-Bittel L**, Kawase, T., Calcitonin gene-related peptide elevates calcium and polarizes membrane potential in MG63 cells by both cAMP-independent and -dependent mechanisms. *Am. J. Physiol. Cell Physiol.* 287(2):C457-67, 2004.
- Fedoryak OD, Searls Y, Smirnova IV, Burns D, **Stehno-Bittel L**, Spontaneous nuclear  $\text{Ca}^{2+}$  oscillations in subcellular compartments of vascular smooth muscle cells rely on different  $\text{Ca}^{2+}$  pools, *Cell Res*, 14(5):379-88, 2004.
- Searls Y, Smirnova IV, Fegley BR, **Stehno-Bittel L**, Exercise attenuates diabetes-induced ultrastructural changes in rat cardiac tissue, *Med. Sci. Sports Ex*, 36(11):1863-70, 2004.

- MacGregor, R., Williams, S.J., Tong, P.Y., Kover, K., Moore, W.V., **Stehno-Bittel, L.** Small rat islets are superior to large islets in function and transplantation outcomes, *Am J Physiol Endocrinol Metab.* 290(5):E771-779, 2006.
- Sui, Y., **Stehno-Bittel, L.**, Li, S., Loganathan, R., Dhillon, NK., Pinson, D., Nath, A., Kolson, D., Narayan, O., Buch, S., CXCL10-induced cell death in neurons: role of calcium dysregulation, *Eur J Neurosci*, 23(4):957-964, 2006
- Loganathan, R., Searls, Y. M., Smirnova, I.V. **Stehno-Bittel, L.** Exercise induced benefits in individuals with Type 1 diabetes, *Physical Therapy Reviews*, 11:77-89, 2006.
- Unruh, J.R., Price, E.S., Molla, R.G., **Stehno-Bittel, L.**, Johnson, C.K., Hui, R. Two-Photon Microscopy with Wavelength Switchable Fiber Laser Excitation, *Optics Express*, 14:9825-9831, 2006.
- Smirnova IV, Kibiryeva N, Vidoni E, Buñag RD, **Stehno-Bittel L:** Abnormal EKG stress test in rats with type 1 diabetes is deterred with low-Intensity exercise program. *Acta Diabetologica*, 2006 43(3): 66-74.
- Al-Jarrah, M., Pothakos, K., Novikova, L., Smirnova, I.V., Kurz, M.J., **Stehno-Bittel, L.**, Lau, YS. Endurance exercise promotes cardiorespiratory rehabilitation without neurorestoration in the chronic mouse model of Parkinsonism with severe neurodegeneration. *Neuroscience*. 2007 149(1):28-37.

## CURRENT GRANTS

- R01 NIH/NICHHD, Lau (PI), 5/2003-4/2008

Impact of Exercise on Parkinson's Disease Therapy

The purpose of the grant is to determine the impact of endurance aerobic exercise on the drug efficacy on a chronic mouse model of Parkinsons Disease. Neurological changes in response to exercise are being monitored as well as behavioral and functional improvements. We are completing EMG studies characterizing the tone in the PD model, as well as microscopy analysis of changes in the brain.

Role: Co-I

- Research Development Grant, Stehno-Bittel (PI), 7/2005-6/2008

Rosebud Diabetes Research Foundation

Subcutaneous Islet Transplants for Type 1 Diabetes

This project is based on previous observations that smaller islets are superior to large ones for transplantation into the liver and kidney capsule. The goals of the project are to utilize small islets (< 125 mm) to attempt subcutaneous transplants in rats with type 1 diabetes.

Role: PI

- NIH/NIMH, Buch (PI), 7/2003 0 4/2008

Mechanism and therapy of SHIV encephalitis in macaques

Mechanism and Therapy of SHIV Encephalitis in Macaques

This grant will explore the role of PDGF in virus replication in macaque macrophage cultures and will also assess the role of IP-10 in neuronal dysfunction/death associated with SHIV-encephalitis. Delivery of liposomes carrying antisense DNA plasmids will be first optimized in macaque macrophage cell cultures followed by delivery and biodistribution in small animals such as rats. These studies will then form the basis for antisense delivery in infected macaques to interdict the disease process.

Role: Co-I

- Proteon Therapeutics, R41 Franano (PI), 8/2004 – 6/2008

Permanent Vasodilators for Improved Hemodialysis

The project is in collaboration with a start-up company that has an enzyme cocktail to permanently dilate vessels. The role of our laboratory is to test the vessels for biomechanical properties and compare them to normal veins and arteries, and to analyze the vessels for morphological changes.

Role: Co-I

- NIH/NICHHD, Buch (PI), 5/2006-4/2011

HIV-Encephalitis and Cocaine Abuse: Mechanism of Synergy and Therapy

The purpose of the project is to identify the interplay between HIV effects and symptoms with cocaine administration. My portion of the project is to complete live-cell experiments from cells infected with HIV and monitor the signaling changes when the cells are exposed to cocaine.

Role: Co-I

- NIH/NCRR, Hui (PI) 3/2006 – 8/2008

Portable and Wavelength-Tunable Two-Photon Microscopy

Portable and Wavelength-Tunable Two Photon Microscopy

The project encompasses testing a small tunable two-photon microscope for use on a variety of biological samples including stained tissue sections, monolayers of cultured cells, and intact islets. I provide the biological samples and analyze images for the engineers who have designed the microscope.

Role: Co-I

## RECENTLY COMPLETED GRANTS

- F31 HL076143, Johnson (Graduate student, PI), 4/01/04 – 3/30/07

NIH/NHLBI

Diabetes SMC changes reversed by islet transplants

This grant explores the ability of islet transplants to reverse the smooth muscle cell pathology associated with type 1 diabetes. Specifically, we are examining the change in calcium regulatory protein and in proteins responsible for proliferation of smooth muscle cells.

Role: Mentor Research Grant,

- Moore (PI), 1/2003-12/2006

Hall Foundation

Islet Transplantation for Type 1 Diabetes

This collaborative initiative investigates the different mechanisms for islet isolation in producing successful islet transplants and in looking for the long-term effects of the islet transplants. Our role in this project is to identify genetic and functional markers in islet cells that correlate with successful transplants.

- R01 HL55290 Stehno-Bittel (PI), 5/1999-4/20/05

NIH/GMS

Nuclear Calcium Regulates Structure/Function of Pore Complex

The long-term objective of this project was to investigate the effect of diabetes on the structure of the nucleus and specifically the nuclear pore complex.

- Training Grant, Fischer (PI), 2/2002-1/2005

NSF REU Site Award

Research Experience for Undergraduates in Biomedical Engineering

The goal of the project was to provide summer research projects for undergraduates in biomechanical engineering.

Role: Co-Director

- Research Grant, Talebi (PI), 7/2001-9/2003

Hall Foundation (years 1-2)

Functional Analysis of Two Mutations of KCNQ4 Potassium Channel

This collaborative project aimed at cloning two genetic mutations responsible for alterations in K channel activity and ultimately hearing loss.

Role: Co-I

- US Army, Hall (PI), 9/2000-2/2003

## Real-Time Imaging for Improved Detection and Discrimination of Breast Abnormalities

This collaborative project was aimed at inventing new forms of image processes to detect and diagnose breast tumors. Our role was to assist with image analysis and to measure the biomechanical properties of collagen-based phantoms used for testing the prototype equipment and software.

Role: Co-I Training Grant, Stehno-Bittel (PI), 5/2001-4/2002

US Dept. of Commerce - SABIT training grant

The purpose of the grant was to train post-doctoral fellows from countries comprising the former Soviet Union. Two fellows were trained on this grant and returned to the Ukraine in research positions.

## RECENT INVITED PROFESSIONAL & SCIENTIFIC PRESENTATIONS

"Metabolic Syndrome X: Evidence, Education, and Effective Intervention Strategies" Combined Sections Meeting of the American Physical Therapy Association, Drs, Patricia Kluding, Irina Smirnova, Yvonne Searls and I presented the opening half-day program at the APTA summer meeting, San Diego, CA, 2006

"Diabetes Induced Vascular Disease - Update" Scientific Forum XIV, Combined Meeting of International Association of Cardiologists (South American Society), Brazilian Society of Cardiology, Brazilian Society of Cardiovascular Surgery, Latin American Chapter of the International Society of Heart Research., Rio de Janeiro, Brazil. 2005

"Why are Large Vessels Affected Differently by Diabetes?" Scientific Forum XIV, Combined Meeting of International Association of Cardiologists (South American Society), Brazilian Society of Cardiology, Brazilian Society of Cardiovascular Surgery, Latin American Chapter of the International Society of Heart Research., Rio de Janeiro, Brazil. 2005

"Stroke Rehabilitation when Diabetes is Present" 38th Annual Underwriters National Conference, Kansas City, MO, 2005. Although this meeting was in Kansas City, it was the national annual meeting for underwriters.

"Islet Transplantation as a Means to Cure Type 1 Diabetes" Kansas Medical Education Foundation, Topeka, KS, 2004.

"Pharmacology for the Rehabilitation" Therapist Workshop, Cleveland, Ohio, 2000

"Cognitive deficits after stroke: Impact on rehabilitation" Physical Therapy 99: Meeting and Exposition of the American Physical Therapy Association, half day workshop with Drs. Pam Duncan, Patricia Pohl, and Joan McDowd, Washington DC. 1999

"Signal regulation in proliferating cells" Univ. of Alabama, Birmingham AL, 1998

"The effects of low energy lasers on fibroblasts, World Association of Laser Therapy Meeting, Kansas City, MO 1998

"Calcium gradients across the nuclear envelope", University of Missouri, Kansas City, MO, 1997

"Calcium regulation of the nuclear pore complex" Gordon Conference, Oxford, England, 1997

"Calcium regulation in the nucleus" Annual meeting of the Society of General Physiologists, Woods Hole, MA, 1995

"Sarcoplasmic reticulum calcium buffering in resting smooth muscle cells" Symposium: electrophysiology of the vascular wall, 5th World Congress for Microcirculation, Louisville, KY, 1991

"The effects of exercise on calcium regulation in coronary artery smooth muscle cells" Departamento de Medicina, Universidad de Sevilla, Spain, 1990

"The effects of exercise on coronary artery smooth muscle cells" Departamento de Fisiologia, Universidad de Madrid, Madrid, Spain, 1990

## **RECENT HONORS & AWARDS**

Travel Award, 1993, International Union of Pure and Applied Biophysics, Budapest, Hungary.

Outstanding Teacher Award, 1998, Physical Therapy Department, University of Kansas Medical Center, Kansas City, KS.

School of Allied Health Investigator of the Year Award, 1999, University of Kansas, Medical Center, Kansas City, KS.

### US patent pending:

Templated small islets and beta cells for diabetes treatment, Inventors: C. Berkland, L. Stehno-Bittel, T. Siahann, 2006

## **PROFESSIONAL & SCIENTIFIC MEMBERSHIPS**

- American Physical Therapy Association, Member.
  - American Diabetes Association, Member.
  - American Stroke Foundation, Board Member.
  - North American Regional Editor for *Physical Therapy Reviews*
- NIH Study Section Member, NCR, Shared Instrument Proposals, 2001-2006  
Reviewer for the following journals (current):

Biophysical Journal  
Laser Therapy  
Journal of Biological Chemistry  
Journal of Orthopaedic and Sports Physical Therapy  
Circulation Research  
American Journal of Physiology

Diabetes Advisory Council, State of Kansas mandated by the Department of Health and Environment, 2006- present.

National Advisory Committee, Diabetes Freedom Foundation, 2005.

Nominating Committee for the Academic Administrator's Special Interest Group within the American Physical Therapy Association, 2005- present.

Co-Founder, Diabetes Research Interest Group of Kansas City, 2002 – present.