

BIOGRAPHICAL SKETCH

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NAME Lyle L. Moldawer, Ph.D.		POSITION TITLE Professor of Surgery and Vice Chairman (Research)	
eRA COMMONS USER NAME LMOLDAWER			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Göteborgs Universitet, Göteborg, SWEDEN	Ph.D.	1986	Experimental Medicine

A. Positions and Honors.

Vice Chairman (Research), University of Florida College of Medicine, Gainesville, Florida, 2004-
Professor of Surgery (Tenure), University of Florida College of Medicine, Gainesville, Florida, 1996-
Associate Professor of Surgery, University of Florida College of Medicine, Gainesville, Florida 1993-1996
Associate Professor of Cell Biology and Anatomy, Cornell University Medical College, New York, New York .1991-1993
Associate Professor of Surgery, Cornell University Medical College, New York, New York. 1991-1993
Assistant Professor of Cell Biology and Anatomy, Cornell University Medical College, New York, New York.1988-1991
Assistant Professor of Surgery, Cornell University Medical College, New York, New York. 1987-1991

Federal Government Public Advisory Groups

Member, Special Scientific Review Group, Burn and Trauma Program Project Review, Biophysics and Biophysiology
Division, National Institutes of General Medical Sciences. 1989, 1991-1998, Chairperson, 1999.
Regular Member, Surgery Anesthesiology and Trauma Study Section, 2004-2009
Regular Member, Surgery B Study Section, Veterans Affairs Scientific Review Group, 2004-
Regular Member, Metabolic Pathology Study Section, DRG, 1995-1999
Special Member, Veterans Affairs/Defense Department Merit Review Committee for Combat Casualty Care and Wound
Repair, Department of Veterans Affairs, 1998
Member, Special Emphasis Panel, NIEHS, 1999, Special Emphasis Panel, NHLBI, 2003

Honors/Awards

University of Florida College of Medicine Prize in Basic Research, 2004
University of Florida Bank Award for Excellence in Research, 1997, 1999
NIH MERIT Award, R37 GM-40586-11, NIGMS, 1998-2006
Lester Dragstedt Scientist-Physician Award, 1998
Florida Blue Key Distinguished Faculty Award, 1999

B. Selected peer-reviewed publications (in chronological order). (Selected from a list of 301 peer reviewed)

- 1) Ginsberg, H., Moldawer, L.L., Sehgal, P.B, Redington, M., Kilian, P.L., Chanock, R.M., Prince, G.A. A unique mouse model to investigate the molecular pathogenesis of adenovirus pneumonia. *Proc Nat. Acad Sci* 88:1651-1655, 1991
- 2) Fischer, E., Poutsiaka, D.D., Van Zee, K.J., Marano, M.A., Rock, C.S., Kenney, J.S., Dinarello, C.A., Lowry, S.F., Moldawer, L.L. Interleukin-1 receptor antagonist circulates in experimental inflammation and in human disease. *Blood* 79:2196-2200, 1992.
- 3) Fischer, E., Marano, M.A., Van Zee, K.J., Rock, C.S., Hawes, A.S., Thompson, W.A., DeForge, L., Kenney, J.S., Remick, D.G., Bloedow, D.C., Thompson, R.C., Lowry, S.F., Moldawer, L.L. Interleukin-1 receptor blockade improves survival and hemodynamic performance in *Escherichia coli* septic shock, but fails to alter host responses to sublethal endotoxemia. *J Clin Invest* 89:1551-1557, 1992.
- 4) Van Zee, K.J., Kohno, T., Fischer, E., Rock, C.S., Moldawer, L.L., Lowry, S.F. TNF soluble receptors protect against excessive TNF during infection and injury. *Proc Nat. Acad Sci.* 89:4845-4849, 1992.
- 5) Van Zee, K.J., Stackpole, S.A., Montegut, W.J., Rogy, M.A., Calvano, S.E., Hsu, K.C., Chao, M., Loetscher, H., Stuber, D., Ettl, U., Wipf, B., Lesslauer, W., Lowry, S.F. Moldawer, L.L. A human tumor necrosis (TNF) γ mutant that binds exclusively to the p55 TNF receptor produces toxicity in the baboon. *J Exp Med* 179:1185-1191, 1994.
- 6) Rogy, M., Auffenburg, T., Espat, N.J., Philip, R., Remick, D.J., Wollenburg, G.K., Copeland, E.M., Moldawer, L.L. Human TNF receptor and interleukin-10 gene transfer in the mouse reduces mortality to lethal endotoxemia and also attenuates local inflammatory responses. *J Exp Med* 181:2289-2293, 1995.
- 7) Solorzano, C.C., Ksontini, R., Pruitt, J.H., Hess, P.J., Edwards, P.D., Kaibara, A., Abouhamze, A., Auffenburg, T., Galardy, R.E., Vauthey, J.N., Copeland, E.M., III., Edwards, C.K., III., Lauwers, G.Y., Clare-Salzler, M., MacKay, S.L.D., Moldawer, L.L. and Lazarus, D.D. Involvement of 26 kD cell-associated TNF α in experimental hepatitis and exacerbation of liver injury with a matrix-metalloproteinase inhibitor. *J Immunol* 158:414-419, 1997.

- 8) van der Poll, T., Jansen, P.M., Montegut, W.J., Braxton, C.C., Calvano, S.E., Stackpole, S.A., Smith, S.M., Swanson, S.W., Hack, C.E., Lowry, S.F., Moldawer, L.L. Effects of IL-10 on systemic inflammatory responses during sublethal primate endotoxemia. *J Immunol*, 158:1971-1975, 1997.
- 9) Ksontini, R., Colagiovanni, D.B., Josephs, M.D., Edwards, C.K. 3rd, Tannahill, C.L., Solorzano, C.C., Norman, J., Denham, W., Clare-Salzler, M., MacKay, S.L., Moldawer, L.L. Disparate roles for TNF- α and Fas ligand in concanavalin A-induced hepatitis. *J Immunol*, 160:4082-4089, 1998.
- 10) Ginsberg, H.S., Moldawer, L.L., Prince, G.A. Role of the type 5 adenovirus gene encoding the early region E1B 55kD protein in pulmonary pathogenesis. *Proc Natl Acad Sci (USA)* 96(18):10409-11, 1999.
- 11) Minter, R.M., Rectenwald, J.E., Fukuzuka, K., LaFace, D., Tsai, V., Hutchins, E., Moyer, R., Moldawer, L.L. TNF α receptor signaling and interleukin-10 gene therapy regulate the innate and humoral immune responses to recombinant adenovirus in the lung. *J Immunol* 164(1):443-451; 2000.
- 12) Fukuzuka, K., Edwards, C.K., Clare-Salzler, M., Copeland, E.M. III, Moldawer, L.L., Mazingo, D.W. Glucocorticoid induced, caspase-dependent organ apoptosis early after burn injury. *Am J Physiol* 278:R1005-18; 2000.
- 13) Minter R.M., Ferry M.A., Rectenwald, J.E., Bahjat F.R., Oberholzer, A., Oberholzer, C., LaFace D., Tsai V., Ahmed, C.M.I., Hutchins B., Copeland E.M., and Moldawer L.L. Extended lung expression and increased tissue localization of viral IL-10 with adenoviral gene therapy *Proc Natl Acad Sci* 98(1):277-282, 2001.
- 14) Oberholzer, A., Oberholzer, C., Minter, R.M., Moldawer, L.L. Considering immunomodulatory therapies in the septic patient: should apoptosis be a potential therapeutic target. *Immunology Letters*, 75(3):221-4, 2001.
- 15) Oberholzer, C., Oberholzer, A., Clare-Salzler, M., Moldawer, L.L. Apoptosis in sepsis: a new target for therapeutic exploration. *FASEB Journal* 15(6):879-92, 2001.
- 16) Oberholzer, A., Oberholzer, C., Bahjat, K., Ungaro, R., Tannahill, C.L., Murday, M., Bahjat, F.R., Abouhamze, Z., LaFace, D., Hutchins, B., Moldawer, L.L., Clare-Salzler, M.J. Increased survival in sepsis by in vivo adenovirus-induced expression of IL-10 in dendritic cells. *J Immunol*. 168(7):3412-8, 2002.
- 17) Li J., Kokkola R., Tabibzadeh S., Yang R., Ochani M., Qiang X., Harris H.E., Czura C.J., Wang H., Ulloa L., Wang H., Warren H.S., Moldawer L.L., Fink M.P., Andersson U., Tracey K.J., Yang H. Structural basis for the proinflammatory cytokine activity of high mobility group box 1. *Mol Med* 9(1-2):37-45, 2003.
- 18) Palladino M.A., Bahjat F.R., Theodorakis E.A., Moldawer L.L.. Anti-TNF-alpha therapies: the next generation. *Nat Rev Drug Discov*. 2(9):736-46, 2003.
- 19) Feezor, R.J., Oberholzer, C., Baker, H.V., Novick, D., Rubinstein, M., Moldawer, L.L., Pribble, J., Souza, S., Dinarello, C.A., Ertel, W., Oberholzer, A. Molecular characterization of the acute inflammatory response to infections with gram-negative versus gram-positive bacteria. *Infect Immun* 71(10):5803-13, 2003.
- 20) Efron P., Moldawer L.L. Sepsis and the dendritic cell. *Shock* 20(5):386-401, 2003.
- 21) Feezor, R.J., Paddock, H.N., Baker, H.V., Varela, J.C., Barreda, J., Moldawer, L.L., Schultz, G.S., Mazingo, D.W. Temporal patterns of gene expression in murine cutaneous burn wound healing. *Physiol Genomics*.16(3):341-8, 2004.
- 22) Efron, P.A., Tinsley, K., Minnich, D.J., Monterroso, V., Wagner, J., Laine, P., Lorr, K., Swanson, P.E., Hotchkiss, R., Moldawer, L.L. Increased lymphoid tissue apoptosis in baboons with bacteremic shock. *Shock*, 21(6):566-571, 2004.
- 23) Feezor, R.J., Baker, H.V., Wenzhong, X., Lee, W.A., Huber, T.S., Mindrinos, M., Kim, R.A., Ruiz-Taylor, L., Moldawer, L.L., Davis, R.W., Seeger, J.M. Genomic and proteomic determinants of outcome in patients undergoing thoracoabdominal aortic aneurysm repair. *J Immunol*. 172(11):7103-9, 2004.
- 24) Efron P.A., Martins A., Minnich D., Tinsley K., Ungaro R., Bahjat F.R., Hotchkiss R., Clare-Salzler M., Moldawer L.L.. Characterization of the systemic loss of dendritic cells in murine lymph nodes during polymicrobial sepsis. *J Immunol* Sep;173(5):3035-43, 2004.
- 25) Feezor, R.J., Baker, H.V., Mindrinos, M., Hayden, D., Tannahill, C.L., Brownstein, B.H., Fay, A., MacMillan, S., Laramie, J., Xiao, W., Moldawer, L.L., Cobb, J.P., Laudanski, K., Miller-Graziano, C.L., Maier, R.V., Schoenfeld, D., Davis, R.W., Tompkins, R.G., and the Inflammation and Host Response to Injury Large Scale Collaborative Research Program. Whole blood and leukocyte RNA isolation for gene expression analyses. *Physiol Genomics* Nov;19(3):247-54, 2004.
- 26) Matsumoto, T., Efron, P.A., Tsujimoto, H., Tschoeke, S.K., Ungaro, R., Fujita, S., Foley, D.P., Hemming, A., Moldawer, L.L. Splenic transposition is superior to caudal shunt as a model of murine total hepatic ischemia. *Lab Invest* 85(1):90-8, 2005.
- 27) Cobb, J.P., Mindrinos, M.N., Miller-Graziano, C., Calvano, S.E., Baker, H.V., Xiao, W., Laudanski, K., Brownstein, B.H., Elson, C.M., Hayden, D.L., Herndon, D.N., Lowry, S.F., Maier, R.V., Schoenfeld, D.A., Moldawer, L.L., Davis, R.W., Tompkins, R.G., Application of genome-wide expression analysis to human health and disease. *Proc Natl Acad Sci*; 102(13):4801-6, 2005.
- 28) Laine, P., Efron, P., Tschoeke, S.K., Elies, L., De Winter, H., Lorre, K., Moldawer, L.L. Delayed neutralization of interferon-gamma prevents lethality in primate Gram-negative bacteremic shock. *Crit Care Med* Apr;33(4):797-805, 2005.
- 29) Oberholzer, C., Tschoeke, S.K., Bahjat, K., LaFace, D., Hutchins, B., Clare-Salzler, M.J., Moldawer, L.L., Oberholzer, A. In vivo transduction of thymic dendritic cells with adenovirus and its potential use in acute inflammatory diseases. *Scand J Immunol*. 2005 Apr; 61(4):309-15.

- 30) Oberholzer, A., Souza, S.M., Tschoeke, S.K., Oberholzer, C., Abouhamze, A., Pribble, J.P., Moldawer, L.L. Plasma cytokine measurements augment prognostic scores as indicators of outcome in patients with severe sepsis. *Shock*. 2005 Jun;23(6):488-93.
- 31) Oberholzer, A., Oberholzer, C., Efron, P., Bahjat, K., Ungaro, R., Tannahill, C., Murday, M., Bahjat, F., Tsai, V., Hutchins, B., Moldawer, L.L., LaFace, D., Clare-Salzler, M. Functional modification of dendritic cells with recombinant adenovirus encoding IL-10 for the treatment of sepsis. *Shock*. 2005 Jun;23(6):507-15.
- 32) Litherland, S.A., Xie, T.X., Grebe, K.M., Davoodi-Semiromi, A., Elf, J., Belkin, N.S., Moldawer, L.L., Clare-Salzer, M.J. Signal transduction activator of transcription 5 (STAT5) dysfunction in autoimmune monocytes and macrophages. *J Autoimmun*. 2005 Jun;24(4):297-310. Epub 2005 Mar 23.
- 33) Efron, P.A., Tsujimoto, H., Bahjat, F.R., Ungaro, R., Debernardis, J., Tannahill, C., Baker, H.V., Edwards, C.K., Moldawer, L.L. Differential maturation of murine bone-marrow derived dendritic cells with lipopolysaccharide and tumor necrosis factor- α . *J Endotoxin Res*. 2005;11(3):145-60.
- 34) Biberthaler, P., Bogner, V., Baker, H.V., Lopez, M.C., Neth, P., Kanz, K., Mutschler, W., Jochum, M., Moldawer, L.L. Genome-wide monocyte mRNA expression in polytrauma patients for identification of clinical outcome. *Shock*. 2005 Jul;24(1):11-19.
- 35) Tsujimoto, H., Uchida, T., Efron, P.A., Scumpia, P.O., Verma, A., Matsumoto, T., Tschoeke, S.K., Ungaro, R.F., Ono, S., Seki, S., Clare-Salzler, M.J., Baker, H.V., Mochizuki, H., Ramphal, R., Moldawer, L.L. Flagellin enhances NK cell proliferation and activation directly and through dendritic cell-NK cell interactions. *J Leukoc Biol*. 2005 78(4):888-97.
- 36) Scumpia, P.O., McAuliffe, P.F., O'malley, K.A., Ungaro, R., Uchida, T., Matsumoto, T., Remick, D.G., Clare-Salzler, M.J., Moldawer, L.L., Efron, P.A. CD11c+ dendritic cells are required for survival in murine polymicrobial sepsis. *J Immunol*. 2005 Sep 1;175(5):3282-6.
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- 38) Feezor, R.J., Cheng, A., Paddock, H.N., Baker, H.V., Moldawer, L.L. Functional genomics and gene expression profiling in sepsis: beyond class prediction. *Clin Infect Dis*. 2005 Nov 15;41 Suppl 7:S427-35.
- 39) McAuliffe, P.F., Murday, M.E., Efron, P.A., Scumpia, P.O., Ungaro, R., Abouhamze, A., Tannahill, C.L., Hutchins, B., Laface, D., Moldawer, L.L. Dose-dependent improvements in outcome with adenoviral expression of interleukin-10 in a murine model of multisystem organ failure. *Gene Ther*. 2005 13(3):276-82.
- 40) Schreiber, J., Efron, P.A., Park, J.E., Moldawer, L.L., Barbul, A. Adenoviral gene transfer of an NF-kappaB super-repressor increases collagen deposition in rodent cutaneous wound healing. *Surgery*. 2005 Nov;138(5):940-946.
- 41) Calvano, S.E., Xiao, W., Richards, D.R., Felciano, R.M., Baker, H.V., Cho, R.J., Chen, R.O., Brownstein, B.H., Cobb, J.P., Tschoeke, S.K., Miller-Graziano, C., Moldawer, L.L., Mindrinos, M.N., Davis, R.W., Tompkins, R.G., Lowry, S.F., Bankey, P.E., Billiar, T.R., Camp, D.G., Casella, G., Chaudry, I.H., Choudhry, M.A., Cooper, C., De, A., Elson, C., Freeman, B., Gamelli, R.L., Campbell-Finnerty, C., Gibran, N.S., Hayden, D.L., Harbrecht, B.G., Herndon, D.N., Horton, J.W., Hubbard, W.J., Hunt, J.L., Johnson, J., Klein, M.B., Lederer, J.A., Logvinenko, T., Maier, R.V., Mannick, J.A., Mason, P.H., McKinley, B.A., Minei, J.P., Moore, E.E., Moore, F.A., Nathens, A.B., O'keefe, G.E., Rahme, L.G., Remick, D.G., Schoenfeld, D.A., Schwacha, M.G., Shapiro, M.B., Silver, G.M., Smith, R.D., Storey, J.D., Toner, M., Warren, H.S., West, M.A. A network-based analysis of systemic inflammation in humans. *Nature*. 2005 Dec 1;438(7068):696.
- 42) Scumpia, P.O., Moldawer, L.L. Biology of interleukin-10 and its regulatory roles in sepsis syndromes. *Crit Care Med*. 2005 Dec;33(12 Suppl):S468-S471.
- 43) Qian, W.J., Jacobs, J.M., Camp, D.G. 2nd, Monroe, M.E., Moore, R.J., Gritsenko, M.A., Calvano, S.E., Lowry, S.F., Xiao, W., Moldawer, L.L., Davis, R.W., Tompkins, R.G., Smith, R.D. Comparative proteome analyses of human plasma following in vivo lipopolysaccharide administration using multidimensional separations coupled with tandem mass spectrometry. *Proteomics* Feb;5(2):572-84, 2005.

C. Research Support. List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

1. R37 GM-40586-17 (NIH/NIGMS) 8/01/88-11/30/07
Lyle L. Moldawer, Ph.D. (Principal Investigator)
ΔCytokine Regulation in Sepsis and Inflammation@

The overall goal of this award is to examine proinflammatory cytokine, cytokine inhibitor and anti-inflammatory cytokine regulation in sepsis, and bacterial infections. Using rodent models of a cecal ligation and puncture, or endotoxemia, the application intends to explore the role of TNF signaling pathways in determining outcome to sepsis and endotoxemic shock.

2. T32 GM-08721-07 (NIH/NIGMS) 7/1/99-6/30/09
Lyle L. Moldawer, Ph.D. (Principal Investigator)
@Molecular Biology and Gene Therapy in Burns and Trauma@

A training grant to provide surgical residents with a two year research experience in the laboratory of an established molecular biologist and gene therapist.

3. R01 GM-63041-05 (NIH/NIGMS) 4/01/01-7/31/09
Lyle L. Moldawer, Ph.D. (Principal Investigator)
ΔTargeted Interleukin-10 Gene Therapy in Sepsis Syndromes@

This application proposes to explore the utility of IL-10 gene therapy as a an anti-inflammatory and anti-apoptotic agent for the treatment of sepsis syndromes.

4. U54 GM-62119-01 (NIH/NIGMS) 09/30/01-9/29/06
Ronald Tompkins, M.D., D.Sc. (Principal Investigator),
Lyle L. Moldawer, Ph.D. (Steering Committee, Director, Protein Analysis and Cell Biology Core)
“Inflammation and the Host Response to Injury”

This large scale program seeks to better understand the gene expression and proteomic changes that follow traumatic and burn injury in humans. Dr. Moldawer’s laboratory is providing administrative oversight for sample collection and coordination, and is responsible for some of the analyses. Dr. Moldawer serves on the Steering Committee that provides oversight for the program.

5. P01 HL051811-02 (NIH/NHLBI) 05/01/04 – 03/31/06
William B. Guggino, M.D. (Principal Investigator)
Lyle L. Moldawer (Co-Investigator)
“Gene and Pharmacological Therapies for Cystic Fibrosis”

This application is examining the potential therapeutic efficacy of gene therapy and protein replacement modalities for the treatment of cystic fibrosis. The support for Dr. Moldawer is to provide analytical support for the determination of apoptosis in epithelial cells and inflammatory cells, in the lungs of murine models of cystic fibrosis.

6. R01 DK066211-01A2 (NIH/NIDDK) 10/01/05 – 09/30/10
Kevin E. Behrns, M.D. (Principal Investigator)
Lyle L. Moldawer (Co-Investigator)
“Growth Control of Normal and Cirrhotic Hepatocytes”

The major aim of this proposal is to continue previous work that examines mechanisms of apoptosis resistance in murine cirrhotic hepatocytes. This proposal will focus differences in signal mechanisms of transforming growth factor beta-induced apoptosis in normal and cirrhotic hepatocytes.