

**BIOGRAPHICAL SKETCH**

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NAME Charles J. Lowenstein	POSITION TITLE Professor of Medicine		
eRA COMMONS USER NAME CLOWENS1			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Harvard College, Cambridge, MA	B.A.	1982	Biochemistry
Harvard Medical School, Boston, MA	M.D.	1986	Medicine
The Johns Hopkins University School of Med. Baltimore, MD		1994	Cardiology

**A. Positions and Honors.****Professional Experience**

1986-1989: Medical Resident, Massachusetts General Hospital, Boston, MA  
 1989-1990: Research Associate, Massachusetts Institute of Technology, Boston, MA  
 1991-1994: Cardiology Fellow, Johns Hopkins School of Medicine, Baltimore, MD  
 1993-1999: Assistant Professor, Department of Medicine, Johns Hopkins School of Medicine  
 1996-1999: Assistant Professor, Department of Pathology, Johns Hopkins School of Medicine  
 1996: Scientific Director, Ciccarone Center for the Prevention of Heart Disease  
 1999-2004: Associate Professor, Department of Medicine, Johns Hopkins School of Medicine  
 2000-2004: Associate Professor, Department of Pathology, Johns Hopkins School of Medicine  
 2004: Professor, Department of Medicine, Johns Hopkins University School of Medicine

**Honors and Awards**

1989-1990: NIH Physician Scientist Award: Beta-globin gene transfer into hematopoietic stem cells.  
 1991-1994: NIH Physician Scientist Award: Macrophage nitric oxide synthase gene characterization.  
 1993: American Heart Association Katz Award Finalist  
 2001-2004: American Heart Association Established Investigator Grant  
 2002: Member, American Society for Clinical Investigation  
 2003: Sir William Osler Young Investigator Award, Interurban Clinical Club  
 2006: Clarence P. Doodeman Professorship of Cardiology

**B. Selected peer-reviewed publications (in chronological order selected from 82 peer-reviewed research publications).**

1. Bredt, D.S., Hwang, P.M., Glatt, C.E., Lowenstein, C.J., Reed, R.R. and Snyder, S.H. Cloned and expressed nitric oxide synthase structurally resembles cytochrome P-450 reductase. *Nature* 351:714-718, 1991.
2. Lowenstein, C.J., Glatt, C.S., Bredt, D.S. and Snyder, S.H. Cloned and expressed macrophage nitric oxide synthase contrasts with the brain enzyme. *Proc.Natl.Acad.Sci.U.S.A.* 89:6711-6715, 1992.
3. Burnett, A.L., Lowenstein, C.J., Bredt, D.S., Chang, T.S. and Snyder, S.H. Nitric oxide: a physiologic mediator of penile erection. *Science* 257:401-403, 1992.
4. Lowenstein, C.J. and Snyder, S.H. Nitric oxide, a novel biologic messenger. *Cell* 70:705-707, 1992.
5. Lowenstein, C.J., Alley, E.W., Raval, P., Snowman, A.M., Snyder, S.H., Russell, S.W. and Murphy, W.J. Macrophage nitric oxide synthase gene: two upstream regions mediate induction by interferon gamma and lipopolysaccharide. *Proc.Natl.Acad.Sci.U.S.A.* 90:9730-9734, 1993.

6. Geller, D.A., Lowenstein, C.J., Shapiro, R.A., Nussler, A.K., Di Silvio, M., Wang, S.C., Nakayama, D.K., Simmons, R.L., Snyder, S.H. and Billiar, T.R. Molecular cloning and expression of inducible nitric oxide synthase from human hepatocytes. *Proc.Natl.Acad.Sci.U.S.A.* 90:3491-3495, 1993.
9. Lowenstein, C.J., Dinerman, J.L. and Snyder, S.H. Nitric oxide: a physiological messenger. *Ann. Intern. Med.* 120(3):227-37, 1994.
10. Lowenstein, C.J. and Snyder, S.H. Purification, Cloning, and Expression of Nitric Oxide Synthase Isoforms. *Methods in Enzymology* 233:264-268, 1994.
11. Balligand J.L., Ungureanu-Longrois D., Simmons W.W., Pimental D., Malinski T.A., Kapturczak, Taha Z., Lowenstein, C.J., Davidoff A.J., Kelly R.A., and Michel, T. Cytokine-inducible nitric oxide synthase (iNOS) expression in cardiac myocytes. Characterization and regulation of iNOS expression and detection of iNOS activity in single cardiac myocytes in vitro. *J. Biol. Chem.* 269(44):27580-8, 1994.
27. Lowenstein, C.J., Allen, G., Rose, N., Snyder, S.H. and Herskowitz, A. Nitric oxide inhibits viral replication in murine myocarditis. *J. Clin. Invest.* 97:1837-1843, 1996.
28. Arnet, U., McMillan, A.M., Ballermann, B.J., and Lowenstein, C.J. Regulation of Endothelial Nitric Oxide Synthase During Hypoxia. *J. Biol. Chem.* 271: 15069-15073, 1996.
33. Lafond-Walker, A., Chen, C., Augustine, S., Wu, T.C., Hruban, R.H., and Lowenstein, C.J. Inducible Nitric Oxide Synthase Expression in Coronary Arteries of Transplanted Human Hearts with Accelerated Graft Arteriosclerosis. *Am. J. Path.* 151:919-925 (1997).
34. Zaragoza, C., Ocampo, C.J., Saura, M., McMillan, A., and Lowenstein, C.J. Nitric Oxide Inhibition of Coxsackievirus Replication In Vitro. *J. Clin. Investig.* 100:1760-1767 (1997).
37. Ratovitski, E.A., Kotbauer, P.T., Milbrandt, J., Lowenstein, C.J., and Burrow, C. Midkine Induces Tumor Cell Proliferation and Binds to a High Affinity Signaling Receptor Associated with JAK Tyrosine Kinases. *J. Biol. Chem.* 273: 3654-3660 (1998).
39. Zaragoza, C., Ocampo, C.J., Saura, M., Leppo, M., Wei, X., Moncada, S., Liew, F.Y., and Lowenstein, C.J. The role of NOS2 in the host response to Coxsackievirus myocarditis. *Proc. Natl. Acad. Sci. U. S. A.* 95:2469-2474 (1998).
45. Ratovitski, E.A., Alam, M.R., Quick, R.A., McMillan, A., Bao, C., Kozlovsky, C., Hand, T.A., Mains, R.E., Eipper, B.A., Lowenstein, C.J. Kalirin Inhibition of Inducible Nitric Oxide Synthase, *J. Biol. Chem.* 274: 993-9, 1999.
46. Saura, M., Zaragoza, C., McMillan, A., Quick, R.A., Hohenadl, C., Lowenstein, J.M., and Lowenstein, C.J. An Anti-Viral Mechanism of Nitric Oxide: Inhibition of a Viral Protease Immunity, *10: 21-8, 1999.*
50. Ratovitski, E.A., Bao, C. Quick, R.A., McMillan, A, and Lowenstein, C.J. An Inducible Nitric Oxide Synthase Associated Protein Inhibits NOS Dimerization *J. Biol. Chem.* 274: 30250-7. (1999).
51. Zaragoza, C., Ocampo, C.J., Saura, M., Bao, C. Leppo, M., Lafond-Walker, A., Thiemann, D.R., Hruban, R., and Lowenstein, C.J. Inducible Nitric Oxide Synthase Protection Against Coxsackievirus Pancreatitis. *J. Immunol.* 163: 5497-504 (1999).
55. Lopez-Ongil S, Senchak V, Saura M, Zaragoza C, Ames M, Ballermann B, Rodriguez-Puyol M, Rodriguez-Puyol D, Lowenstein, C.J. Superoxide regulation of endothelin-converting enzyme. *J. Biol. Chem.* 275(34):26423-7 (2000).
57. Rothstein, N.M., Quinn, T.C., Madico, G., Gaydos, C.A., Lowenstein, C.J. The Effect of Azithromycin upon Murine Arteriosclerosis Exacerbated by Chlamydia. *J. Infect. Dis.* 183(2):232-238 (2001).
59. Tendler, D.T., Bao, C., Wang, T., Huang, E.L., Ratovitski, E.A., Pardoll, D.A., and Lowenstein, C.J. Intersection of Interferon and Hypoxia Signal Transduction Pathways in Nitric Oxide Induced Tumor Apoptosis. *Cancer Res.* 61:3682-8 (2001).
60. Qian Z, Gelzer-Bell R, Yang SX, Cao W, Ohnishi T, Wasowska BA, Hruban RH, Rodriguez ER, Baldwin WM 3rd, Lowenstein CJ. Inducible nitric oxide synthase inhibition of Weibel-Palade body release in cardiac transplant rejection. *Circulation.* 2001 Nov 6;104(19):2369-75.
65. Cao, W., Bao, C., Lowenstein CJ. Inducible nitric oxide synthase expression inhibition by adenovirus E1A. *Proc Natl. Acad. Sci. U. S. A.* 2003 Jun 24; 100(13):7773-8.
67. Matsushita K, Morrell CN, Cambien, B, Yang SX, Yamakuchi M, Bao C, Hara M, Quick RA, Cao W, O'Rourke B, Lowenstein JM, Pevsner J, Wagner DD, and Lowenstein CJ. Nitric Oxide Regulation of Exocytosis by S-Nitrosylation of N-ethylmaleimide Sensitive Factor. *Cell* 2003;115(2):139-50.
69. Bhatia R, Matsushita K, Yamakuchi M, Morrell CN, Cao W, Lowenstein CJ. Ceramide Triggers Weibel-Palade Body Exocytosis. *Circ Res.* 2004 Jun 24; 95: 319-324.

70. Matsushita, K., C.N. Morrell, and Lowenstein, C.J. 2004. Sphingosine 1-phosphate activates Weibel-Palade body exocytosis. *Proc Natl Acad Sci U S A* 101:11483-11487.
71. Padalko, E., T. Ohnishi, K. Matsushita, H. Sun, K. Fox-Talbot, C. Bao, W.M. Baldwin, 3rd, and Lowenstein C.J. 2004. Peroxynitrite inhibition of Coxsackievirus infection by prevention of viral RNA entry. *Proc Natl Acad Sci U S A* 2004; 101:11731-11736.
72. Matsushita K, Yamakuchi M, Morrell CN, Ozaki M, O'Rourke B, Irani K, Lowenstein CJ. Vascular endothelial growth factor regulation of Weibel-Palade body exocytosis. *Blood*. 2005 Jan 1;105(1):207-14
73. Matsushita K, Morrell CN, Lowenstein CJ. A novel class of fusion polypeptides inhibits exocytosis. *Mol Pharmacol*. 2005 Apr;67(4):1137-44.
74. Morrell CN, Matsushita K, Chiles K, Scharpf RB, Yamakuchi M, Mason RJ, Bergmeir W, Mankowski JL, Baldwin WM 3rd, Faraday N, Lowenstein CJ. Regulation of platelet granule exocytosis by S-nitrosylation. *Proc Natl Acad Sci U S A*. 2005 Mar 8;102(10):3782-7.
77. Matsushita K, Morrell CN, Mason RJ, Yamakuchi M, Khanday FA, Irani K, Lowenstein CJ. Hydrogen peroxide regulation of endothelial exocytosis by inhibition of N-ethylmaleimide sensitive factor. *J Cell Biol*. 2005 Jul 4;170(1):73-9.
80. Ferlito M, Irani K, Faraday N, Lowenstein CJ. Nitric oxide inhibits exocytosis of cytolytic granules from lymphokine-activated killer cells. *Proc Natl Acad Sci U S A*. 2006 Aug 1;103(31):11689-94.
81. Saura M, Zaragoza C, Bao C, Herranz B, Rodriguez-Puyol M, Lowenstein CJ. Stat3 mediates interleukin-6 inhibition of human endothelial nitric-oxide synthase expression. *J Biol Chem*. 2006 Oct 6;281(40):30057-62
82. Zaragoza C, Saura M, Padalko EY, Lopez-Rivera E, Lizarbe TR, Lamas S, Lowenstein CJ. Viral protease cleavage of inhibitor of kappaBalpha triggers host cell apoptosis. *Proc Natl Acad Sci U S A*. 2006 Dec 12;103(50):19051-6.
83. Yamakuchi M, Kirkiles-Smith NC, Ferlito M, Cameron SJ, Bao C, Fox-Talbot K, Wasowska BA, Baldwin III WM, Pober JS, Lowenstein CJ. Antibody to Human Leukocyte Antigen Triggers Endothelial Exocytosis *Proc Natl Acad Sci U S A*. 2007 Jan 23;104(4):1301-6.

### C. Research Support.

#### Ongoing Research Support

P01 HL56091                      Baldwin (PI)                      05/01/03 - 04/30/08  
NIH/NHLBI

*The Role of Mediators in Accelerated Graft Arteriosclerosis.*

The major goal of this Project within a PPG is to examine the effect of nitric oxide on accelerated arteriosclerosis in cardiac transplants.

Role: Project Leader.

R01 HL74061                      Lowenstein (PI)                      05/01/04 – 03/31/08  
NIH/NHLBI

*Regulation of Vascular Inflammation*

The major goal of this R01 is to explore mechanisms by which nitric oxide inhibits vascular inflammation.

Role: Principal Investigator.

R01 HL078635                      Lowenstein (PI)                      9/24/04 – 8/31/08  
NIH/NHLBI

*Exocytosis and Vascular Inflammation*

The major goal of this proposal is to determine mechanisms that protect NSF from oxidation.

Role: Principal Investigator

Industry Support                      Lowenstein (PI)                      02/01/05 – 9/30/07  
Pfizer HDL Award  
*HDL Regulation of Endothelial Exocytosis*

The Aims of this proposal are to define mechanisms by which HDL regulates endothelial activation.

Role: Principal Investigator

P01 HL65608                      Becker (PI)    04/01/06 – 03/31/11

NIH/NHLBI

*The Regulation of Exocytosis in the Post-Ischemic Myocardium*

The major goal of this Project within a PPG is to examine molecular mechanisms of exocytosis during ischemia and reperfusion.

Role: Project Leader.

**Completed Research Support**

R01 HL63706                      Lowenstein (PI)    02/01/00 - 01/31/04

NIH/NHLBI

*The Regulation of NOS2 in Ischemic Myocardium*

The major goal of this R01 is to examine molecular mechanisms of murine NOS2 regulation.

Role: Principal Investigator.

P01 HL65608                      Becker (PI)    01/01/00 - 12/31/04

NIH/NHLBI

*The Regulation of NOS2 in Ischemic and Post-Ischemic Myocardium.*

The major goal of this Project within a PPG is to examine molecular mechanisms of human NOS2 regulation.

This grant partially overlaps with R01 HL63706 listed above.

Role: Project Leader.

EIG 0140210N                      Lowenstein (PI)    01/01/01 - 12/31/04

AHA

*Host Defenses Against Coxsackievirus Myocarditis*

The major goal of this Established Investigator Award from the American Heart Association is to examine host targets of viral proteases that regulate apoptosis.

Role: Principal Investigator.