

BIOGRAPHICAL SKETCH

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NAME Salvemini, Daniela	POSITION TITLE Associate Professor		
eRA COMMONS USER NAME SALVEMD			
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as</i>)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of London, UK	B.Sc.	1987	Pharmacology
University of London, UK	Ph.D.	1990	Pharmacology
William Harvey Research Institute, London, UK	Postdoctoral	1990-1992	Pharmacology
Monsanto, St Louis, MO, USA	Postdoctoral	1992-1994	Pharmacology

Personal Statement: I am an *in vivo* pharmacologist trained by the Nobel Laureate Sir John R. Vane with extensive experience in pain & inflammation. Chronic severe pain is a significant global health problem. In the US alone, one third of Americans suffer some form of chronic pain, and in these individuals over 30% of reported pain is resistant to analgesic therapy. The economic impact of pain is equally large at approximately \$100 billion annually. Novel therapeutics agents are clearly needed. Using a multidisciplinary approach including genetic, molecular, bioanalytical, biochemical and pharmacological tools my lab is interested in 1) understanding the signaling pathways engaged by nitroxidative species and sphingolipids in pain with a particular focus on chronic pain states and 2) identifying novel chemical entities that specifically target these pathways with the ultimate goal of providing viable therapeutic approaches in pain management.

B. Positions and Honors.

Positions and Employment

1994-1995	Senior Research Investigator, Discovery Pharmacology, G.D. Searle, St Louis, MO
1995-1997	Research Scientist, Discovery Pharmacology, G.D. Searle, St Louis, MO
1997-1999	Research Scientist II & Project Leader, Discovery Pharmacology, G.D. Searle, St Louis, MO
1996-2009	Adjunct Professor, Department of Pharmacological and Physiological Sciences, Saint Louis University Medical School, St Louis, MO
1999-2001	Director of Biology, Metaphore Pharmaceuticals, St Louis, MO
2000-present	Adjunct Professor of Molecular Pharmacology, Department of Pharmacology (Faculty of Pharmacy of Catanzaro, Italy)
2001-2003	Vice President, Biological and Pharmacological Research, Metaphore Pharmaceuticals, St Louis, MO
2003-2005	Senior Vice President of Research, Metaphore Pharmaceuticals, St Louis, MO
2005- June 2009	Research Professor of Internal Medicine, Department of Internal Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine, Saint Louis University, St Louis, MO
2009-present	Adjunct Associate Professor of Internal Medicine, Department of Internal Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine, Saint Louis University, St Louis, MO
2010-present	Adjunct Associate Professor, Pharmaceutical Sciences, School of Pharmacy, Southern Illinois University Edwardsville
2009-present	Associate Professor, Department of Pharmacological and Physiological Sciences, Saint Louis University Medical School, St Louis, MO

Honors and Awards: **2010:** Premio Internazionale Maria Luisa de' Medici Award from Italy for her distinguished contribution to science. **2002:** The Oxygen Club of Greater Washington, D.C and the Society for Experimental Biology and Medicine, D.C Award for her research in free radical biology. **2000:** Magna Graecia Prize for her contribution of the scientific advancement of research in Southern Italy. **1997:** Searle Discovery Research Achievement Award for her achievements and leadership in the Superoxide Dismutase Project. **1997:** Novartis Prize In Pharmacology for her research on free radicals, nitric oxide and cyclooxygenases in inflammation. **1996:** Searle Discovery Research Achievement Award for her achievements and leadership in Nitric Oxide Synthase and Superoxide Dismutase Projects. **1991:** The University of London William Julius Mickle Fellowship, For: "An investigator under 35 years of age, who has in the opinion of the Committee, done most to advance medical art or science within the preceding five years". **1989:** The British Society of Thrombosis and Haemostasis Young Investigators Award for the excellence and originality of the work presented on the interactions between nitric oxide, platelets and vascular smooth muscle cells.

Referee (ad hoc) for Scientific Journals: Pain, J. Neuroscience, Neuroscience, Molecular Pain, JBC, Proc. Natl. Acad. Sci. USA, Nature Med, J. Pharmacol. Exp. Ther, Free Radical Biology and Medicine, Molecular and Cell Biology of Lipids, Pharmacological Research, American Journal of Physiology.

C. Selected peer-reviewed publications (selected from over 150 peer-reviewed publications, excluding book chapters)

1. Rausaria S, Kamadulski A, Rath NP, Bryant L, Chen Z, **Salvemini D**, Neumann WL. (2011) Manganese(III) Complexes of Bis(hydroxyphenyl)dipyrromethenes Are Potent Orally Active Peroxynitrite Scavengers. *J Am Chem Soc.* 133:4200-3. PMID: 21370860.
2. **Salvemini, D.**, Little, J. W., Doyle, T., Neumann, W. L. (2011) Roles of reactive oxygen and nitrogen species in pain. *Free Radic Biol Med* (Jan 27, Epub ahead of print). PMID:21277369.
3. Doyle, T., Finley, A., Chen, Z., and **Salvemini, D.** (2011) Role for peroxynitrite in sphingosine 1-phosphate induced hyperalgesia in rats. *Pain* (Jan 14, Epub ahead of print, PMID:21239112)
4. L. Batinic-Haberle, I. (2011). Methoxy-derivatization of alkyl chains increases the efficacy of cationic Mn porphyrins. Synthesis, characterization, SOD-like activity, and SOD-deficient E. coli study of meta Mn(III) N-methoxyalkylpyridylporphyrins. *Dalton Transaction.* 40:4111-21. PMID:21370860
5. Doyle, TD, Chen, Z, Muscoli, Cm Obeid, L.M, **Salvemini, D.** (2011) Ceramide Induced Peripheral Sensitization and Hyperalgesia is Mediated by a NF-kB and p38 Kinase Dependent Cyclooxygenase 2 /Prostaglandin E2 Pathway: Role for Sphingosine kinase and Sphingosine-1-Phosphate. *FASEB J.* May 6. [Epub ahead of print] PMID: 21551240
6. T. Doyle, Z. Chen, L. M. Obeid, **D. Salvemini.** (2011). Sphingosine-1-phosphate Acting via the S1P1 Receptor is a Downstream Signaling Pathway in Ceramide-Induced Hyperalgesia. *Neuro. Letts.* May 13. [Epub ahead of print] PMID: 21605625
7. Muscoli, C., Doyle, T., Dagostino, C., Bryant, L., Chen, Z., Watkins, L. R., Ryerse, J., Bieberich, E., Neumann, W., **Salvemini, D.** (2010) Counter-Regulation of Opioid Analgesia by Glial-Derived Bioactive Sphingolipids. *J Neurosci* **30**, 15400-15408. PMCID:PMC3000610. Comment in *Nat. Rev. Drug Discov.* 2011, 10, 20-21.
8. Chen, Z., Muscoli, C., Doyle, T., Bryant, L., Cuzzocrea, S., Mollace, V., Mastroianni, R., Masini, E., **Salvemini, D.** 2010. NMDA-receptor activation and nitroxidative regulation of the glutamatergic pathway during nociceptive processing. *Pain* 149:100-106. PMCID:PMC2837917
9. Doyle, T., Bryant, L., Muscoli, C., Cuzzocrea, S., Esposito, E., Chen, Z., **Salvemini, D.** 2010. Spinal NADPH oxidase is a source of superoxide in the development of morphine-induced hyperalgesia and antinociceptive tolerance. *Neurosci Lett.* 483, 85-89. PMCID:PMC2933278
10. Little, J.W., Doyle, T., **Salvemini, D.** 2010. Reactive nitroxidative species and nociceptive processing: determining the roles for nitric oxide, superoxide, and peroxynitrite in pain. *Amino Acids.* Jun 16, Epub ahead of print. PMID:20552384.

- 11. Salvemini, D.,** Neumann, W. 2010. Targeting peroxynitrite driven nitroxidative stress with synzymes: A novel therapeutic approach in chronic pain management. *Life Sci* 86:604-614. PMID:19576230.
- 12. Batinic-Haberle, I., Cuzzocrea, S., Reboucas, J.S., Ferrer-Sueta, G., Mazzon, E., Di Paola, R., Radi, R., Spasojevic, I., Benov, L., Salvemini, D.** 2009. Pure MnTBAP selectively scavenges peroxynitrite over superoxide: Comparison of pure and commercial MnTBAP samples to MnTE-2-PyP in two models of oxidative stress injury, an SOD-specific Escherichia coli model and carrageenan-induced pleurisy. *Free Radic Biol Med* 46:192-201. PMID:PMC2742324.
- 13. Salvemini, D.** 2009. Peroxynitrite and opiate antinociceptive tolerance: a painful reality. *Arch. Biochem Biophys* 484:238-244. PMID:PMC2714174.
- 14. Doyle, T., Bryant, L., Batinic-Haberle, I., Little, J., Cuzzocrea, S., Masini, E., Spasojevic, I., Salvemini, D.** 2009. Supraspinal inactivation of mitochondrial superoxide dismutase is a source of peroxynitrite in the development of morphine antinociceptive tolerance. *Neuroscience*. PMID:PMC2860430.
- 15. Ndengele, M.M., Cuzzocrea, S., Esposito, E., Mazzon, E., Di Paola, R., Matuschak, G.M., Salvemini, D.** 2008. Cyclooxygenases 1 and 2 contribute to peroxynitrite-mediated inflammatory pain hypersensitivity. *Faseb J* 22:3154-3164. PMID:18497304.

Patents

- Salvemini, D. (2001)** US 6,180,620: Analgesic methods using synthetic catalysts for the dismutation of superoxide radicals.
- Stern, M and **Salvemini, D. (2001)** US 6,245,758 B1. Methods of use for peroxynitrite decomposition catalysts, pharmaceutical compositions therefore.
- Salvemini, D. (2002)**. US 6,395,725 B1. Analgesic methods using synthetic catalysts for the dismutation of superoxide radicals.
- Salvemini, D. (2002)**. "Synthetic low molecular weight catalysts for the dismutation of superoxide are potent analgesics that are effective in elevating the pain threshold in hyperalgesic conditions such as arthritis, and also operate to prevent or reverse tolerance to opioid analgesics." US Patent 6395725.
- Salvemini, D. (2004)**. "Combinations of synthetic low molecular weight catalysts for the dismutation of superoxide and opioids are potent analgesics that are effective in elevating the pain threshold in hyperalgesic conditions." US Patent Appl. US 2004/0219138 A1.

D. Research Support (contracts not listed)

Ongoing Research Support

R01 DA024074 (NIH/NIDA) Salvemini (PI) 07/01/2008 - 05/31/2013
 Role of peroxynitrite in morphine hyperalgesia and tolerance
 Use of novel SODm/PN catalysts to unravel importance of nitroxidative stress in morphine induced hyperalgesia.

1RC1AR058231-01 (NIH/NIAMSD) Salvemini (PI) 09/30/2009 - 08/31/2011
(no-cost extension)
 Targeting the relief of chronic pain with orally active peroxynitrite decomposition catalysts
 The goals are design and pharmacological evaluation of novel orally bioavailable polyazamacrocyclic metalloporphyrin as peroxynitrite decomposition for the relief of chronic arthritic pain.

C: Completed

Title: Role of ceramide in morphine hyperalgesia and tolerance.

R21, NIH/NIDA (2008-2010)
 Principle investigator: Daniela Salvemini, PhD

Title: Role of peroxynitrite in the development of chemotherapy-induced pain.

Principle investigator: Daniela Salvemini, PhD
 President's Research Award
 Saint Louis University Seed Funds (2010-2011)

Title: Ceramide- novel target in the development of opiate-induced hyperalgesia and tolerance.

Principle investigator: Daniela Salvemini, PhD
Saint Louis University Seed Funds (2007-2008)

Title: Ceramide- novel target in the development of opiate-induced hyperalgesia and tolerance.

Principle investigator: Daniela Salvemini, PhD
Saint Louis University Seed Funds (2006-2008)

Title: Pulmonary Collectins, Hyaluronan and Macrophages

HL073896 4/1/04 - 3/31/09
NIH/NHLBI

Principle investigator: Rashmin Savani MD; **Salvemini** (collaborator)

Title: M40403 and IL-2 Induced Hypotension

1 R43 CA93203-01 8/06/01-7/31/02
NIH/NCI

Principle investigator: Daniela Salvemini, PhD

Title: SODm for Management of Ischemic Heart Disease

1 R43 HL68362-01 9/30/01-3/29/02
NIH/NHLBI

Principle investigator: Daniela Salvemini, PhD

Title: Superoxide Dismutase Mimetics for Management of Pain

1R43 DA13534-01 7/01/00 -12/31/00
NIH/NIDA

Principle investigator: Daniela Salvemini, PhD

Title: Inactivation of Catecholamines in Septic Shock

R43 FD-01585-01 9/30/00-3/31/01
DHHS/FDA

Principle investigator: Daniela Salvemini, PhD

Title: Deactivation of catecholamines by nitric oxide, superoxide and peroxynitrite

R01 HL61836-03 3/07/00-2/28/04
NIH/NHLBI

Principle investigator: Heather Macarthur, PhD
Role: Consultant