

CURRICULUM VITAE

Lawrence H. Lazarus, Ph.D.

Present Address

Head, Medicinal Chemistry Group
Laboratory of Pharmacology and Chemistry
National Institute of Environmental Health Sciences
MD C3-04
PO Box 12233
111 South TW Alexander Drive
Research Triangle Park, North Carolina 27709
Tel: (919) 541-3238
Fax: (919) 541-5737
E-mail: lazarus@niehs.nih.gov
Website: <http://dir.niehs.nih.gov/dir/lpc/medchem/>

Education

1960 BA University of California, Los Angeles, CA. Zoology
1962 MA University of California, Los Angeles, CA. General Physiology
1966 PhD University of California, Los Angeles, CA. Cell
Physiology/Biochemistry

Employment History

1960-1962 Teaching and Research Assistants, Department of Zoology, UCLA, Los Angeles, CA. OH Scherbaum, mentor
1966-1968 Postdoctoral Fellow, Microbiology Institute, University of Copenhagen, Copenhagen, Denmark. NO Kjeldgård, sponsor
1968-1973 Assistant Professor, Department of Virology, Hebrew University-Hadassah Medical School, Jerusalem, Israel. N Goldblum, Chair
1973-1975 Visiting Research Chemist, Department of Chemistry, School of Medicine, University of California, San Diego, La Jolla, CA. NO Kaplan, sponsor
1975-1977 Senior Research Associate, Neuroendocrinology Laboratory, Salk Institute, La Jolla, CA. R Guillemin (Nobel Laureate, Medicine, 1977)
1977-date Research Chemist, National Institute of Environmental Health Sciences, Research Triangle Park, NC. Current Position: Head, Medicinal Chemistry Group, Laboratory of Pharmacology. D. Miller, Acting Chief.

- 1978-date Adjunct, Department of Pharmacology, School of Medicine,
University of North Carolina, Chapel Hill, NC
- 1978-date Adjunct, Lineberger Cancer Research Institute, University of North
Carolina, Chapel Hill, NC

Society Membership

American Association for the Advancement of Science
American Chemical Society
American Society of Biochemistry and Molecular Biology

Honors, Special Recognition, Committees

- 1956 Bausch & Lomb Honorary Science Award.
- 1956 Rotary Club of America Design Award
- 1956 Southern California Science Fair Award
- 1973 Friends of Hadassah Science Award
- 1991-1994 Animal Care and Use Committee
- 1995 Graphics and Photography Focus Group
- 1995-date Structural Biology Faculty
- 1995-date Neuroscience Faculty
- 1996 Outstanding Performance Award
- 1998 Supply Advisory Committee
- 1999 Outstanding Performance Award
- 2000 Promotion to GS-15
- 2002 Special Service Award
- 2003 Reviewer: International Cooperative Biodiversity Groups Program
(ICBG) supported by NIH, NSF and USDA, in cooperation with the
Fogarty Center
- 2004-2007 NIEHS Committee on Promotions (COP-3)
- 2004-2007 TIPS Award Committee
- 2007 Performance Award
- 2008 Reviewer for the Akabori Memorial Award 2008 presented by the
Japanese Peptide Society once every two years to an outstanding
scientist for meritorious lifetime achievement

Grants, Fellowships

- 1962-1966 USPHS Training Grant in Protozoology and Parasitology,
Department of Zoology, University of California, Los Angeles
- 1966-1968 USPHS Postdoctoral Fellowship, Microbiology Institute, University of
Copenhagen, Denmark, NO Kjeldgård, sponsor
- 1973-1974 American Friends of the Hebrew University, Special Research
Fellowship

- 1973-1975 USPHS Fellowship, Department of Chemistry, University of California, San Diego, NO Kaplan, sponsor
- 1999-2002 Grant-in-Aid for Scientific Research, (C) 11694326, Japan Society for the Promotion of Science. Title: Design and synthesis of μ -selective opioidmimetic peptides. Okada Y, Yokoi T, Tsuda Y, **Lazarus LH**, Bryant SD.

Research Interests

- 1960-1966 Identification, isolation, purification, characterization of RNases, acid phosphatase, phosphodiesterase from *Tetrahymena pyriformis*
- 1966-1968 Induction of the galactokinase operon in *E. coli*
- 1968-1973 Characterization, isolation of FMDV replicase; viral enzymology; RNA and DNA synthesis; isolation, characterization DNA Pol α , β
- 1973-1975 General ligand affinity chromatography
- 1975-1977 Peptide endocrinology, neurochemistry
- 1977-1987 Identification of bioactive peptides in mammalian tissue
- 1987-date Rational design of opioid drugs and biochemical, pharmacological, and physiological mode of action of ligands; computational modeling

Major Research Achievements

- 1964 Inhibited synchronized cell division in *Tetrahymena* by actinomycin D
- 1967 Discovered, isolated of three base-specific RNases from *Tetrahymena*
- 1968 Discovered a phosphodiesterase in *Tetrahymena*
- 1972 Detailed kinetics of phosphorus analysis
- 1973 Discovered requirement for RNA in DNA synthesis in intact nuclei
- 1973 Discovered polymeric nature of DNA Pol α
- 1973 Discovered differential heparin inhibition of DNA Pol α and β
- 1973 Discovered the requirement for viral ssRNA in dsRNA replication
- 1976 Applied general-ligand affinity chromatography to enzyme purification
Quoted in Pharmacia PL-Biochemicals catalog
- 1976 Discovered β -LH as a precursor for endogenous opioids. Summarized in *Chemistry* **1976**, 48, 22-24. Most cited article in endocrinology 1977
- 1977 Discovered neurotensin receptors in extraneural tissue (mast cells)
- 1980 Discovered a mammalian physalaemin-related peptide
- 1982 Discovered bombesin-related peptide in human lung small-cell carcinoma.
Cover Story in *Oncology Today*, 1982
- 1983 Discovered physalaemin-related peptide in human lung small-cell carcinoma. Abstracted by the Public Affairs Office of FASEB Feature Service, 1983. Summarized in *Biomedicine et Pharmacotherapie*, 1983. Discussed in *Selecta* **1983**, 33 (XXV): 2864. Appeared as a feature article in the *Durham Morning Herald*, Sunday 30 January 1983

- 1983 Discovered mammalian bombesin-related peptide in milk
- 1985 Isolated physalaemin-related peptide from mammalian tissue
- 1989 Identified amphibian deltorphin as a δ -opioid receptor selective ligand
Quoted in Bachem California catalog
- 1989 Discovered bradykinin in bovine milk
- 1995 Developed potent Dmt-Tic pharmacophore (δ -opioid receptor antagonist)
- 1998 Awarded *U.S. Patent No. 5,780,589* for δ -opioid receptor di- and tripeptide
Dmt-Tic pharmacophore antagonists
- 2000 Inhibited hMDR-1 by hydrophobic δ -opioid receptor antagonists
- 2002 Transformed δ -opioid antagonist into potent δ -opioid agonist
- 2003 Discovered synthetic μ -opioid pyrazinone ligands with CNS analgesia.
Patent application No. 03703014.5-2103-JP0300516
- 2004 Demonstrated oral bioavailability of synthetic μ -opioid agonist
- 2004 Awarded *U.S. Patent No. 6,753,317* for δ -opioid receptor ligands
- 2004 Developed fluorescent δ -opioid antagonist.
- 2005 Developed Dmt-Tic dual μ -/ δ -opioid receptor antagonists; interconversion
between δ -antagonist and δ -agonist ligands
- 2006 Converted selective μ -agonist into a potent μ -antagonist
- 2007 Prevented morphine withdrawal symptoms by selective μ -antagonists
- 2007 Patent application for ^{18}F -opioids for PET screening for δ receptors in lung
cancer. *Patent pending.*

Ad Hoc Reviewer

Analytical Biochemistry
Bioorganic & Medicinal Chemistry
Bioorganic & Medicinal Chemistry Letters
Canadian Journal of Biochemistry
Cancer Research
Chemico-Biological Interactions
Comparative Biochemistry and Physiology
Critical Reviews in Oncology/Hematology
Current Medicinal Chemistry
Endocrine Journal
Endocrinology
Environmental Health Perspectives
European Journal of Cell Biology
 International Foundation for Science (<http://www.ifs.se>)
Journal of Biological Chemistry
Journal of Endocrine Investigation
Journal of Medicinal Chemistry
Journal of Pharmacology and Experimental Therapeutics
Journal of Peptide Research

Journal of Peptide Science
Journal of the American Chemical Society
Letters in Peptide Science
Medicinal Chemistry Research
Mini-Reviews in Medicinal Chemistry
Molecular and Cellular Neuroscience
Molecular Pharmacology
Peptides
Photochemistry and Photobiology
Proceedings of the National Academy of Science, USA
Protein Science
Regulatory Peptides
Science
Society for Experimental Biology and Medicine
Trends in Biotechnology
Trends in Pharmacological Sciences

Mentorship Activities

- 1978-1980 Michael D. Erisman PhD, Postdoctoral Fellow, American Lung Association, University of California, San Diego.
Current position: Vice President for Research, A/F Protein, Waltham, MA 02154.
- 1984-1987 Antonio Guglietta MD, PhD, IRTA Fellow, Rome, Italy.
Current position: Director of Research and Development, Grupo Ferrer Internacional, S.A., Gran Via Carles III, 98, E-08028 Barcelona, Spain.
- 1991-1993 L Martti J Attila PhD, IRTA Fellow, Helsinki, Finland
Current position: Faculty of Veterinary Medicine, Department of Clinical Sciences, Pharmacology and Toxicology, POB 57, University of Helsinki, Helsinki, Finland FIN-00014.
- 1996-1998 Peter S. Cooper PhD, IRTA Fellow, University of Virginia.
Current position: National Center for Biotechnology Information, National Library of Medicine, Bethesda, MD.
- 2001-2006 Yunden Jinsmaa PhD, IRTA Fellow, Ulaanbaatar, Mongolia and Kyoto University, Japan.
Current position: College of Pharmacy, Division of Medicinal and Natural Products Chemistry, S328, University of Iowa, Ames, Iowa 52240

2004-present Ewa D Marczak PhD, Research Fellow. Biotechnology Laboratory of Industrial Chemistry Research Institute, Warsaw, Poland

Guest Investigators

1983-1984 Giovanni Gaudino PhD, NATO Fellow and Visiting Scientist, Fogarty International Center.

Current position: Professor, School of Pharmacy, Department of Medical Sciences, Università degli Studi del Piemonte Orientale *Amedeo Avogadro*, 28100 Novara, Italy

1987-1988 Antonio Guglietta MD, PhD, Visiting Research Associate

1994 L Martti J Attila PhD, Consultant.

Students

1993 James Dixon BA, Summer Award Program, American Society of Biochemistry and Molecular Biology for High School Teachers

1997 Summer of Discovery Program: Jennifer Hardisty (UNC), Tara Lovekamp (NCSU)

2006 Summers of Discovery Program: Jennifer Williams (Native American, University of Oklahoma) and Jillian Fine (UNC)

2008 Summers of Discovery Program: Nicole Capik (George Mason University)

Invited Presentations

1966 Fluctuation of nuclease activity in heat-synchronized *T. pyriformis*: Carlsberg Biological Laboratories, Copenhagen, Denmark; E Zeuthen PhD, Chair and host. October, 1966.

1967 Properties of the nucleases from *T. pyriformis* and their fluctuation during synchronized growth: Department of Zoology, University of Lund, Lund, Sweden. May, 1967.

1968 Isolation of gal⁻ lambda phage and induction of the gal operon in *E. coli* temperature-sensitive mutants: Department of Microbiology, University of Copenhagen, Copenhagen, Denmark; NO Kjeldgaard PhD, host. April, 1968.

- 1970 Capsid structure of foot-and-mouth disease virus: Department of Virology, Hebrew University-Hadassah Medical School, Jerusalem, Israel; N Goldblum PhD, Chair and host. October, 1970.
- 1973 **Special Lecturer:** International Conference on Herpes and Related Viruses, Glasgow, Scotland. Biochemical properties of foot-and-mouth disease virus RNA polymerase. 23 February 1973.
- 1975 NIH conference on Mammalian DNA Polymerase, Monterey, CA. Biochemical and molecular properties affecting the activity of mammalian DNA polymerase. 28-31 January 1975.
- 1973 Interconversion between eukaryotic polymeric DNA polymerases: Diabetes Branch, NIAMDD, NIH, Bethesda, MD; J Roth MD, host. 24 August 1973.
- 1973 Interconversion between eukaryotic nuclear and cytoplasmic DNA polymerases: Department of Microbiology, University of Arizona, College of Medicine, Tucson, AZ; H Bernstein MD, host. 6 November 1973.
- 1973 Interconvertibility among eukaryotic polymeric DNA polymerases: Department of Biology, New Mexico State University, Las Cruces, NM; RT O'Brien PhD, host. 7 November 1973.
- 1973 Eukaryotic polymeric DNA polymerases: Action of heparin and conversion into monomeric enzyme. Department of Microbiology, University of New Mexico, Albuquerque, NM; LC McLaren PhD, host. 8 November 1973.
- 1974 Dissociation and specific inhibition of eukaryotic DNA polymerases: Department of Biology, California State University, Pomona, CA; L Cohen PhD, Chair and host. January 1974.
- 1974 Interrelationship between eukaryotic DNA polymerases: Department of Biology, California State University, Northridge, CA; M Cantor PhD and P Sheeler PhD, hosts. March 1974.
- 1975 Isolation of RNase free from DNase and protease contamination by general ligand affinity chromatography: Department of Chemistry, University of California San Diego, School of Medicine, La Jolla, CA; NO Kaplan PhD, host. June 1975.
- 1975 **Special Lecturer:** Engineering Foundation Conferences on Enzyme Engineering, Reed College, Portland, OR. Purification of dehydrogenase and kinases by affinity chromatography. 3-8 August 1975.
- 1976 Interaction of neurotensin with membrane receptor sites: NIEHS, Research Triangle Park, NC; RP DiAugustine PhD, host. August 1976.
- 1978 Specificity of the binding of neurotensin to mast cell receptor sites: Diabetes Branch, NIAMDD, NIH, Bethesda, MD; J Roth MD, host. June 1978.
- 1979 Evidence on the presence of [Leu⁵]enkephalin precursor in a murine mastocytoma: Department of Pharmacology, University of North Carolina, School of Medicine, Chapel Hill, NC; J Perkins PhD, host. December 1979.
- 1981 Physalaemin-like peptide from rabbit stomach: Diabetes Branch, NIAMDD, NIH, Bethesda, MD; J Roth MD, Chief, host. 28 March 1981.

- 1982 Of frogs and man—the peptide connection: Department of Pharmacology, University of North Carolina School of Medicine, Chapel Hill, NC; T-C Peng PhD, host. October 1982.
- 1984 International Workshop on Peptides in Lung Cancer, Marburg, Germany. Physalaemin-like immunoreactivity in human lung small-cell carcinoma: isocratic reversed-phase HPLC analysis of the chemically modified peptide. 15-19 June 1984.
- 1985 International Conference on Nonmammalian Peptides, National Academy of Lincci, Rome, Italy. Evolutionary relationships between nonmammalian and mammalian peptides. 11-15 May 1985.
- 1985 **Session Chairman:** Nonmammalian Peptides: Amphibia, Birds and Reptiles. Nonmammalian Peptides, Rome, Italy, 11-15 May 1985.
- 1987 **Member, Scientific Committee:** Bombesin-like Peptides in Health and Disease, New York Academy of Sciences, Rome, Italy. Neuromedin B: Physiology and pharmacological perturbations. 13-16 October 1987.
- 1987 Neuromedin B: Application of antibody probes on physiological function. Department of Medical Science and Human Oncology, University of Turin, Torino, Italy; P Comoglio MD, Chairman; 20 October 1987.
- 1992 **Special Lecturer:** Gordon Conference on Biology and Chemistry of Peptides, Ventura, CA. Molecular determinants required for high selectivity of deltorphin opioid peptides. 10-14 February 1992.
- 1989 Correlation between gastric acid secretion and brain μ receptors: Brain Research Institute, UCLA; J Fried, host; 26 January 1989.
- 1990 **Special Lecturer:** Design of selective opioid peptide ligands: Department of Chemical Engineering, UCLA; Y Cohen PhD, host; 17 August 1990.
- 1994 **Plenary Lecturer:** Friends of the Library Series, North Carolina State University, Raleigh, NC. The toad, ugly and venomous, wears yet a precious jewel in his skin. 29 August 1994.
- 1995 **Special Lecturer Series:** Center for Drug Evaluation and Research Staff College, Food and Drug Administration, Rockville, MD. Of frogs and man: the opioid bond that cannot be loosed. L Kaus PhD, host; 20 September 1995.
- 1998 **Invited Lecturer:** Size matters: new frontiers in designing potent δ -opioid antagonists. Department of Pharmaceutical Sciences, Kobe Gakuin University, Kobe, Japan; Y Okada PhD, host; 14 August 1998.
- 1998 **Plenary Lecturer:** The 3rd Symposium on Frontiers in Protein Chemistry and Biotechnology, Jilin University, Changchun, China. Size matters: new frontiers in designing potent δ -opioid antagonists. 17-20 August 1998.
- 1998 **Session Chairman:** *ibid*, Jilin University, Changchun, China, 17-20 August 1998.
- 2000 **Plenary Lecturer:** Annual Conference on Opioid Mimetic Analgesics 1999, Kobe Gakuin University, Kobe, Japan. Recent developments in the design and application of potent opioidmimetics. 24 March 2000.
- 2000 **Plenary Lecturer:** 120th Annual Meeting of the Pharmaceutical Society of Japan, Gifu, Japan. The Dmt-Tic pharmacophore: exquisite probes for the

- internal environment and bioactivity of opioid receptors. 28-31 March 2000.
- 2001 **Special Lecturer:** Dmt: the opioid affair. The 32nd Meeting of the International Narcotics Research Conference, Helsinki, Finland 14-19 July.
- 2001 **Plenary Lecturer:** The 4th Symposium on Frontiers in Protein Chemistry and Biotechnology, Chengde, China, 16-20 August.
- 2001 **Session Chairman:** *ibid*, Chengde, China, 16-20 August.
- 2002 **Organizing Committee and Plenary Lecturer:** Annual Conference on Opioid Mimetic Analgesics 2001, Kobe Gakuin University, Kobe, Japan, 18-19 March 2002.
- 2002 **Guest Lecturer:** Methods in opioid peptide research. Department of Pharmaceutical Sciences, Kobe Gakuin University, Kobe, Japan; Y Okada PhD, host; 25 March 2002.
- 2004 **Special Lecturer:** Designer opioids: ligand formation predicated on hydrophobic correlates. The 35th Meeting of the International Narcotics Research Conference, Kyoto, Japan, 17-23 July 2004.
- 2004 **Plenary Lecturer:** On the design of opioid mimetic peptides from chemistry to pharmacology: The new frontier in medicinal chemistry and medicine. Kobe Gakuin University, Kobe, Japan, Y Tsuda PhD, host; 26 July 2004.
- 2005 Pain and pleasure: the opioid conundrum. NIEHS, Laboratory of Pharmacology and Chemistry, John Pritchard, PhD, Chief, host: 24 February 2005.
- 2006 **Culture Event Lecturer:** Impressionism: interpretation of light and color. Kathy Oldenwald, EEO Director, NIEHS, and Eli Ney, sponsors; 15 November and 6 December 2006.

BIBLIOGRAPHY

1. Peer Reviewed Journals

1. **Lazarus LH**, Levy MR, Scherbaum OH. Inhibition of synchronous cell division in *Tetrahymena pyriformis* by actinomycin D. *Exp. Cell Res.* **1964**, 35, 672-676
2. **Lazarus LH**, Scherbaum OH. Effect of temperature on the activity of ribonuclease from *Tetrahymena pyriformis*. *J. Cell Physiol.* **1966**, 68, 95-97.
3. **Lazarus LH**, Scherbaum OH. Activity of a ribosomal phosphodiesterase from a protozoan. *Nature* **1967**, 213, 887-888.
4. **Lazarus LH**, Scherbaum OH. Isolation and specificity of the intracellular ribonuclease from *Tetrahymena pyriformis*. *Biochem. Biophys. Acta* **1967**, 142, 368-384
5. **Lazarus LH**, Scherbaum OH. Some properties of the acid phosphatases of *Tetrahymena pyriformis*. *Life Sci.* **1967**, 6, 2401-2407.
6. **Lazarus LH**, Scherbaum OH. Activity of ribonuclease, acid phosphatase and phosphodiesterase in *Tetrahymena pyriformis* during growth. *J. Cell Biol.* **1968**, 36, 415-418
7. Popescu M, **Lazarus LH**, Goldblum N. Simplified adaptor for electroelution. *Anal. Biochem.* **1971**, 40: 247-253.
8. **Lazarus LH**, Olshevsky U, Cymbalista S, Einav G, Goldblum N. On the architecture of foot-and-mouth disease virus. *Rev. Roum. Inframicrobiol.* **1971**, 8, 205-208.
9. Popescu M, **Lazarus LH**, Goldblum N. Electroelution of RNA: Simplified adaptor for continuous flow and characteristics of the system. *Rev. Roum. Inframicrobiol.* **1971**, 8, 237-246
10. Popescu M, **Lazarus LH**, Goldblum N. Electroelution of RNA: Characteristics of the system. *Anal. Biochem.* **1972**, 45, 35-41.
11. **Lazarus LH**, Chou S-C. Modification of the analysis of phosphorus and kinetics of the reaction. *Anal. Biochem.* **1972**, 45, 557-566
12. Barzilai R, **Lazarus LH**, Goldblum N. Viscosity-density gradient for purification of FMDV. *Arch. gesamt. Virusforsch.* **1972**, 36, 141-146

13. **Lazarus LH**, Popescu M, Barzilai R, Goldblum N. Spermidine stimulation of RNA-dependent polymerase activity. *Arch. gesamt. Virusforsch.* **1972**, 36, 311-316, 1972.
14. **Lazarus LH**, Itin A, Popescu M, Goldblum N. Mono- and divalent cationic parameters of foot-and-mouth disease virus replicase. *Eur. J. Biochem.* **1973**, 27, 335-340.
15. **Lazarus LH**, Itin A. Activity of foot-and-mouth disease virus RNA polymerase in vitro: Inhibition by polyamines and polyamino acids. *Arch. Biochem. Biophys.* **1973**, 154, 156-160.
16. **Lazarus LH**. A novel system for DNA synthesis in isolated nuclei. *FEBS Lett.* **1973**, 35, 166-168.
17. **Lazarus LH**, Kitron N. Neomycin inhibition of DNA polymerase. *Biochem. Pharmacol.* **1973**, 22, 3115-3117.
18. **Lazarus LH**, Kitron N. Cytoplasmic DNA polymerase: Polymeric forms and their conversion to monomers resembling nuclear DNA polymerase. *J. Mol. Biol.* **1973**, 81, 529-534
19. **Lazarus LH**, Kitron N. Lithium depresses DNA polymerase activity. *Lancet* **1974**, 2, 225-226
20. **Lazarus LH**, Kitron N. Inhibition and dissociation of mammalian polymeric DNA polymerase by heparin. *Arch. Biochem. Biophys.* **1974**, 164, 414-419
21. **Lazarus LH**, Barzilai, R. Association of foot-and-mouth disease virus replicase with RNA template and cytoplasmic membranes. *J. Gen. Virol.* **1974**, 23, 213-218
22. **Lazarus LH**, Itin A. Requirement for double-stranded RNA during the synthesis of FMDV RNA in vitro. *Arch. gesamt. Virusforsch.* **1974**, 45, 135-140
23. Barzilai R, Finkelkraut E, **Lazarus LH**, Goldblum N. Inhibition of SV40 DNA synthesis by FV3. *J. Gen. Virol.* **1974**, 23, 335-339
24. Barzilai R, **Lazarus LH**. Inhibition of foot-and-mouth disease virus replicase by FV3 virions. *J. Gen. Virol.* **1974**, 24, 39-44
25. **Lazarus LH**, Kitron, N. Differentiation and characterization of the cytoplasmic and nuclear deoxyribonucleic acid polymerase from baby hamster kidney cells. *Biochem. Biophys. Acta* **1975**, 402, 309-322

26. **Lazarus LH**, Kitron N. Fluctuation in activity of the molecular forms of cellular DNA polymerase during infection by SV40. *Arch. Virol.* **1976**, *52*, 113-133.
27. **Lazarus LH**, Lee C-Y, Wermuth B. Application of general ligand affinity chromatography for the mutual separation of deoxyribonuclease and ribonuclease free of protease contamination. *Anal. Biochem.* **1976**, *74*, 138-144
28. Lee C-Y, **Lazarus LH**, Kabakoff DS, Russel PJ, Lavel, M, Kaplan NO. Purification of kinases by general ligand chromatography. *Arch. Biochem. Biophys.* **1976**, *178*, 8-18
29. **Lazarus LH**, Ling N, Guillemin R. β -Lipotropin as a prohormone for the morphinometric peptides, endorphins and enkephalin. *Proc. Natl. Acad. Sci USA* **1976**, *73*, 2156-2159
30. Lee C-Y, **Lazarus LH**, Kaplan NO. Purification of dehydrogenases and kinases by affinity chromatography. *Enzyme Eng.* **1977**, *3*, 299-311
31. **Lazarus LH**, Brown MR, Perrin MH. Distribution, localization and characteristics of neurotensin binding sites in the rat brain. *Neuropharmacol.* **1977**, *16*, 625-629
32. **Lazarus LH**, Brown MR, Perrin MH. Mast cell binding of neurotensin. I. Iodination of neurotensin and characterization of the interaction of neurotensin with mast cell receptor sites. *J. Biol. Chem.* **1977**, *252*, 7174-7179
33. **Lazarus LH**, Brown MR, Perrin MH, Rivier JE. Mast cell binding of neurotensin. II. Molecular conformation of neurotensin involved in the stereospecific binding to mast cell receptor sites. *J. Biol. Chem.* **1977**, *252*, 7180-7183
34. **Lazarus LH**, Brown MR, Perrin MH, Rivier JE. Verification of both the sequence and conformation of neurotensin in binding to mast cells. *Biochem. Biophys. Res. Commun.* **1977**, *76*, 1079-1085
35. Rivier JE, **Lazarus LH**, Perrin MH, Brown MR. Neurotensin analogs: structure-activity relationships. *J. Med. Chem.* **1977**, *20*, 1409-1414
36. **Lazarus LH**, DiAugustine RP. Radioimmunoassay of the tachykinin peptide physalaemin. Detection of physalaemin-like immunoreactivity in rabbit stomach. *Anal. Biochem.* **1980**, *107*, 350-357
37. **Lazarus LH**, Linnoila, RI, Hernandez O, DiAugustine RP. Neuropeptide in mammalian tissues with physalaemin-like immunoreactivity. *Nature* **1980**, *287*, 555-558

38. DiAugustine RP, **Lazarus LH**, Jahnke GD, Kahn MN, Erisman MD, Linnoila RI: Corticotropin/ β -endorphin immunoreactivity in rat mast cells. Peptide or protease? *Life Sci.* **1980**, *27*, 2663-2668
39. Jahnke GD, **Lazarus LH**, DiAugustine RP, Soldato CM, Erisman MD. Peptide degradation by mast cell chymase-heparin complex. *Life Sci.* **1981**, *29*, 397-403.
40. **Lazarus LH**, DiAugustine RP, Khan MN, Jahnke GD, Erisman MD. Application of a sequence-specific radioimmunoassay for the carboxyl terminal region of adrenocorticotropin. *Clin. Chem.* **1981**, *27*, 542-552.
41. Erisman MD, Linnoila RI, Hernandez O, DiAugustine RP, **Lazarus LH**. Human lung small-cell carcinoma contains bombesin. *Proc. Natl. Acad. Sci. USA* **1982**, *79*, 2379-2383
42. **Lazarus LH**, DiAugustine RP, Soldato CM. A substance with immunoreactivity to the peptide physalaemin in mammalian respiratory tissue. *Exp. Lung Res.* **1982**, *3*, 329-341
43. **Lazarus LH**, DiAugustine RP, Jahnke GD, Hernandez O. Physalaemin: An amphibian peptide in human lung small-cell carcinoma. *Science* **1983**, *219*, 79-81 (**48 citations**)
44. Erisman MD, **Lazarus LH**, Jahnke GD, Soldato CM, DiAugustine RP. Joining peptide of proopiomelanocortin. I. Radioimmunoassay and extraction of related peptides from pituitary glands. *Peptides* **1983**, *4*, 475-482
45. Jahnke GD, Soldato CM, Erisman MD, DiAugustine RP, **Lazarus LH**. Joining peptide of proopiomelanocortin. II. Interspecies heterogeneity of the joining peptide fragment. *Peptides* **1983**, *4*, 483-492
46. Jahnke GD, **Lazarus LH**. A bombesin immunoreactive peptide in milk. *Proc. Natl. Acad. Sci. USA* **1984**, *81*, 578-583
47. Hernandez O, Dermott K, **Lazarus LH**. High-performance liquid chromatography of amphibian peptides. Selectivity changes induced by pH. *J. Liquid Chromat.* **1984**, *7*, 893-905
48. Khan MN, Mirel RD, Ontjes DA, Gosh AP, **Lazarus LH**, DiAugustine RP. Adrenocorticotropin radioimmunoassay: Properties of antisera against synthetic ACTH(1-24) and its clinical application. *Hormone Res.* **1984**, *20*, 129-137

49. Conlon JM, Schmidt WE, **Lazarus LH**, Becker HD, Creutzfeldt W. Partial characterization of substance P-like immunoreactivity and physalaemin-like activity in a carcinoid tumor. *Reg. Peptides* **1985**, *11*, 117-123
50. **Lazarus LH**, Hernandez O. Physalaemin-like immunoreactivity from human small-cell carcinoma: Isocratic reversed-phase HPLC analysis of the chemically modified peptide. *Rec. Resul. Cancer Res.* **1985**, *99*, 56-66.
51. Guglietta A, Strunk CL, Irons BJ, **Lazarus LH**. Central neuromodulation of gastric secretion by bombesin-like peptides. *Peptides* **1985**, *6*, 75-81
52. Gaudino G, Fasolo A, Merlo G, **Lazarus LH**, Renda T, D'Este L, Melchiorri P, Vandesande F. Active peptides from amphibian skin are also amphibian neuropeptides. *Peptides* **1985**, *6*, 209-214
53. **Lazarus LH**, Wilson WE, Gaudino G, Irons BJ, Guglietta A. Evolutionary relationship between nonmammalian and mammalian peptides. *Peptides* **1985**, *6*, 295-307
54. Van Dongen PAM, Theodorsson-Norheim E, Brodin E, Hökfelt T, Grillner S, Peters A, Cuello AC, Forssmann WG, Reinecke M, Singer E, **Lazarus LH**. Immunohistochemical and chromatographic studies of peptides with tachykinin-like immunoreactivity in the central nervous system of the lamprey. *Peptides* **1986**, *7*, 297-314
55. Wilson WE, Harvan DJ, Hamm C, **Lazarus LH**, Klapper DG, Yajima H, Hayashi Y. Physalaemin-like immunoreactive peptides from rabbit stomach. *Int. J. Peptide Prot. Res.* **1986**, *28*, 58-66
56. **Lazarus LH**, Gaudino G, Wilson WE, Erspamer V. An immunoreactive peptide in milk contains bombesin-like bioactivity. *Experientia* **1986**, *42*, 822-823.
57. Fujii N, Hayashi Y, Akaji K, Funakoshi S, Shimamura M, Yuguchi S, **Lazarus LH**, Yajima H. Studies on peptides. CXLIX. Solid-phase synthesis of a rabbit stomach peptide by application of a new polymer support and a new deprotecting procedure. *Chem. Pharm. Bull.* **1987**, *35*, 1266-1269
58. Guglietta A, Irons BJ, **Lazarus LH**, Melchiorri P. Structure-activity relationship of dermorphin on gastric secretion. *Endocrinology* **1987**, *120*, 2137-2143
59. **Lazarus LH**, Irons BJ, Grimes LM, Wilson WE, Guglietta A, Yajima H. Assessment of neuromedin B polyclonal antibodies as molecular probes in neural tissue. *J. Neurosci. Meth.* **1988**, *23*, 161-172

60. Guglietta A, Irons BJ, **Lazarus LH**, Sivam SP. Effects and mechanism of action of lithium chloride on gastric acid secretion in rats. *Gastroenterology* **1988**, *95*, 1454-1459
61. Guglietta A, Irons BJ, **Lazarus LH**. Effect of bombesin, dermorphin and salmon calcitonin on gastric secretion in rats. *Methods Find. Exp. Clin. Pharmacol.* **1988**, *10*, 481-485
62. Renda T, D'Este L, Fasolo A, **Lazarus LH**, Minniti F, Erspamer V. Brain-gut-skin peptides: An update and overview. *Arch. Histol. Cytol.* **1989**, *52*, 317-323
63. **Lazarus LH**, Guglietta A, Wilson WE, Irons BJ, de Castiglione R. Dimeric dermorphin analogues as specific μ -receptor probes on rat brain membranes. Positive correlation between central μ -receptors and suppression of gastric acid secretion. *J. Biol. Chem.* **1989**, *264*, 354-362
64. **Lazarus LH**, de Castiglione R, Guglietta A, Wilson WE. Dermorphin gene sequence peptide with high affinity and selectivity for δ -opioid receptors. *J. Biol. Chem.* **1989**, *264*, 3047-3050
65. Wilson WE, **Lazarus LH**, Tomer K. Bradykinin and kininogen in bovine milk. *J. Biol. Chem.* **1989**, *264*, 17777-17783
66. Guglietta A, Irons BJ, **Lazarus LH**, de Castiglione R, Melchiorri P. Dimeric dermorphin peptides: Central administration suppresses gastric acid secretion through interaction with μ -type opioid receptor. *Meth. Find. Clin. Pharmacol.* **1989**, *11*, 663-670
67. Guglietta A, Nardi RV, **Lazarus LH**. Central administered indomethacin blocks the inhibitory action of several neuropeptides on gastric acid secretion. *Eur. J. Pharmacol.* **1989**, *170*, 87-90
68. **Lazarus LH**, Wilson WE, Guglietta A, de Castiglione, R. Dermorphin interaction with rat brain opioid receptors: Involvement of hydrophobic sites in the binding domain. *Mol. Pharmacol.* **1990**, *37*, 886-892
69. **Lazarus LH**, Salvadori S, Santagada S, Tomatis R, Wilson WE. Function of negative charge in the "address domain" of deltorphins. *J. Med. Chem.* **1991**, *34*, 1350-1355
70. **Lazarus LH**, Salvadori S, Tomatis R, Wilson WE. Opioid receptor selectivity reversal in deltorphin tetrapeptide analogues. *Biochem. Biophys. Res. Commun.* **1991**, *178*, 110-115

71. Marastoni M, Tomatis R, **Lazarus LH**, Salvadori S. On the degradation of deltorphin peptides by plasma and brain homogenate. *Farmaco* **1991**, *46*, 1273-1279
72. Panzanelli P, Multatero B, **Lazarus LH**, Fasolo A. Ranatensin-like immunoreactivity in the brain of the green frog (*Rana exulenta* L.). *Basic Appl. Histochem.* **1991**, *35*, 359-370
73. Ordronneau P, Woodley JC, Grossman G, Abdullah LA, **Lazarus LH**, Petrusz P. Characterization of an antiserum to glycyl-D-aspartate (GDA) and its use as a probe for endogenous N-methyl-D-aspartate (NMDA)-like compounds. *Mol. Cell. Neurosci.* **1992**, *3*, 259-266
74. **Lazarus LH**, Salvadori S, Balboni G, Tomatis R, Wilson WE. Stereospecificity of amino acid side chains in deltorphin defines binding to opioid receptors. *J. Med. Chem.* **1992**, *35*, 1222-1227
75. **Lazarus LH**, Salvadori S, Greico P, Wilson WE, Tomatis R. Unique sequence in deltorphin C confers structural requirements for δ opioid receptor selectivity. *Eur. J. Med. Chem.* **1992**, *27*, 791-797
76. Salvadori S, Bianchi C, **Lazarus LH**, Scaranari V, Attila M, Tomatis R. Para-substituted Phe³ deltorphin analogues: Enhanced selectivity of halogenated derivatives for δ opioid receptor sites. *J. Med. Chem.* **1992**, *35*, 4651-4657
77. **Lazarus LH**, Salvadori S, Bundy DM, Greico P, Wilson WE, Tomatis R. Interaction of deltorphin with opioid receptors: Molecular determinants for affinity and selectivity. *Peptides* **1993**, *14*, 21-28
78. Salvadori S, Bryant SD, Temussi PA, Bundy DM, Attila M, Tomatis R, **Lazarus LH**. Relationship between receptor affinity and topography of N-terminally extended and bridged [Tyr¹ \rightarrow Asp⁴]deltorphin C analogues: Novel probes for the δ opioid receptor. *Eur. J. Pharmacol.* **1993**, *230*, 357-363
79. Bryant SD, Salvadori S, Attila M, **Lazarus LH**. Topographical conformation of the deltorphins predicate δ receptor affinity. *J. Amer. Chem. Soc.* **1993**, *115*, 8503-8504
80. Attila M, Salvadori S, Balboni G, Bryant SD, **Lazarus LH**. Synthesis and receptor binding analysis of dermorphin hepta-, hexa- and pentapeptide analogues. Evidence for one- and two-site binding models for the δ -opioid receptor. *Int. J. Peptide Prot. Res.* **1993**, *42*, 550-559
81. Salvadori S, Bryant S D, Bianchi C, Balboni G, Attila M, **Lazarus LH**. Phe³-substituted analogues of deltorphin C. Spatial conformation and topography of the

aromatic ring in peptide recognition by δ opioid receptors. *J. Med. Chem.* **1993**, *36*, 3748-3756

82. **Lazarus LH**, Attila M. The toad, ugly and venomous, wears yet a precious jewel in his skin. *Prog. Neurobiol.* **1993**, *41*, 473-507

83. Temussi PA, Salvadori S, Amodeo P, Bianchi C, Guerrini R, Tomatis R, **Lazarus LH**, Picone D, Tancredi T. Selective opioid dipeptides. *Biochem. Biophys. Res. Commun.* **1994**, *198*, 933-939

84. Bryant SD, Attila M, Salvadori S, Guerrini R, **Lazarus L H**. Molecular dynamics conformations of deltorphin analogues advocate δ opioid binding site models. *Peptide Res.* **1994**, *7*, 175-184

85. Tancredi T, Salvadori S, Amodeo P, Picone D, **Lazarus LH**, Bryant SD, Guerrini R, Marzola G, Temussi PA. Conversion of enkephalin and dermorphin into δ -selective opioid antagonists by single-residue substitution. *Eur. J. Biochem.* **1994**, *224*, 241-247

86. Jones LS, Grooms SY, Salvadori S, **Lazarus LH**. Dermorphin-induced hyperexcitability in hippocampal CA3 and CA1 in vitro. *Eur. J. Pharmacol.* **1994**, *264*, 39-48

87. Salvadori S, Guerrini R, Forlani V, Bryant SD, **Lazarus LH**. Prerequisite for His⁴ in deltorphin A for high δ opioid receptor selectivity. *Amino Acids* **1994**, *7*, 291-304

88. **Lazarus LH**, Bryant SD, Attila M, Salvadori S. Frog opioid peptides. A case for environmental mimicry. *Environ. Health Perspect.* **1994**, *102*, 648-654

89. Balboni G, Salvadori S, D'Angeli F, Marchetti P, **Lazarus LH**, Bryant SD, Bianchi C. Single diastereomeric desamino tyrosyl-alanyl-tetra- and heptapeptides with opioid antagonistic activity. *Int. J. Peptide Prot. Res.* **1995**, *45*, 187-193

90. Salvadori S, Attila M, Balboni G, Bianchi C, Bryant SD, Crescenzi O, Guerrini R, Picone D, Tancredi T, Temussi P A, **Lazarus LH**. δ Opioidmimetic antagonists: prototypes for designing a new generation of ultrasensitive opioid peptides. *Mol. Med.*, **1995**, *1*, 678-689

91. Breveglieri A, Guerrini R, Salvadori S, Bianchi C, Bryant SD, Attila M, **Lazarus LH**. Design and synthesis of 1-aminocycloalkane-1-carboxylic acid substituted deltorphin analogues: unique δ and μ opioid activity in modified peptides. *J. Med. Chem.*, **1996**, *39*, 773-780

92. Guerrini R, Capasso A, Sorrentino L, Anacardio R, Bryant SD, **Lazarus LH**, Attila M, Salvadori S. Opioid receptor selectivity alteration by single residue replacement: synthesis and activity profile of [Dmt¹]deltorphin B. *Eur. J. Pharmacol.*, **1996**, 206, 37-42
93. Capasso A, Guerrini R, Balboni G, Sorrentino L, Temussi PA, **Lazarus L**, Bryant S D, Salvadori S. Dmt-Tic-OH, a highly selective and potent δ -opioidmimetic receptor antagonist after systemic administration in the mouse. *Life Sci.*, **1996**, 59, PL93-PL98
94. Lazarus LH, Bryant SD, Salvadori S, Attila M, Jones LS. Opioid infidelity: novel opioid peptides with dual high affinity for delta- and mu-receptors. *Trends Neurosci.* **1996**, 19, 31-35
95. Balboni G, Guerrini R, Salvadori S, Tomatis R, Bianchi C, Attila M, Bryant SD, **Lazarus LH**. Opioid diketopiperazines: Synthesis and activity of a prototypic class of unique opioid antagonists. *Biol. Chem.*, **1997**, 378, 19-29
96. Bryant SD, Balboni G, Guerrini R, Salvadori S, Tomatis R, **Lazarus LH**. Opioid diketopiperazines: Refinement of the δ opioid antagonist pharmacophore. *Biol. Chem.*, **1997**, 378, 107-114
97. Salvadori S, Picone D, Tancredi T, Guerrini R, Spadaccini R, **Lazarus LH**, Regoli D, Temussi PA. Solution conformation of nociceptin. *Biochem. Biophys. Res. Commun.*, **1997**, 233, 640-643
98. Guerrini R, Calo G, Rizzi A, Bianchi C, **Lazarus LH**, Salvadori S, Temussi PA, Regoli D., Address and message sequences for the nociceptin receptor. A structure-activity study of nociceptin-(1-13)-amide. *J. Med. Chem.*, **1997**, 40, 1789-1793
99. Crescenzi O, Fraternali F, Picone D, Tancredi T, Balboni G, Guerrini R, **Lazarus LH**, Salvadori S, Temussi PA. Design and solution structure of a partially rigid opioid antagonist lacking the basic center. Models of antagonism. *Eur. J. Biochem.* **1997**, 247, 66-73
100. Bryant SD, Guerrini R, Salvadori S, Bianchi C, Tomatis R, Attila M, **Lazarus LH**. Helix inducing α -aminoisobutyric acid in opioidmimetic deltorphin C analogues. *J. Med. Chem.*, **1997**, 40, 2579-2587
101. Tomatis R, Marastoni M, Balboni G, Guerrini R, Capasso A, Sorrentino L, Santagada V, Caliendo G, **Lazarus LH**, Salvadori S. Synthesis and pharmacological activity of deltorphin and dermorphin-related glycopeptides. *J. Med. Chem.*, **1997**, 40, 2948-2952

102. Salvadori S, Balboni G, Guerrini R, Tomatis R, Bianchi C, Bryant SD, Cooper PS, **Lazarus LH**. Evolution of the Dmt-Tic pharmacophore: N-terminal methylated derivatives with extraordinary δ opioid antagonist activity. *J. Med. Chem.*, **1997**, *40*, 3100-3108
103. Capasso A, Amodeo P, Balboni G, Guerrini R, **Lazarus LH**, Temussi PA, Salvadori S. Design of μ selective opioid dipeptides antagonists. *FEBS Lett.* **1997**, *417*, 141-144
104. Bryant SD, Salvadori S, Cooper PS, **Lazarus LH**. New δ -opioid antagonists as pharmacological probes. *Trends Pharmacol. Sci.* **1998**, *19*, 42-46
105. Guerrini R, Capasso A, Marastoni M, Bryant SD, Cooper PS, **Lazarus LH**, Temussi PA, Salvadori S. Rational design of dynorphin A analogues with δ -receptor selectivity and antagonism for δ - and κ -receptors. *Bioorg. Med. Chem.* **1998**, *6*, 57-62
106. Okada Y, Tsukatani M, Taguchi H, Yokoi T, Bryant SD, **Lazarus LH**. Amino acids and peptides. LII. Design and synthesis of opioidmimetics containing pyrazinone ring and examination of their opioid receptor binding activity. *Chem. Pharm. Bull.*, **1998**, *46*, 1374-1382
107. **Lazarus LH**, Bryant SD, Salvadori S, Attila M, Jones LS. Opioid infidelity. Novel opioid agonists with dual high affinities for δ and μ receptors. *Trends Neurosci.*, **1998**, *19*, 31-35
108. Kertész I, Balboni G, Guerrini R, Salvadori S, **Lazarus LH**, Tóth G. Synthesis of 2',6'-dimethyltyrosine containing tritiated δ opioid-receptor selective antagonist dipeptide ligands with extraordinary affinity. *J. Labelled Compd. Radiopharm.* **1998**, *41*, 1083-1091
109. Marastoni M, Guerrini R, Balboni G, Salvadori S, Fantin G, Fogagnolo M, **Lazarus LH**, Tomatis R. Opioid deltorphin C analogues containing *cis*- or *trans*-2 or 3- or 4-aminocyclohexanecarboxylic acid residue. *Arzneimittel-Forsch./Drug Res.* **1999**, *49*, 6-12
110. Okada Y, Fukumizu A, Takahashi M, Yokoi T, Tsuda Y, Bryant SD, **Lazarus LH**. Synthesis of pyrazinone ring-containing opioid mimetics and examination of their opioid receptor-binding activity. *Chem. Pharm. Bull.* **1999**, *46*, 1374-1382
111. Okada Y, Fukumizu A, Takahashi M, Yokoi T, Tsuda Y, Bryant SD, **Lazarus LH**. Synthesis of pyrazinone ring-containing opioid mimetics and examination of their opioid receptor-binding activity. *Chem. Pharm. Bull.* **1999**, *47*, 1193-1195

112. Salvadori S, Guerrini R, Balboni G, Bianchi C, Bryant SD, Cooper PS, **Lazarus LH**. Further studies on the Dmt-Tic pharmacophore: Hydrophobic substituents at the C-terminus endow δ antagonists to manifest δ agonism and μ antagonism. *J. Med. Chem.* **1999**, *42*, 5010-5019
113. Okada Y, Fukumizu A, Takahashi M, Yamazaki J, Yokoi T, Tsuda Y, Bryant SD, **Lazarus LH**. Amino acids and peptides. LVI. Synthesis of pyrazinone ring-containing opioid mimetics and examination of their opioid receptor binding activity. *Tetrahedron* **1999**, *55*, 14391-14406
114. Bryant SD, Salvadori S, Cooper PS, **Lazarus LH**. New δ opioid antagonists as pharmacological probes. *Trends Pharmacol. Sci.*, **1999**, *19*, 42-46
115. **Lazarus LH**, Bryant SD, Cooper PS, Salvadori S. What peptides these deltorphins be. *Prog. Neurobiol.*, **1999**, *57*, 377-420
116. Monory K, Bryant SD, Kertész I, Balboni G, Guerrini R, Tóth G, Salvadori S, **Lazarus LH**, Borsodi A. [³H]N,N(Me)₂-Dmt-Tic-OH, a new delta selective opioid dipeptide antagonist: binding characteristics and effects on G protein activation. *NeuroReport* **2000**, *11*, 2083-2086
117. Balboni G, Salvadori S, Guerrini R, Bianchi C, Santagada V, Calliendo G, Bryant SD, **Lazarus LH**. Opioid pseudopeptides containing heteroaromatic or heteroaliphatic nuclei. *Peptides*, **2000**, *21*, 1663-1671
118. Okada Y, Fukumizu A, Takahashi M, Shimizu Y, Tsuda Y, Yokoi T, Bryant SD, **Lazarus LH**. Synthesis of stereoisomeric analogues of endomorphin-2, H-Tyr-Pro-Phe-Phe-NH₂, and examination of their opioid receptor binding activities and solution conformation. *Biochem. Biophys. Res. Commun.* **2000**, *276*, 7-11
119. Labarre M, Butterworth J, St-Onge S, Payza K, Schmidhammer H, Salvadori S, Balboni G, Guerrini R, Bryant SD, **Lazarus LH**. Inverse agonism by Dmt-Tic analogues and HS 378, a naltrindole analogue. *Eur. J. Pharmacol.* **2000**, *406*, R1-R3
120. Santagada V, Balboni G, Calliendo G, Guerrini R, Salvadori S, Bianchi C, Bryant SD, **Lazarus LH**. Assessment of substitution in the second pharmacophore of Dmt-Tic analogues. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2745-2748
121. Lovekamp T, Cooper PS, Hardison J, Bryant SD, Guerrini R, Balboni G, Salvadori S, **Lazarus LH**. Inhibition of human multidrug resistance P-glycoprotein-1 by analogues of a potent δ -opioid antagonist. *Brain Res.*, **2001**, *902*, 131-134

122. Santagada V, Fiorino F, Severino B, Salvadori S, **Lazarus LH**, Bryant SD, Caliendo G. A convenient synthesis of *N*-Fmoc-*N,N*-bis-Boc-7-guanyl-1,2,3,4-tetrahydro-3-isoquinoline carboxylic acid (Fmoc-*N,N*-bis-Boc-7-guanyl-Tic-OH, GTIC). *Tetrahedron Lett.* **2001**, *42*, 3507-3509
123. Balboni G, Guerrini R, Salvadori S, Bianchi C, Rizzi D, Bryant SD, **Lazarus LH**. Evaluation of the Dmt-Tic Pharmacophore: conversion of a potent δ -opioid receptor antagonist into a potent δ -agonist and ligands with mixed properties. *J. Med. Chem.* **2002**, *45*, 713-720
124. Okada Y, Fujisawa Y, Morishita A, Shiotani K, Miyazaki A, Fujita Y, Tsuda Y, Yokoi T, Bryant SD, **Lazarus LH**. Deamination of 2(1*H*)-pyrazinone derivatives during catalytic hydrogenation. *Tetrahedron Lett.* **2002**, *43*, 8137-8139
125. Bryant SD, George C, Flippen-Anderson J, Deschamps JR, Salvadori S, Balboni G, Guerrini R, **Lazarus LH**. Crystal structures of dipeptides containing the Dmt-Tic pharmacophore. *J. Med. Chem.* **2002**, *45*, 5506-5513
126. Balboni G, Salvadori S, Guerrini R, Negri L, Gianinni E, Yunden J, Bryant SD, **Lazarus LH**. Potent δ -opioid receptor agonists containing the Dmt-Tic pharmacophore. *J. Med. Chem.* **2002**, *45*, 5556-5563
127. Okada Y, Fujita Y, Motoyama T, Tsuda Y, Yokoi T, Li T, Sasaki Y, Ambo A, Yunden J, Bryant SD, **Lazarus LH**. Structural studies of [2',6'-dimethyl-L-tyrosine¹]endomorphin-2 analogues: enhanced activity and *cis* orientation of the Dmt-Pro amide bond. *Bioorg. Med. Chem.* **2003**, *11*, 1983-1984
128. Okada Y, Tsuda Y, Yokoi T, Sasaki Y, Ambo A, Nagata M, Yunden J, Bryant SD, **Lazarus LH**. Unique high-affinity synthetic μ -opioid receptor agonists with central- and systemic-mediated analgesia. *J. Med. Chem.* **2003**, *46*, 3201-3209
129. Ingman K, Salvadori S, **Lazarus L**, Korpi ER, Honkanen A. Selective δ -opioid receptor antagonist *N,N*(CH₃)₂-Dmt-Tic-OH does not reduce ethanol intake in alcohol-preferring AA rats. *Addic. Biol.* **2003**, *8*, 173-179.
130. Balboni G, Salvadori S, Guerrini R, Negri L, Giannini E, Bryant SD, Jinsmaa Y, **Lazarus LH**. Synthesis and opioid activity of *N,N*-dimethyl-Dmt-Tic-NH-CH(R)-R' analogues: acquisition of potent δ antagonism. *Bioorg. Med. Chem.* **2003**, *11*, 5435-5441
131. Jinsmaa Y, Okada Y, Tsuda Y, Sasaki Y, Ambo A, Bryant SD, **Lazarus LH**. Novel 2',6'-dimethyl-L-tyrosine-containing pyrazinone opioid mimetic μ agonists with potent antinociceptive activity in mice. *J. Pharmacol. Exp. Ther.* **2004**, *309*, 1-7

132. Jinsmaa Y, Miyazaki A, Fujita Y, Fujisawa Y, Shiotani K, Li T, Tsuda Y, Yokoi T, Ambo A, Sasaki Y, Bryant SD, **Lazarus LH**, Okada Y. Oral availability of a new class of μ -opioid receptor agonists containing 3,6-bis-[Dmt-NH-(CH₂)_n]-2(1*H*)-pyrazinone with central mediated analgesia. *J. Med. Chem.*, **2004**, *47*, 2599-2610
133. Fujita Y, Tsuda Y, Li T, Motoyama T, Takahashi M, Shimizu Y, Yokoi T, Sasaki Y, Ambo A, Kita A, Jinsmaa Y, Bryant SD, **Lazarus LH**, Okada Y. Development of potent bifunctional endomorphin-2 analogs with mixed μ/δ -opioid agonist/ δ -opioid antagonist properties. *J. Med. Chem.* **2004**, *47*, 3591-3599.
134. Balboni G, Salvadori S, Guerrini S, Negri L, Giannini E, Bryant SD, Jinsmaa Y, **Lazarus LH**. Direct influence of C-terminally substituted amino acids in the Dmt-Tic pharmacophore alters high δ -opioid receptor selectivity and potent antagonism. *J. Med. Chem.* **2004**, *47*, 4061-4071
135. Balboni G, Salvadori S, Dal Piazz, A, Bortolotti, F, Argazzi R, Negri L, Lattanzi R, Bryant SD, Jinsmaa Y, **Lazarus LH**. Highly selective fluorescent analogue of the potent δ -opioid receptor antagonist Dmt-Tic. *J. Med. Chem.*, **2004**, *47*, 6541-6546
136. Li T, Fujita Y, Tsuda Y, Miyazaki A, Jinsmaa Y, Bryant SD, **Lazarus LH**, Ambo A, Sasaki Y, Okada Y. Development of potent μ -opioid receptor ligands using unique tyrosine analogues at the N-terminus of endomorphin-2. *J. Med. Chem.*, **2005**, *48*, 586-592
137. Fujita Y, Tsuda Y, Motoyama T, Li T, Miyazaki A, Yokoi T, Sasaki Y, Ambo A, Jinsmaa Y, Bryant SD, **Lazarus LH**, Okada Y. Studies on the structure-activity relationship of 2',6'-dimethyl-L-tyrosine (Dmt) derivatives: bioactivity profile of H-Dmt-NH₃. *Bioorg. Med. Chem. Lett.*, **2005**, *15*, 599-602
138. Troyen-Tóth P, Décaillor FM, Fillol D, **Lazarus LH**, Schiller PW, Schidhammer H, Keiffer BL. Inverse agonism and neutral antagonism at wild-type and constitutively mutant delta opioid receptors. *J. Pharmacol. Exp. Ther*, **2005**, *313*, 410-421
139. Jinsmaa Y, Shiotani K, Fujita Y, Miyazaki A, Li T, Tsuda Y, Okada Y, Ambo A, Sasaki Y, Bryant SD, **Lazarus LH**. Differentiation of opioid receptor preference by [Dmt¹]endomorphin-2-mediated analgesia in the mouse. *Eur. J. Pharmacol.*, **2005**, *509*, 37-42.
140. Balboni G, Cocco MT, Salvadori S, Romagnoli R, Sasaki Y, Okada Y, Bryant SD, Jinsmaa Y, **Lazarus LH**. From the potent and selective μ -opioid receptor

agonist H-Dmt-Tic-D-Arg-Phe-Lys-NH₂ to the potent δ antagonist H-Dmt-Tic-Phe-Lys(Z)-OH. *J. Med. Chem.* **2005**, *48*, 5608-5611

141. Miyazaki A, Fujisawa Y, Shiotani K, Morishita A, Fujita Y, Li T, Tsuda Y, Yokoi T, Bryant SD, **Lazarus LH**, Okada Y. Studies on the mechanism of 1,2-dihydropyrazin-2-one ring formation from dipeptidyl chloromethyl ketone and its chemical properties: immediate deamination during catalytic hydrogenation. *Chem. Pharm. Bull.*, **2005**, *53*, 1152-1158

142. In Y, Minoura K, Tomoo K, Sasaki Y, **Lazarus LH**, Okada Y, Ishida T. Structural function of C-terminal amidation of endomorphin: conformational comparison of μ -selective endomorphin-2 with its C-terminal free acid, studied by ¹H-NMR spectroscopy, molecular calculation, and X-ray crystallography. *FEBS J.*, **2005**, *272*, 5079-5097

143. Li T, Tsuda Y, Shiotani K, Miyazaki A, Fujita Y, Ambo A, Sasaki Y, Jinsmaa Y, Marczak E, Bryant SD, **Lazarus LH**, Okada Y. New series of potent heterodimeric δ -opioid antagonists containing the H-Dmt-Tic-NH-hexyl-NH-R motif. *Bioorg. Med. Chem. Lett.*, **2005**, *15*, 5517-5520

144. Li T, Fujita Y, Shiotani K, Miyazaki A, Tsuda Y, Ambo A, Sasaki Y, Jinsmaa Y, Marczak E, Bryant SD, Salvadori S, **Lazarus LH**, Okada Y. Potent Dmt-Tic pharmacophoric δ - and μ -opioid receptor antagonists. *J. Med. Chem.*, **2005**, *48*, 8035-8044

145. Balboni G, Guerrini R, Salvadori S, Negri L, Giannini E, Bryant SD, Jinsmaa Y, **Lazarus LH**. Conversion of the potent δ -opioid agonist H-Dmt-Tic-NH-CH₂-Bid into δ -opioid antagonists by N¹-benzimidazole alkylation. *J. Med. Chem.* **2005**, *48*, 8112-8114

146. Li T, Tsuda Y, Minoura K, In Y, Ishida T, **Lazarus LH**, Okada Y. Enantioselective synthesis of a phenylalanine library containing alkyl groups on the aromatic moiety: confirmation of stereostructure by X-ray analysis. *Chem. Pharm. Bull.* **2006**, *54*, 873-877

147. Vazquez ME, Blanco JB, Salvadori S, Argazzi R, Bryant SD, Jinsmaa Y, **Lazarus LH**, Negri L, Giannini E, Lattanzi R, Colucci M, Balboni G. 6-*N,N*-Dimethylamino-2,3-naphthalimide, a new environment-sensitive fluorescent probe for δ -selective and μ -selective opioid peptides. *J. Med. Chem.*, **2006**, *49*, 3653-3658

148. Ballet S, Salvadori S, Bryant SD, Jinsmaa Y, **Lazarus LH**, Negri L, Giannini E, Lattanzi R, Tourwé D, Balboni G. New Dmt opioid peptidomimetics based on

the Aba-Gly scaffold: development of unique μ -opioid receptor ligands. *J. Med. Chem.*, **2006**, *49*, 3990-3993

149. Jinsmaa Y, Marczak E, Fujita Y, Shiotani K, Miyazaki A, Li T, Tsuda Y, Ambo A, Sasaki Y, Bryant SD, Okada Y, **Lazarus LH**. Potent in vivo antinociception and opioid receptor preference of the novel analogue [Dmt¹]endomorphin-1. *Pharmacol. Biochem. Behav.*, **2006**, *84*, 252-258

150. Balboni G, Onnis V, Salvadori S, Zotti M, Sasaki Y, Ambo A, Bryant SD, Jinsmaa Y, **Lazarus LH**. Effect of lysine at C-terminus of the Dmt-Tic opioid pharmacophore. *J. Med. Chem.*, **2006**, *49*, 5610-5617

151. Neumeyer JL, Peng X, Knapp BI, Bidlack JM, **Lazarus LH**, Salvadori S, Trapella C, Balboni G. New opioid designed multiple ligand from Dmt-Tic and morphinan pharmacophores. *J. Med. Chem.*, **2006**, *49*, 5640-5643

152. Shiotani K, Li T, Miyazaki A, Tsuda Y, Bryant SD, Ambo A, Sasaki Y, **Lazarus LH**, Okada Y. Synthesis of 3,6-bis[H-Tyr/H-Dmt-NH(CH₂)_{m,n}]-2(1H)pyrazinone derivatives: function of alkyl chain length on opioid activity. *Bioorg. Med. Chem. Lett.*, **2006**, *16*, 5793-5796

153. Li T, Jinsmaa Y, Nedachi M, Shiotani K, Miyazaki A, Tsuda Y, Ambo A, Sasaki Y, Bryant SD, Marczak E, Li Q, Swartzwelder HS, **Lazarus LH**, Okada Y. Transformation of a μ -opioid agonist into biologically potent μ -opioid antagonists. *Bioorg. Med. Chem.*, **2007**, *15*, 1237-1251

154. Balboni G, Onnis V, Congiu C, Zotti M, Sasaki Y, Ambo A, Bryant SD, Jinsmaa Y, **Lazarus LH**, Lazzari I, Trapella C, Salvadori S. Further studies on the effect of lysine at the C-terminus of the Dmt-Tic opioid pharmacophore. *Bioorg. Med. Chem.* **2007**, *15*, 3143-3151

155. Li T, Shiotani K, Miyazaki A, Tsuda Y, Ambo A, Sasaki Y, Jinsmaa Y, Marczak ED, Bryant SD, **Lazarus LH**, Okada, Y. Bifunctional [2',6'-dimethyl-L-tyrosine]endomorphin-2 analogues substituted at position 3 with alkylated phenylalanine derivatives yield potent mixed μ -agonist/ δ -antagonist and dual μ -/ δ -agonist opioid ligands. *J. Med. Chem.* **2007**, *50*, 2753-2766

156. Salvadori S, Trapella C, Fiorini S, Negri L, Lattanzi R, Bryant SD, Jinsmaa Y, **Lazarus LH**, Balboni G. A new opioid designed multiple ligand derived from the μ -opioid agonist endomorphin-2 and the δ -opioid antagonist pharmacophore Dmt-Tic. *Bioorg. Med. Chem. Lett.*, **2007**, *15*, 6876-6881

157. Marczak ED, Jinsmaa Y, Bryant SD, Li T, Okada Y, **Lazarus LH**. [N-allyl-Dmt¹]endomorphins are μ -opioid receptor antagonists lacking inverse agonist properties. *J. Pharmacol. Exp. Ther.*, **2007**, *323*, 374-380

158. Shiotani K, Li T, Miyazaki A, Tsuda Y, Yokoi T, Ambo A, Sasaki Y, Bryant SD, **Lazarus LH**, Okada Y. Design and synthesis of opioidmimetics containing 2',6'-dimethyl-L-tyrosine and a pyrazinone ring platform. *Bioorg. Med. Chem. Lett.*, **2007**, *17*, 5768-5771
159. Shiotani K, Miyazaki A, Li L, Tsuda Y, Yokoi T, Ambo A, Sasaki Y, Bryant SD, Jinsmaa Y, **Lazarus LH**, Okada Y. Synthesis of opioidmimetics, 3-[H-Dmt-NH(CH₂)_m]-6-[H-Dmt-NH(CH₂)_n]-2(1*H*)-pyrazinones and studies on structure-activity relationships. *Med. Chem.*, **2007**, *3*, 583-598
160. Salvadori S, Fiorini S, Porreca F, Davis P, Sasaki Y, Ambo A, Marczak ED, **Lazarus LH**, Balboni G. Role of benzimidazole (Bid) in the δ -opioid agonist pseudopeptide H-Dmt-Tic-NH-CH₂-Bid (UFP-502). *Bioorg. Med. Chem.*, **2008**, *16*, 3032-3038
161. Vergura R, Balboni B, Spagnolo B, Gavioli E, Lambert DG, McDonald J, Trapella C, **Lazarus LH**, Regoli D, Guerrini R, Salvadori S, Calo' G. Anxiolytic- and antidepressant-like activities of H-Dmt-Tic-NH-CH(CH₂-COOH)-Bid (UFP-512), a potent selective delta-opioid receptor agonist. *Peptides*, **2008**, *29*, 93-103
162. Ryu EK, Wu Z, Chen K, **Lazarus LH**, Marczak ED, Sasaki Y, Ambo A, Salvadori S, Ren C, Zhao H, Balboni G, Chen X. Synthesis of a potent and selective ¹⁸F-labeled δ -opioid receptor antagonist derived from the Dmt-Tic pharmacophore for peripheral imaging. *J. Med. Chem.*, **2008**, *51*, 1817-1823
163. Koda Y, Del Borgo M, Wessling ST, **Lazarus LH**, Okada Y, Toth I, Blanchfield JT. Synthesis and in vitro evaluation of a library of modified endomorphin 1 peptides. *Bioorg. Med. Chem.*, **2008**, *16*, 6286-6296
164. Jinsmaa Y,* Marczak ED,* Balboni G, Salvadori S, Bryant SD, **Lazarus LH**. Inhibition of morphine tolerance development by a potent dual μ -/ δ -opioid antagonist, H-Dmt-Tic-Lys-NH-CH₂-Ph. *Pharmacol. Biochem. Behav.*, **2008**, *90*, 651-657
165. Balboni G, Fiorini S, Baldisserotto A, Trapella C, Sasaki Y, Ambo A, Marczak ED, **Lazarus LH**, Salvadori S. Further studies on lead compounds containing the opioid pharmacophore Dmt-Tic. *J. Med. Chem.*, **2008**, *51*, 5109-5117
166. Li Q, Marczak ED, Okada Y, Wilson W, **Lazarus LH**, Swartzwelder HS. The novel μ -opioid receptor antagonist [*N*-allyl-Dmt¹]-endomorphin-2 attenuates alcohol-induced GABAergic neurotransmission in rat hippocampus. *Alcohol Alcoholism*, **2009**, *44*, 13-19

167. Ballet S, Feytens, D, De Wachter R, De Vlaeminck M, Marczak ED, Salvadori S, de Graf C, Rognan D, Negri L, Lattanzi R, **Lazarus LH**, Tourwé D, Balboni G. Conformationally constrained opioid ligands: the Dmt-Aba and Dmt-Aia vs. Dmt-Tic pharmacophore. *Bioorg. Med. Chem. Lett.*, **2009**, *19*, 433-437

2. Invited Reviews, Book Chapters

1. **Lazarus LH**, Ling N, Guillemin R. β -Lipotrophin as a prohormone for the morphinomimetic peptides, endorphins and enkephalin. In Langlen LL (ed.), *Benchmark Papers in Human Physiology*. Sowers JR (ed.), *Hypothalamic Hormones*, **1980**, 14

2. **Lazarus LH**, Wilson WE. Recognition, purification, and structural elucidation of mammalian physalaemin related molecules. In Abelson JN, Simon MI (eds.), *Methods in Enzymology*. Conn PM (ed.), *Hormone Action. Neuroendocrine Peptides*, Academic Press, New York, **1989**, 168, 444-462

4. **Lazarus LH**, Salvadori S, Temussi PA, Balboni G, Guerrini R, Bryant SD, Cooper PS. Ultraselective antagonists of the δ -opioid receptor. *Emerging Ther. Targets.*, **1998**, 2 (1)

5. **Lazarus LH**, Bryant SD, Cooper PS, Guerrini R, Balboni G, Salvadori S. Design of δ -opioid peptide antagonists for emerging drug applications. *Drug Discov. Today*, **1998**, 3, 284-294

6. Okada Y, Tsuda Y, Bryant SD, **Lazarus LH**. Endomorphins and Related Opioid Peptides, In Litwack G (ed.), *Vitamins and Hormones*, **2002**, 65, 257-279

7. Bryant SD, Yunden J, Salvadori S, Okada Y, **Lazarus LH**. Dmt and opioid peptides: a potent alliance. *Biopolymers/Pept. Sci.*, **2003**, 71, 86-102

8. **Lazarus LH**, Marczak ED, Okada Y, Balboni G, Salvadori S. Overdosed, underutilized: the pathos of addictive drugs. In, Langer T, Bryant SD (eds.), *Why Drugs Fail. Methods and Principles in Medicinal Chemistry*, **2009**, in press

PATENTS

1. **Lazarus LH**, Salvadori S, Temussi PA. Ultraselective opioidmimetic peptides and pharmacological and therapeutic uses thereof. U.S. Patent No. 5,780,589, issued 14 July 1998

2. **Lazarus LH**, Salvadori S. Dmt-Tic di- and tri-peptide derivatives and related compositions and methods of use. U.S. Patent No. 6,753,317, issued 22 June 2004
3. **Lazarus LH**, Salvadori S. Dmt-Tic di- and tri-peptidic derivatives and related compositions and methods of use. U.S. Patent No. 6,916,905, issued 12 July 2005
4. Okada Y., Yokoi T., Tsuda Y., Bryant SD, **Lazarus LH**. New Opioid Derivatives. Patent Application, No. 03703014.5-2103-JP0300516, by Teikoku Seiyaku Co., Ltd.; US filing 29.01.02/USA 58192. International Publication Number WO 03/064375 A1
5. **Lazarus LH**, Salvadori S, Guerrini R, Balboni G. New biologically potent analogues of the Dmt-Tic pharmacophore and methods of use. US Provisional Patent Application no. 60/628,147, filed on 16 November 2004, DHHS reference E-103-2000/2-US-01, LVM reference 231871
6. **Lazarus LH**, Okada Y, Li T. Dmt-derivative compounds and related compositions and methods of use. US Provisional Patent Application filed 1 September 2005, application no. DHHS reference E-305-2005/0-PCT-02. International patent applications no. PCT/US06/33560 filed 8 March 2007 and PCT/US07/74839 filed 31 July 2007
7. **Lazarus LH**, Balboni G, Salvadori S, Chen S. Fluorine-substituted Dmt-Tic compounds and methods of use. U.S. Provisional Patent Application No. 60/970,143, filed 5 September 2007, DHHS reference E-317-2007/0-US-01