CURRICULUM VITAE

Lawrence H. Lazarus, Ph.D.

Present Address

PI, 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 or 541-0696
E-mail: lazarus@niehs.nih.gov
Website: http://dir.niehs.nih.gov/dirlpc/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

1966-1968	Postdoctoral Fellow, Microbiology Institute, University of Copenhagen, Copenhagen, Denmark.
1968-1973	Assistant Professor, Department of Virology, Hebrew University-Hadassah Medical School, Jerusalem, Israel.
1973-1975	Visiting Research Chemist, Department of Chemistry, School of Medicine, University of California, San Diego, La Jolla, CA.
1975-1977	Senior Research Associate, Neuroendocrinology Laboratory, The Salk Institute, La Jolla, CA with R Guillemin (Nobel Laureate, Medicine, 1977)
1977-date	Research Chemist, National Institute of Environmental Health Sciences, Research Triangle Park, NC. Current Position: PI, Medicinal Chemistry Group, Laboratory of Pharmacology and Chemistry.
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

Societies

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

Major Research Achievements

1964	Inhibited synchronized cell division in *Tetrahymena* by actinomycin D
1967	Discovered, isolated of three base-specific RNases from *Tetrahymena*
1968	Identified a phosphodiesterase in *Tetrahymena*
1972	Detailed the kinetics of phosphorus analysis
1973	Discovered requirement for RNA in DNA synthesis
1973	Discovered polymeric nature of DNA polymerase α
1973	Discovered differential heparin inhibition of DNA polymerases α and β
1973	Proved viral ssRNA replication required dsRNA
1976	Applied general-ligand affinity chromatography to enzyme purification. Quoted in Pharmacia PL-Biochemicals catalog
1976	Discovered β-LH is a precursor for opioid peptides. Summarized in *Chemistry* **1976**, *48*, 22-24. Most cited article in endocrinology in 1977
1977	Discovered neurotensin receptors in mast cells
1980	Discovered a mammalian neuropeptide related to physalaemin
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	Discovered amphibian deltorphin as a δ-opioid receptor selective ligand. Quoted in Bachem California catalog
1989	Discovered bradykinin in bovine milk
1995	Developed 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 a potent δ-opioid agonist
2003	Produced synthetic μ-opioid ligands with CNS analgesia. Patent application No. 03703014.5-2103-JP0300516
2004	Demonstrated oral bioavailability of a 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	Dmt-Tic pharmacophoric dual μ-/δ-opioid receptor antagonists; interconversion between μ- and δ-opioid agonists
2006	Conversion of a selective μ-agonist into a potent dual μ-/δ-antagonists

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 Heath 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
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

BIBLIOGRAPHY

1. Peer Reviewed Journals (> 20 citations marked)

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 (**47 citations**).

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 (**22 citations**)

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 (**21 citations**)

7. Popescu M, **Lazarus LH**, Goldblum N. Simplified adaptor for electoelution. *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 (**24 citations**)

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 (**28 citations**)

12. Barzilai R, **Lazarus LH**, Goldblum N. Viscosity-density gradient for purification of FMDV. *Arch. gesamt. Virusforsch*. **1972**, *36*, 141-146 (**26 citations**)

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. (**52 citations**)

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*. **1977**, *178*, 8-18 (**32 citations**)

29. **Lazarus LH**, Ling N, Guillemin R. ß-Lipotropin as a prohormone for the morphinometic peptides, endorphins and enkephalin. *Proc. Natl. Acad. Sci USA* **1976**, *73*, 2156-2159. (**228 citations**)

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 (**97 citations**)

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. (**80 citations**)

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. (**52 citations**)

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. (**98 citations**)

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 (**31 citations**)

37. **Lazarus LH**, Linnoila, RI, Hernandez O, DiAugustine RP. Neuropeptide in mammalian tissues with physalaemin-like immunoreactivity. *Nature* **1980**, *287*, 555-558. (**91 citations**)

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 (**28 citations**)

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. (**213 citations**)

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 (**60 citations**)

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. *Recent Results. 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 (**34 citations**)

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 (**39 citations**)

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. (**88 citations**)

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 (**21 citations**)

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. (**61 citations**)

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 (**35 citations**)

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 Phe^3 deltorphin analogues: Enhanced selectivity of halogenated derivatives for δ opioid receptor sites. *J. Med. Chem*. **1992**, *35*, 4651-4657 (**27 citations**).

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 (**34 citations**)

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 [$Tyr^1 \rightarrow Asp^4$]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**. Phe^3-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 (**41 citations**)

82. **Lazarus LH**, Attila M. The toad, ugly and venomous, wears yet a precious jewel in his skin. *Prog. Neurobiol*. **1993**, *41*, 473-507. (**124 citations**)

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. (**76 citations**)

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 (**20 citations**)

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 His^4 in deltorphin A for high δ opioid receptor selectivity. *Amino Acids* **1994**, *7*, 291-304.

88. Balboni G, Salvadori S, D'Angeli F, Marchetti P, **Lazarus L**H, 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.

89. 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 ultraselective opioid peptides. *Mol. Med*., **1995**, *1*, 678-689. (**76 citations**)

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90. 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 (**27 citations**)

91. 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 $[Dmt^1]$deltorphin B. *Eur. J. Pharmacol*., **1996**, *206*, 37-42 (**35 citations**)

92. 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.

93. 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 (**29 citations**)

94. 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 (**26 citations**)

95. 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 (**20 citations**)

96. 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 (**119 citations**)

97. 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.

98. 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.

99. 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 (**27 citations**)

100. 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 (**65 citations**)

101. 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.

102. 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.

103. 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.

104. **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.

105. 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.

106. 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. *Arzeimittel-Forsch./Drug Res*. **1999**, *49*, 6-12.

107. 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.

108. 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.

109. 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 (**40 citations**)

110. 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.

111. Bryant SD, Salvadori S, Cooper PS, **Lazarus LH.** New δ opioid antagonists as pharmacological probes. *Trends Pharmacol. Sci*., **1999**, *19*, 42-46.

112. **Lazarus LH**, Bryant SD, Cooper PS, Salvadori S. What peptides these deltorphins be. *Prog. Neurobiol*., **1999,** *57*, 377-420 (**38 citations**)

113. Monory K, Bryant SD, Kertész I, Balboni G, Guerrini R, Tóth G, Salvadori S, **Lazarus LH**, Borsodi A. [^{3}H]*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.

114. 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.

115. 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-NH_2, and examination of their opioid receptor binding activities and solution conformation. *Biochem. Biophys. Res. Commun*. **2000**, *276*¸ 7-11 (**20 citations**)

116. 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.

117. Santagada V, Balboni G, Caliendo 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.

118. 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.

119. 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.

120. 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 (**33 citations**)

121. 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.

122. 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.

123. 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 (**21 citations**)

124. 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-

tyrosine[1]]endomorphin-2 analogues: enhanced activity and *cis* orientation of the Dmt-Pro amide bond. *Bioorg. Med. Chem*. **2003**, *11*, 1983-1984.

125. 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.

126. Ingman K, Salvadori S, **Lazarus L**, Korpi ER, Honkanen A. Selective δ-opioid receptor antagonist *N,N*$(CH_3)_2$-Dmt-Tic-OH does not reduce ethanol intake in alcohol-preferring AA rats. *Addic. Biol.* **2003**, *8*, 173-179.

127. 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.

128. 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.

129. 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-$(CH_2)_n$]-2(1*H*)-pyrazinone with central mediated analgesia. *J. Med. Chem*., **2004**, *47*, 2599-2610.

130. Fujita Y, Motoyama T, Takahashi M, Shimizu Y, Tsuda Y, Yokoi T, Li 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.

131. 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.

132. Balboni G, Salvadori S, Dal Piaz, 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.

133. 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.

134. 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-NH_3. *Bioorg. Med. Chem. Lett.*, **2005**, *15*, 599-602.

135. 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.

136. 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 [Dmt^1]endomorphin-2-mediated analgesia in the mouse. *Eur. J. Pharmacol*., **2005**, *509*, 37-42.

137. 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-NH_2 to the potent δ antagonist H-Dmt-Tic-Phe-Lys(Z)-OH. *J. Med. Chem*. **2005**, *48*, 5608-5611.

138. 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.

139. 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 ^{1}H-NMR spectroscopy, molecular calculation, and X-ray crystallography. *FEBS J*., **2005**, *272*, 5079-5097.

140. 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.

141. 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.

142. 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-CH_2-Bid into δ-opioid antagonists by N^1-benzimidazole alkylation. *J. Med. Chem*. **2005**, *48*, 8112-8114.

143. 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.

144. 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.

145. 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.

146. 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 [Dmt^1]endomorphin-1. *Pharmacol. Biochem. Behav*., **2006**, *84*, 252-258.

147. 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.

148. 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.

149. 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$(CH_2)_{m,n}$]-2(1*H*)pyrazinone derivatives: function of alkyl chain length on opioid activity. *Bioorg. Med. Chem. Lett*., **2006**, *16*, 5793-5796.

150. 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.

151. 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.

152. 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**, in press.

153. 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(CH_2)$_m$]-6-[H-Dmt-NH(CH_2)$_n$]-2(1*H*)-pyrazinones and studies on structure-activity relationships. *Med. Chem*., **2007**, in press

2. Submitted

1. Jinsmaa Y, Marczak ED, Balboni G, Salvadori S, Bryant SD, **Lazarus LH**. H-Dmt-Tic-Lys-NH-CH_2-Ph, a potent dual μ-/δ-opioid receptor antagonist, inhibits morphine- and deltorphin C-induced antinociception and morphine tolerance in mice. *Eur. J. Pharmacol.*, **2007**

2. Marczak ED, Jinsmaa Y, Bryant SD, Li T, Okada Y, **Lazarus LH.** Alleviation of morphine withdrawal symptoms by [*N*-allyl-Dmt^1]-endomorphins: potent and selective neutral antagonists for the μ-opioid receptor. *J. Pharmacol. Exp. Ther*., **2007**.

3. Invited Reviews, Articles, 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.), B*enchmark 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.

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

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), 1998.

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, 1998 (**28 citations**)

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 (**26 citations**).

8. **Lazarus LH**, Marczak ED, Bryant SD, Okada Y, Salvadori S. Overdosed, underutilized: the pathos of addictive drugs. *In*, Langer T and Bryant SD (eds), *Why Drugs Fail*, series on *Methods and Principles in Medicinal Chemistry*, **2007**.

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 application no. PCT/US06/33560 filed 8 March 2007.

LICENSING AGREEMENTS

1. Opioid analogues, coded as UFP-000, are being commercialized by the Biotechnology Center at the University of Ferrara, Ferrara, Italy.