

**BIOGRAPHICAL SKETCH**

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NAME Garland Marshall	POSITION TITLE Principal Investigator		
eRA COMMONS USER NAME			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
California Institute of Technology, Pasadena, CA	B.S.	1962	Biology
The Rockefeller University, New York, NY	Ph.D.	1966	Biochemistry

**A. Positions and Honors.****Positions and Employment**

1966 – 1967 Instructor; 1967 – 1972 Assistant Professor; 1972 – 1976 Associate Professor  
1976 – 1986 Professor, Departments of Physiology and Biophysics and of Biological Chemistry, Washington University School of Medicine, St. Louis, Missouri.  
1985 – 2000 Professor of Molecular Biology and Pharmacology and of Biomedical Engineering, Washington University School of Medicine, St. Louis, Missouri.  
1988 – 2000 Director, Center for Molecular Design and Professor of Biomedical Computing, Institute for Biomedical Computing at Washington University, St. Louis, Missouri.  
2000 – present Professor of Biochemistry and Molecular Biophysics and of Biomedical Engineering, Washington University School of Medicine, St. Louis, Missouri

**Other Experience and Professional Memberships**

1970 – 1975 Established Investigator, American Heart Association  
1993 – 1996 National Institutes of Health, Bioorganic and Natural Products Study Section  
2000 Co-Chairman, Gordon Research Conference on Chemistry & Biology of Peptides  
2001 – present Member, Scientific Advisory Board, Institute for Molecular Biosciences, University of Queensland, Brisbane, Australia  
2002 – 2006 Member, Scientific Advisory Board, MDS Capital/Canadian Medical Discoveries Fund Inc. Toronto, Canada  
2005 – present Board of Trustees, Torrey Pines Institute of Molecular Sciences, La Jolla, CA  
2005 – present Board of Trustees, Alzheimer's and Aging Research Center, La Jolla, CA  
2006 – present Member, Scientific Advisory Board, Center for Drug Design, University of Minnesota  
2004 - present Member, Center for Computational Biology, WUMS, St. Louis, MO  
2005 - present Member, Alvin J. Siteman Cancer Center, WUMS, St. Louis, MO  
2004-2005 Member/Co-chair, NIH Roadmap Study Section – Centers for Computational Biology  
2006 Screening Committee, NIH Director's Pioneer Awards

**Honors**

1987 – Medal XL-Lecia Politechniki Lodzkiej (40th Anniversary of Polytechnika, Lodz, Poland)  
1988 – Medicinal Chemistry Award, Medicinal Chemistry Division, American Chemical Society  
1993 – Doctora Honoris Causa, Politechniki Lodzkiej, Oct. 1, 1993 (Polytechnika, Lodz, Poland)  
1994 – Vincent duVigneaud Award, Gordon Conference on Peptides, Ventura, CA, Feb. 17, 1994  
1996 – Midwest Award, St. Louis Regional Division, American Chemical Society  
1996 – Science and Technology Award, St. Louis Regional Commerce and Growth Association  
1996 – George B. Koelle Award, Mid-Atlantic Pharmacology Society  
1997 – Medal 50-Lecia Politechniki Lodzkiej (50th Anniversary of Polytechnika, Lodz, Poland)  
2000 – Cathay Award, Chinese Peptide Society, Mt. Huangshan, China  
2000 – Taito M. Soine Memorial Award, Department of Medicinal Chemistry, University of Minnesota.

- 2001 – Merrifield Award, American Peptide Society, San Diego, CA  
2003 – Excellence in Life Sciences Award for Serial Entrepreneurship, Missouri Biotechnology Association  
2005 – Inaugural Lee Wing Nam Professor, School of Biological Sciences, Nanyang Technological University, Singapore  
2006 – 16<sup>th</sup> Smissman Memorial Lecturer, Department of Medicinal Chemistry, University of Kansas

**B. Selected publications (in chronological order, from over 350 peer-reviewed publications)**

1. Huston SE, Marshall GR.  $\alpha/3_{10}$ -Helix Transitions in  $\alpha$ -Methylalanine Homopeptides: Conformational Transition Pathway and Potential of Mean Force. *Biopolymers*; 34:75-90 (1994).
2. Smythe ML, Huston SE, Marshall GR. The molten helix: effects of solvation on the  $\alpha$ - to  $3_{10}$ -transition. *J Am Chem Soc*; 117:5445-5452 (1995).
3. Smythe ML, Nakaie CR, Marshall GR.  $\alpha$ -versus  $3_{10}$ -helical conformation of alanine-based peptides in aqueous solution: An electron spin resonance investigation. *J Am Chem Soc*; 117:10555-10562 (1995).
4. Beusen DD, Zabrocki J, Slomczynska U, Head RD, Kao J, Marshall GR. Conformational mimicry: Synthesis and solution conformation of a cyclic somatostatin hexapeptide containing a tetrazole *cis*-amide bond surrogate. *Biopolymers*; 36:181-200 (1995).
5. Head RD, Smyte ML, Oprea TI, Waller CL, Green SM, Marshall GR. VALIDATE: A new method for the receptor-based prediction of binding affinities of novel ligands. *J Am Chem Soc*, 118:3959-3969 (1996).
6. Kisselev OY, Fann C, Kao J, Ponder J, Gautam N, Marshall GR. Light-Activated Rhodopsin Induces Structural Binding Motif in G-Protein Alpha Subunit. *Proc Natl Acad Sci USA*; 95:4270-4275 (1998).
7. Takeuchi Y, Marshall GR. Conformational Analyses of Reverse-Turn Constraints on Peptides and Non-Peptide Mimetics. *J Am Chem Soc*; 120:5363-5372 (1998).
8. Pappu RV, Marshall GR, Ponder JW. A potential smoothing algorithm accurately predicts transmembrane helix packing. *Nature Struct Biol*; 6:50-55 (1999).
9. Nikiforovich GV, Kover KE, Zhang W-J, Marshall GR. Cyclopentapeptides as Flexible Conformational Templates for Receptor Probes. *J Am Chem Soc*; 122:3262-3273 (2000).
10. Tong Y, Zabrocki J, Gershengorn MC, Marshall GR, Moeller KD. Constrained Peptidomimetics for TRH: *Cis*-Peptide Bond Analogs. *Tetrahedron*; 56:9791-9800 (2000).
11. Marshall, G.R., R.H. Head, R. Ragno. Affinity Prediction: The Sina Qua Non. In: *Thermodynamics in Biology*, E. Di Cera, ed. Oxford University Press, 87-111 (2000).
12. Galaktionov S, Nikiforovich GV, Marshall GR. Ab Initio Modeling of Small, Medium and Large Loops in Proteins. *Biopolymers (Peptide Sci.)*; 60:153-168 (2001).
13. Nikiforovich GV, Galaktionov S, Balodis J, Marshall GR. Novel approach to Computer Modeling of Seven-Helical Transmembrane Proteins: Current Progress in Test Case of Bacteriorhodopsin. *Acta Biochim Polonica*; 48(1):53-64 (2001).
14. Nikiforovich GV, Marshall GR. 3D Model for TM Region of the AT-1 Receptor in Complex with Angiotensin II Independently Validated by Site-Directed Mutagenesis Data. *Biochem Biophys Res Comm*; 286:1204-1211 (2001).
15. Arimoto R, Kisselev O, Makara G, Marshall GR. The Rhodopsin-Transducin Interface: Studies with Conformationally Constrained Peptides. *Biophys. J.*, 81:3285-3293 (2001).
16. Marshall GR, Peptide Interactions with G-Coupled Protein Receptors. *Biopolymers (Peptide Sci.)*; 60(3):246-277 (2001).
17. Marshall GR. From Merrifield to MetaPhore: A Random Walk with Serendipity. In: *Peptides: The Wave of the Future (Proc. 17<sup>th</sup> Am. Peptide Symp.)*, RA Houghten and M. Lebl, Eds., Am. Peptide Soc. 2001; 3-11.
18. Marshall GR, Nauk A, Reddy PA, Schall OF, Beusen DD, Ye Y, Slomczynska U. Chapt. 5: Combinatorial Chemistry of Metal-Binding Ligands. In: *Adv. Supramolecular Chem.*, vol. 8, GW Gokel, Ed., SunCoast Press, Inc., 175-243 (2001).
19. Bourne GT, Golding SW, McGeary RP, Meutermans WDF, Jones A, Marshall GR, Alewood PF, Smythe MR. The Development and Application of a Novel Safety Catch Linker for BOC-Based Assembly of Libraries of Cyclic Peptides. *J. Org. Chem.*, 66:7706-7713 (2001).
20. Simpson JC, Ho CMW, Berkley Shands EF, Gershengorn MC, Marshall GR, Moeller KD. Conformationally Restricted TRH Analogues: Constraining the Pyroglutamate Region. *Bioorg. Med. Chem.*, 10:291-302 (2002).

21. Arimoto R, Sha W, Marshall GR. Is a  $\pi$ -Cation Interaction Significant in Binding of Transducin  $\alpha$ -Subunit to Rhodopsin? Abstr. 46<sup>th</sup> Annual Meeting, Biophysical Society, February 23-27, 2002, San Francisco, CA. *Biophys J* 2002; 82(1, II):451a.
22. Reaka AJH, Ho CMW, Marshall GR. Metal Complexes of Chiral Pentaazacrowns as Conformational Templates for  $\beta$ -Turn Recognition. *J. Comput.-Aided. Mol. Des.*; 16:585-600 (2002).
23. Marshall, GR. Solid-Phase Synthesis: A Paradigm Shift. *J. Peptide Sci.*, 9:534-544 (2003).
24. Zhang W-J, Berglund A, Kao J, Couty J-P, Gershengorn MC, Marshall GR. Impact of Azaproline on Amide *Cis-Trans* Isomerism: Conformational Analyses and NMR Studies of Model Peptides Including TRH Analogs. *J. Am. Chem. Soc.*, 125:1221-1235 (2003).
25. Ye Y, Liu M, Kao JL-K and Marshall GR. Peptide-bond modification for metal coordination: peptides containing two hydroxamate groups. *Biopolymers (Peptide Sci.)* 71(4):489-515 (2003).
26. Nikiforovich, G.V. and G.R. Marshall. 3D Model for Meta-II Rhodopsin, an Activated G-Protein-Coupled Receptor. *Biochemistry*. 42:9110-9120 (2003).
27. Poreddy, A.R., O.F. Schall, G.R. Marshall, C. Ratledge and U. Slomczynska. Solid-Phase Synthesis of Carboxymycobactin T and Analogs as Potential Antimycobacterial Agents. *Bioorg. Med. Chem. Lett.* 13:2553-2556 (2003).
28. Poreddy, A.R., O.F. Schall, T.A. Osiek, J.R. Wheatly, D.D. Beusen, G.R. Marshall and U. Slomczynska. Hydroxamate-Based Iron Chelators: Combinatorial Syntheses of Desferrioxamine B Analogs and Evaluation of their Iron Affinities. *J. Comb. Chem.* 6:239-254 (2004).
29. Berglund, A., R.D. Head, E. Welsh and G.R. Marshall. ProVal: A Protein Scoring Function for the Selection of Native and Near-Native Folds. *PROTEINS: Structure, Function, and Bioinformatics* 54:289-302 (2004).
30. Che, Y. and G.R. Marshall. Impact of Azaproline on Peptide Conformation. *J. Org. Chem.*, 69, 9030-9042 (2004).
31. Marshall, G.R. and I.A. Vakser. Protein-Protein Docking Methods. In *Proteomics and Protein-Protein Interactions: Biology, Chemistry, Bioinformatics and Drug Design*. G. Waksman, ed. Springer, NY pp. 115-145 (2005).
32. Marshall, G.R. Introduction to Chemoinformatics in Drug Discovery – a Personal View. In *Cheminformatics in Drug Discovery*. T.I. Oprea, ed. Wiley-VCH Verlag, Weinheim, Germany pp. 1-22 (2005).
33. Marshall, G.R. and I.A. Vakser. Protein-Protein Docking Methods. In *Proteomics and Protein-Protein Interactions: Biology, Chemistry, Bioinformatics and Drug Design*. G. Waksman, ed. Springer, NY pp. 115-145 (2005).
34. Anderson, L. L., G. R. Marshall, G. R. and T. J. Baranski, Using Expressed Protein Ligation to Study Protein Interactions: Semi-synthesis of the G-Protein Alpha Subunit. *Protein Peptide Lett.* 12(8), 783-787 (2005).
35. Anderson, L.L., G.R. Marshall, E. Crocker, S.O. Smith, and T.J. Baranski. Motion of Carboxyl Terminus of Ga is Restricted Upon G-Protein Activation: A Solution NMR Study Using Semi-Synthetic Ga Subunits. *J Biol Chem* 260:31019-31026 (2005).
36. Kuster, D.J. and G.R. Marshall. Validated Ligand Mapping of ACE Active Site. *J Comp-Aided Mol Des* 19:609-615 (2005).
37. Nikiforovich, G.V. and G. R. Marshall. Modeling Conformational Changes of the Flexible Loops in the Dark-Adapted and Activated States of Rhodopsin, A Prototypical G-Protein-Coupled Receptor. *Biophysics J* 89:3780-3789 (2005).
38. Nikiforovich, G. V., B. Mihalik, K.J. Catt and G. R. Marshall. Molecular mechanisms of constitutive activity: mutations at position 111 of the angiotensin AT<sub>1</sub> receptor. *J Peptide Res* 66:236-248 (2005).
39. Che, Y. and G.R. Marshall. Impact of Proline Analogs on Amide *Cis-Trans* Isomerism. *Biopolymers* 81:392-406 (2006) (online 2005; DOI 10.1002/bip.20431).
40. Vabeno, J., G. V. Nikiforovich and G. R. Marshall. A Minimalistic 3D Pharmacophore Model for Cyclopentapeptide CXCR4 Antagonists. *Biopolymers (Peptide Sci.)* (2006); DOI 10.002/bip 20508
41. Marshall, G. R. and D. P. Riley. Design of Protein and Enzyme Mimetics. In *Handbook of Theoretical and Computational Nanotechnology*. M. Rieth and W. Sommers, eds. American Scientific Publishers, Vol. 1, Chapter 137, pp. 1-37 (2006).
42. Che, Ye and G. R. Marshall. Engineering Cyclic Tetrapeptides Containing Chimeric Amino Acids as Preferred Reverse-Turn Scaffolds. *J Med Chem* 49:111-124 (2006).

43. Nikiforovitch, G.V. and G. R. Marshall. 3D modeling of the activated states of constitutively active mutants of rhodopsin. *Biochem Biophys Res Comm* 345:430-437 (2006).
44. Che, Ye and G.R. Marshall. Engineering Cyclic Tetrapeptides Containing Chimeric Amino Acids as Preferred Reverse-Turn Scaffolds. *J Med Chem* 49(1):111-124 (2006).
45. Marshall, G.R. and D.D. Beusen. Molecular Modeling in Drug Design. In: *Burger's Medicinal Chemistry and Drug Discovery*, 6th edition, D. Abraham, Ed., John Wiley & Sons, Inc., New York, Vol. 1, Chapter 3. (2006).
46. Marshall, G.R. and C. M. Taylor. Introduction to Computer-Assisted Drug Design: CADD – Overview & perspective for the future. In *Comprehensive Medicinal Chemistry II, Volume 4*. J. Taylor and D Triggler, eds. Elsevier, Oxford, England (in press, 2006).
47. Anderson, M.A., B. Ogbay, R. Arimoto, W. Sha, O.G. Kisselev, D. P. Cistola and G.R. Marshall. Relative Strength of Cation- $\pi$  Vs. Salt-Bridge Interactions: The G<sub>t</sub> $\alpha$ (340-350) Peptide/Rhodopsin System. *J Am Chem Soc* (in press, June, 2006).
48. Ye, Y. and G.R. Marshall. Trihydroxamate-containing Peptides: Design, Synthesis, Metal Coordination, and Cytotoxicity. *Biopolymers* (in press, 2006).
49. Che, Y., B. R. Brooks, and G. R. Marshall. Development of Small Molecules Designed to Modulate Protein-Protein Interactions. *J Comp-Aided Mol Des.* (in press, 2006).
50. Vabenoe, J., G. V. Nikiforovitch and G. R. Marshall. Insight into the Binding Mode of Cyclopentapeptide Antagonists of the CXCR4 Receptor. *Chem Biol Drug Des* (in press, 2006).

### Research Support Available

#### Marshall Ongoing Research Support

R01 GM068460 Marshall (PI) 12/01/04 – 11/30/09 NIH

#### **Heterochiral Dipeptides of Chimeric Cyclic Amino Acids -**

Semi-rigid cyclic tetrapeptides composed of chimeric cyclic amino acids will be prepared and used as probes of receptor recognition. **The therapeutic target is the CXCR4 receptor with antiviral and oncology therapeutic applications.**

Role: PI

#### Completed Research Support

R01 GM53630-05 Marshall (PI) 03/01/96 – 06/30/03 NIH

#### **Reverse-Turn Recognition and Mimetic Propensity**

Computational tools will be used to predict the reverse-turn propensities of potential mimetics prior to their synthesis. Detailed structural analyses (NMR, FTIR, CD) will be used to characterize the populations of turn structures in this model peptide.

Role: PI

R01 EY1211301 Marshall (PI) 03/01/98 – 06/31/02 NIH

#### **Characterization of the Rhodopsin/Transducin Interface**

This project focused on the rhodopsin-transducin interface and development of inhibitors of transduction.

Role: PI