PART I: General Information

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Name: Michael S. Wolfe

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Place of Birth: Fayetteville, North Carolina

Education:

1984	B.S.	Philadelphia College of Pharmacy and Science (Chemistry), Magna Cum Laude
1986	M.S.	University of Kansas (Medicinal Chemistry)
1990	Ph.D.	University of Kansas (Medicinal Chemistry), with honors
2008	M.A.	Harvard University (Honorary)

Postdoctoral Training:

Research Fellowships:

1990-1992	Postdoctoral Fellow, University of Kansas, Department of Medicinal Chemistry
1992-1994	Pharmacology Research Associate Training (PRAT) Fellow, National Institutes of Health, Laboratory of Cell Biology, National Institute of Mental Health

Academic Appointments:

1984-90	Graduate Research Assistant in Medicinal Chemistry, University of Kansas
1994-98	Assistant Professor of Medicinal Chemistry, University of Tennessee
1998-99	Associate Professor of Medicinal Chemistry, University of Tennessee
1999-2008	Associate Professor of Neurology, Harvard Medical School
2008-	Professor of Neurology, Harvard Medical School

Hospital or Affiliated Institution Appointments:

1999-2008	Associate Scientist, Center for Neurologic Diseases, Brigham and Women's Hospital
2008	Scientist, Center for Neurologic Diseases, Brigham and Women's Hospital

Other Professional Positions and Major Visiting Appointments:

1998	Visiting Scientist, Center for Neurologic Diseases, Brigham and Women's Hospital, Harvard Medical School
2002-	Faculty Affiliate, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School
2002-	Faculty Member, Graduate Programs in Biological and Biomedical Sciences (BBS)
2002-	Faculty Affiliate, Graduate Program in Neuroscience
2007-	Faculty Member, Graduate Program in Human Biology and Translational Medicine (in BBS)

Major Administrative Responsibilities:

1997-99 Director, Graduate Seminar Program, Department of Pharmaceutical Sciences, University of Tennessee

2005- Founder of and Advisor for the Laboratory for Experimental Alzheimer Drugs (LEAD), Harvard Medical School and Brigham and Women's Hospital

Major Committee Assignments:

University of Tennessee:

1995 Curriculum Committee, Department of Pharmaceutical Sciences, Graduate School
1995-8 Honors and Awards Committee, College of Pharmacy
1995-8 Academic Standing Committee, College of Pharmacy

Harvard Medical School:

Preliminary Qualifying Exam Committees:

2003 Steven Boyden, BBS Program. Proposal title: Possible role of the monoamine oxidase-like protein KIAA0601 in models of Parkinson's disease
2004 Alice Lu, Neuroscience Program, Proposal title: The role of ubiquilin-1 in Alzheimer's disease.
2005 Jennifer Baltz, BBS Program. Proposal title: The role of copper in prion disease propagation.
2006 Sarah Mahoney, BBS Program. Proposal title: Potential roles for cellular PrP in scrapie Prp propagation.
2006 Elaine Gee, Biophysics Program. Proposal title: Control of early tau-microtubule thermodynamics and binding kinetics by intraneuronal-oligomeric amyloid-β.
2008 Sidharth Puram, BBS Program. Proposal title: Role of centrosomal CaMKIIβ in dendritic morphogenesis in post-mitotic neurons.
2009 Heather Rice, Neuroscience Program. (*committee chair) Proposal title: Investigation of extracellular interactions with APP: implications for APP processing & function in neurodevelopment
2010 Natalie German. BBS Program. Proposal: SIRT4 substrates and interactors.
2010 Derek Drake. BBS Program. Proposal title: A cell type-specific analysis of the aging brain epigenome and its impact on cognitive decline.
2011 Bethany Bush. BBS Program. Proposal title: Investigating the regulation of Escherichia coli penicillin binding protein 1b by LpoB.
2011 Aswin Sekar. BBS Program. Proposal title: The role of complement receptor 1 in Alzheimer's disease.

Thesis Advisory Committees:

2001-5 Yunsun Nam, BBS Program. Advisor: Stephen Blacklow
2002-5 Zhihua Lui, BBS Program. Advisor: Peter Lansbury
2004-5 Brendan Lilley, BBS Program. Advisor: Hidde Plough
2005-8 Alice Lu, Neuroscience Program. (*committee chair) Advisor: Rudolph Tanzi
2005-9 Allen Chen, BBS Program. (*committee chair) Advisor: Dennis Selkoe
2009- Leila Ross, BBS Program. (*committee chair) Advisor: John Clardy
2009-12 Heather Rice, Neuroscience Program. (*committee chair) Advisor: Dennis Selkoe
2010- Heather McLaughlin, BBS Program. (*committee chair) Advisor: Bruce Yankner
2010-11 Robert Koffie, Biophysic Program. Advisor: Bradley T. Hyman

Doctoral Dissertation Defense Committees:

2003 Michael Volles, BBS Program. Thesis title: The Aggregation and Membrane Permeabilizing Activity of α-Synuclein. Advisor: Peter Lansbury
2005 Brendon Lilley, BBS Program. Thesis title: Viral Manipulation of Endoplasmic Reticulm Protein Degradation Machinery. (*committee chair) Advisor: Hidde Plough

2005 Cheryll Sánchez-Irizarry, BBS Program. Thesis title: Functional and Biochemical Characterization of the Negative Regulatory Region of Mammalian Notch. Advisor: Steven Blacklow
2005 Ross Fredenberg, BBS Program. Thesis title: An Evaluation of the Molecular Model of α-Synuclein-Mediated Cytotoxicity. Advisor: Peter Lansbury
2007 Betty Chan, BBS Program. Thesis title: Functional Studies of the Calcineurin-DSCR1 Complex. Advisor: Tom Ellenberger
2007 Michael Malecki, BBS Program. Thesis title: The Notch Negative Regulatory Region: Mutations and Mechanisms. Advisor: Steven Blacklow
2008 Andrew Choi, BBS Program. Thesis title: Dimer Stabilization and Aggregation of Superoxide Dismutase. Advisor: Peter Lansbury
2008 Kenneth Colodner, Neuroscience Program, Thesis title: Using Drosophila to Investigate the Glial Contribution to Neurodegenerative Disorders. Advisor: Mel Feany
2008 Alice Lu, Neuroscience Program, Thesis title: Potential Roles for Ubiquilin 1 in Alzheimer's Disease Pathogenesis. (*committee chair) Advisor: Rudolph Tanzi
2011 Robert Koffie, Biophysics Program, Thesis title: Molecular Imaging of Synaptic Changes in Alzheimer's Disease. Advisor: Brad Hyman

Other Committees:

2001 Harvard Center for Neurodegeneration and Repair—Core D Task Force (Laboratory for Drug Discovery in Neurodegeneration)
2005-7, -9, -12 Admissions Committee, BBS Program
2005- Credentialing Committee for the Department of Neurology at Brigham and Women's Hospital
2006 Symposium organizer, "Neurodegenerative Diseases: From Mechanism to Medicine", Harvard Center for Neurodegeneration and Repair (May 12, 2006)
2006-8 Review Committee, Partners Center for Drug Discovery Grant Program
2007 Review Committee, Dubai Harvard Found'n for Medical Research Collaborative Research Awards
2008 Symposium organizer, "Protein Misfolding in Neurodegenerative Diseases", Harvard Center for Neurodegeneration and Repair (September 29, 2008)
2009 Review Committee, Alzheimer's Disease Research Center & Harvard NeuroDiscovery Center Pilot Study Grant Program
2010 Evaluator of Harvard Catalyst Type I Diabetes Challenge applications
2010- Prequalifying Exam Committee, BBS Program

Harvard University:

2001 Doctoral dissertation defense committee for Kenneth V. Mills, Department of Chemistry and Chemical Biology. Thesis title: Protein Splicing in Trans by Intein Segments. Advisor: Henry Paulus
2004 Undergraduate thesis evaluation for Daniel M.S. Raper. Thesis title: γ-Secretase Function and Localization at the Cell Surface:Implications for APP Function and Alzheimer's Disease. Advisor: Dennis Selkoe

Harvard-MIT Health Sciences & Technology (HST):
2012 MD Senior Thesis defense committee for Xin Gao. Thesis title: Tyrosine Residues are Functionally Important in Tau-induced Neurodegeneration *in vivo*. Advisor: Mel Feany

Outside Universities:

2004 Doctoral dissertation examiner for Hanna Laudon, Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden. Thesis title: Functional Domains in the Alzheimer's Disease-Associated Presenilin 1 Protein. Advisor: Jan Naslund
2008 Doctoral dissertation defense committee for Sonia Podvin, Department of Pharmacology, Boston University. Thesis title: Characterization of the Anti-Aging Protein Klotho in Normal Brain Aging and Neurodegeneration. Advisor: Carmela Abraham
2012 Doctoral dissertation defense committee for Vincent Mecozzi, Department of Biochemistry, Brandeis University. Thesis title: Validating the Retromer Complex as a Target in Treating Alzheimer's Disease. Advisors: Gregory Petsko and Dagmar Ringe.

Memberships in Professional Societies:

1984- American Chemical Society: Divisions of Organic and Medicinal Chemistry.
1990- American Association for the Advancement of Science.
1998-11 Society for Neuroscience
2003-10 American Society for Biochemistry and Molecular Biology
2003-10 New York Academy of Sciences
2005- International Proteolysis Society
2008- International Society for the Advancement of Alzheimer Research and Treatment (ISTAART)

Community Service Related to Professional Work:

1999, 2000, 2003	Presentation to 4th or 5th grade classes at Horace Mann School, Newton, MA: "Making New Medicines"
2005-10	Series of 3 presentations to high school chemistry and biology classes at Boston Trinity Academy, Brookline, MA: "The Chemistry of Life", "The Chemistry of Disease", and "The Chemistry of Medicine"
2006, 2010	Presentation to 12th grade advanced biology class at Boston Trinity Academy, Brookline, MA: "Evolutionary Theory and Biomedical Research"

Public Communications

2006	Featured in a Japanese public television station NHK program on Alzheimer's disease.
2008	Participated in a National Public Radio current affairs program called "The Sound of Ideas", produced out of WCPN in Cleveland, Ohio. The program, aired live on May 14th, discussed a new book called "The Myth of Alzheimer's", with the authors also participating in the discussion.
2009	Provided opening remarks to the screening of an HBO special on Alzheimer's disease and fielded questions afterwards from a lay audience, an event sponsored by "Science in the News", a Harvard Medical School graduate student group.

Editorial Boards:

1996-	Ad hoc reviewer: Biochemistry, Biological Chemistry, Bioorganic and Medicinal Chemistry Letters, Cell, EMBO Journal, Expert Opinion on Investigational Drugs, FEBS Journal, Genes and Development, Human Molecular Genetics, Journal of Biological Chemistry, Journal of Cell Biology, Journal of Medicinal Chemistry, Journal of Neuroscience, Journal of Neuroscience Research, Journal of Organic Chemistry, Journal of Neurochemistry, Journal of Pharmacology and Experimental Therapeutics, Journal of the American Chemical Society, Molecular and Cellular Neuroscience, Molecular Medicine Today, Nature, Nature Cell Biology, Nature Medicine, Nature Reviews Drug Discovery, Nature Reviews Molecular Cell Biology, Neurobiology of Aging, Neuron, Pharmaceutical Research, Proceedings of the National Academy of Science USA, Science.
2003-8	Editorial Board Member: Journal of Biological Chemistry
2008-9	Editorial Board Member: Current Drug Discovery Technologies
2012	Guest Editor, Journal of Medicinal Chemistry, for special issue on Alzheimer's disease

Advisory Boards

2000-	Institute for the Study of Aging/Alzheimer Drug Discovery Foundation (New York, NY), Scientific Advisory Board member
2002-4	Trophos, S. A. (Marseilles, France), Scientific Advisory Board member
2005-6	Alzheimer Centennial Conference, Tübingen, Germany
2008-10	American Federation for Aging Research (AFAR), National Scientific Advisory Council

2008-10 International Society for the Advancement of Alzheimer Research and Treatment (ISTAART), Founding Council Member
2009- Alzheimer Research Forum, Advisor Board

National Service

2001-4 NIH Study Section: Molecular, Cellular and Developmental Neuroscience-1
2003 NIH Study Section: Medicinal Chemistry A (ad hoc, Feb 2003)
2006 NIH Study Section: Synthetic and Biological Chemistry B (ad hoc, Oct 2006)
2007 NIH Study Section: Special Emphasis Panel on Biological Chemistry and Macromolecular Biophysics (Feb 2007)
2008-11 NIH Study Section: Special Emphasis Panel: Roadmap High Throughput Screening R21 Applications (Jul 2008; Feb 2009; Jun, Nov 2010; Mar 2011)
2012 NIH Blueprint for Neuroscience Study Section (Mar, Dec 2012)

Other Service

2001- Alzheimer's Association: Reviewer, grant applications
2003-5 New York Academy of Science: Program committee member for discussion group on Age Related Neurodegenerative Diseases
2003-5 American Chemical Society, Division of Medicinal Chemistry: Predoctoral Fellowship Award Selection Committee
2004-5 American Chemical Society, Division of Medicinal Chemistry: Executive Committee
2009-12 American Association for the Advancement of Science, Section on Neuroscience: Electorate Nominating Committee
2009- Sato Memorial International Award Nominating Committee, Pharmaceutical Society of Japan and the National Institutes of Health. Committee Chair: 2010-
2010-11 Co-chair of inaugural Gordon Research Conference on Regulated Proteolysis of Cell Surface Proteases, Davidson, N.C., July 10-15, 2011

Awards and Honors:

1980 Hudson Scholarship, Philadelphia College of Pharmacy and Science
1981-82 Rohrer Scholarship, Philadelphia College of Pharmacy and Science
1983 Science Scholarship, Philadelphia College of Pharmacy and Science
1984 American Chemical Society Undergraduate Analytical Chemistry Award, Philadelphia College of Pharmacy and Science
1984 Undergraduate American Chemical Society Award, Philadelphia College of Pharmacy and Science
1984 Magna cum Laude, Philadelphia College of Pharmacy and Science
1985-89 Trainee, National Institutes of Health Training Grant, University of Kansas Department of Medicinal Chemistry
1989 Graduate Honors Seminar Award, University of Kansas School of Pharmacy
1989 Irsay-Dahle Award for outstanding graduate work. University of Kansas Department of Medicinal Chemistry
1991 Argersinger Award for outstanding doctoral dissertation, University of Kansas.
1990-92 American Heart Association, Kansas Affiliate, postdoctoral fellowship
1992-94 Pharmacology Research Associate Training (PRAT) fellowship, National Institute of Health
1997 Junior Faculty Award, University of Tennessee Research Day
1998 Excellence in Teaching Award, University of Tennessee Student Government Association
2003 Sato Memorial International Award, Pharmaceutical Society of Japan
2007 Alzheimer Drug Discovery Foundation and Elan Pharmaceuticals, Award for Innovative Research
2007 Annual Alumni Award, University of the Sciences in Philadelphia
2008-11 Zenith Fellows Award, Alzheimer's Association
2008 MetLife Award for Medical Research, MetLife Foundation
2009 Potamkin Prize for Research in Pick's, Alzheimer's and Related Diseases, American Academy of Neurology

PART II: Research and Teaching Contributions

A. Narrative Report

The Wolfe lab studies intramembrane proteases that play critical roles both in normal biology and in human disease. The last place in the cell to expect hydrolysis is within the hydrophobic environment of the lipid bilayer. Nevertheless, a number of multi-pass membrane proteins appear to carry out this seemingly paradoxical process (Wolfe and Kopan, *Science*, 2004; see publications list for references in this section). Such proteases cut within the transmembrane region of their respective substrates, and consistent with this observation, these proteases contain putative catalytic residues located within transmembrane domains. The specific focus of the lab has been on the chemistry and biology of γ-secretase. This protease is critical to the pathogenesis of Alzheimer's disease (Esler and Wolfe, *Science*, 2001) and to cell differentiation during embryonic development. Small organic inhibitors were developed and used as tools to characterize and identify γ-secretase (Wolfe *et al., J Med Chem*, 1998; Wolfe *et al., Biochemistry*, 1999a). Findings from the lab implicate a multi-pass membrane protein called presenilin as the catalytic component of a larger γ-secretase complex (Wolfe *et al., Nature*, 1999; Esler *et al., Nat Cell Biol*, 2000). Missense mutations in presenilin cause hereditary Alzheimer's disease, and these mutations specifically affect γ-secretase activity.

The lab found that presenilin and a presenilin-associated protein called nicastrin copurify with γ-secretase activity from an immobilized inhibitor, evidence that nicastrin is also a member of the protease complex (Esler *et al., Proc Natl Acad Sci USA*, 2002). Moreover, a γ-secretase substrate also copurified, suggesting an initial substrate docking site on the protease complex distinct from the active site. Helical peptides designed to interact with this docking site can potently inhibit γ-secretase activity both in cell-free and cell-based assays (Das *et al., J Am Chem Soc*, 2003; Kornilova *et al., Proc Natl Acad Sci USA*, 2005). The lab also determined the stoichiometry of the active γ-secretase complex, which had been unknown (and, with respect to presenilin, controversial). The four essential components (presenilin, nicastrin, Aph-1 and Pen-2) are each represented only once per complex (Sato *et al., J Biol Chem*, 2007). Disease-causing mutations in presenilin alter processive proteolysis by γ-secretase, leading to increased proportions of long Aβ peptides (Quintero-Monzon *et al., Biochemistry*, 2011).

The lab also discovered a nucleotide binding site on the γ-secretase complex. Small organic molecules that interact with this site can selectively block γ-secretase proteolysis of the amyloid-β precursor protein (APP), critical to the pathogenesis of Alzheimer's disease, without affecting proteolysis of an alternative substrate, the Notch receptor. Notch signaling, critical in many cell differentiation events, requires proteolysis by γ-secretase (De Strooper *et al., Nature*, 1999), and blocking Notch signaling with γ-secretase inhibitors causes severe toxicity in mice. The finding that compounds can selectively block the cleavage of APP without affecting that of Notch (Fraering *et al., J Biol Chem*, 2005) has revived this protease as a therapeutic target. In 2006, Dr. Wolfe cofounded the Laboratory for Experimental Alzheimer Drugs (LEAD) at HMS to advance the development of such selective agents as disease-modifying therapeutics for Alzheimer's disease.

The Wolfe lab has also investigated the structure, mechanism, and inhibition of other intramembrane proteases, such as the serine protease Rhomboid (Urban and Wolfe, *Proc Natl Acad Sci USA*, 2005) and the presenilin homolog signal peptide peptidase (Sato *et al., Biochemistry*, 2006; Narayanan *et al., J Biol Chem*, 2007; Sato *et al., J Biol Chem*, 2008), both of which are highly conserved across evolution and play critical roles in biology. In this way, the lab helped establish common biochemical principles and strategies for designing inhibitors for this family of membrane-embedded enzymes.

The lab has also begun to combine chemistry and biology toward the study of another factor critical to the pathogenesis of dementias: the microtubule-associated protein tau. Filaments of tau are a common feature in a variety of different neurodegenerative diseases, including Alzheimer's disease. Mutations in the gene encoding this protein are associated with dominant, familial forms of frontotemporal dementia, and many of these mutations alter pre-mRNA splicing to increase inclusion of exon 10. The Wolfe lab has validated the *in vivo* existence of a hypothetical stem-loop at the end of exon 10, where many of the dementia-associated mutations occur (Donahue *et al., J Biol Chem*, 2006). These mutations destabilize this RNA stem-loop structure, allowing more ready access to splicing factors. High-throughput screening has led to identification of small molecules that interact with and stabilize this structure (Donahue *et al., J Biomol Screen*, 2007), and NMR studies have elucidated how one of these compounds interacts with the tau mRNA stem-loop (Zhang *et al., Chem Biol*, 2009). Efforts are ongoing to improve the potency and selectivity of these agents (Liu *et al., J Med Chem*, 2009) to provide new tools for chemical biology as well as new prototype therapeutics. In addition, the lab has studied alternative splicing of the β-site APP-cleaving enzyme 1 (BACE1; β-secretase), determining that alternative splice isoforms are catalytically inactive and that shunting BACE1 down these

alternative pathways with antisense oligonucleotides effectively lowers Aβ production in cells (Mowrer and Wolfe, *J Biol Chem*, 2008). A G-quadruplex structure in exon 3 of BACE1 mRNA partly regulates alternative splicing (Fisette *et al., J Neurochem*, 2012). Thus, modulation of BACE1 alternative splicing represents a new strategy for developing therapeutics for Alzheimer's disease.

Dr. Wolfe is committed to graduate-level teaching at HMS. In 2003, he co-directed and taught a new quarter course, Neurobiology 300, "Biochemistry and Biology of Neurodegenerative Diseases", a 2-hour-per-week class with some didactic presentation but primarily discussion of seminal and current research articles in the field. In 2005 and 2007, he directed and taught this course in its entirety, and in 2009 and 2011, he was joined by Dr. Matthew Lavoie, a junior faculty expert in Parkinson's disease. Each time it has been offered, the course has received high praise from students. From 2002-5, Dr. Wolfe was also involved in leading a discussion section of BCMP 201, "Proteins: Structure, Function, and Catalysis"; in 2006-10, he presented lectures on enzyme mechanisms and inhibition for this course. In 2004, he also led a discussion section for Med Sci 300, the Conduct of Science, an ethics course required of all DMS graduate students. During the fall of 2012 he has been participating for 3 hours each week in BBS 230, "Analysis of the Biological Literature", required of all first-year BBS graduate students.

B. Research Funding Information

Past:

1994-95	American Cancer Society (through an institutional research grant)	PI
	Mechanism-Based Inactivators of Ribonucleotide Reductase as Potential Anticancer Agents	
1995-96	American Association of Colleges of Pharmacy/New Investigator Award	PI
	Design, Synthesis, and Evaluation of Potential Ribonucleotide Reductase Inhibitors	
1995-96	Oak Ridge Associated Universities/Junior Faculty Enhancement Award	Co-PI
	Inhibition of Alzheimer's β–Amyloid Aggregation by Amphipathic Peptides.	
1996-99	NIH/R15 (NCI)	PI
	Potential Inactivators of Ribonucleotide Reductase	
1998-2001	NIH/R29 (NINDS)	PI
	Molecular Probes for Alzheimer's γ-Secretases	
2000-01	Institute for the Study of Aging	PI
	Helical Peptidomimetics as Inhibitors of Alzheimer's γ-Secretases	
2001-04	Alzheimer's Association	PI
	In Search of Presenilinase	
2002-05	Alzheimer's Association	PI
	Probing the Initial Substrate Binding Site of γ-Secretase	
2004-09	NIH/R01 (NINDS)	co-investigator
	γ-Secretase in Alzheimer's Disease	
	P.I. Todd Golde (Mayo Clinic-Jacksonville)	
2005-08	Alzheimer's Association	PI
	Inhibitors of Amyloid Production Selective for APP vis-à-vis Notch	
2007	Fidelity Foundation	PI
	Toward a Crystal Structure of Presenilin Homologues	
2007-09	Alzheimer Drug Discovery Foundation	PI
	Selective Amyloid-Lowering Agents	
2000-10	NIH/R01(NIA)	PI
	The Role of Presenilins in γ-Secretase Activity	
2007-11	NIH/R01(NIGMS)	PI
	Structure and Mechanism of Signal Peptide Peptidase	
2007-11	Leukemia and Lymphoma Society	co-investigator
	Specialized Center of Research (SCOR) Grant: Targeting the Notch Signaling Pathway	
	P.I. Jon Aster (Brigham and Women's Hospital)	
2008-11	Alzheimer's Association, Zenith Fellow Award	PI
	Regulation of RNA Splicing in Alzheimer's and Related Dementias	
2011-12	Alzheimer Drug Discovery Foundation	PI
	Targeting Tau Pre-mRNA for Frontotemporal Dementia and Related Disorders	
2001-12	NIH/R01(NINDS)	PI
	Molecular Probes for Alzheimer's γ-Secretases	

2011-12 Fidelity Biosciences Research Foundation PI
Targeting Tau Pre-mRNA Structure for Dementias

Current:

2003-13 NIH/P01 (NINDS) co-investigator
Presenilin Biology and the Mechanism of Alzheimer's Disease
P.I. Dennis Selkoe. Project 1: Structure and Function of the γ-Secretase Complex

2010-13 American Health Assistance Foundation PI
Gamma-Secretase Modulators for Alzheimer's Disease

2012-14 NIH/R21 (NINDS)
Targeting Tau Splicing for Dementias PI

2012-14 NIH/R03 (NINDS)
Trimming of Long Amyloid Peptides by Gamma-secretase PI

C. Report of Other Current Research Activities

None

D. Report of Teaching

1. Local Contributions

University of Kansas School of Pharmacy

1984-89 Drug Assay Laboratory
Laboratory coordinator for NMR section
80 pharmacy students
Contact time: 20 hours/year

University of Tennessee School of Pharmacy

1995-99 Organic Medicinal Chemistry
Lecturer
75 pharmacy students (1995-97); 100 pharmacy students (1998-99)
Contact time: 15 hours/year (Preparation time ~ 100 hours)

University of Tennessee Graduate School

1994-98 Research Techniques in Medicinal Chemistry
Lecturer
2-6 graduate students
Contact time: 3 hours/year in alternate years (1994, 96, and 98)

1995-99 Organic Medicinal Chemistry
Lecturer
4-6 graduate students
Contact time: 6 hours/year (Preparation time ~ 40 hours)

1997, 99 Bioorganic Chemistry and Drug Design
Coordinator and Lecturer
4 graduate students
Contact time: 30 hours/year (Preparation time: ~ 200 hours)

Harvard Medical School

2001-05	BCMP 201 (Protein Structure, Function and Catalysis) Section leader 6-12 graduate students Contact time: 8 hours/year (Preparation time ~ 50 hours)
2006-10	BCMP 201 (Protein Structure, Function and Catalysis) Lecturer (on Enzyme Mechanism and Inhibition) 18-35 graduate students Contact time: 6 hours/year (Preparation time ~ 60 hours)
2003-11 (alt. years)	Neurobiology 300/305qc (Biochemistry and Biology of Neurodegenerative Diseases) Course co-organizer (03), organizer (05-) and lecturer 5-20 graduate students Contact time: 7 hours/year (03) (Preparation time: ~ 60 hours) Contact time: 14 hours/year (05, 07, 09, 11) (Preparation time: ~120 hours)
2004	Conduct of Science (MED SCI 300) Section leader 16 students Contact time: 8 hours/year (Preparation time: ~30 hours)
2005	Seminar Series in Neuroscience to Neurology Residents (December 14, 2005) Seminar Title: Molecular Basis of Alzheimer's Disease and Strategies Toward Therapeutics
2007-10	BCMP 207 (Molecular Approaches to Drug Action and Drug Discovery) Lecturer (on the design of enzyme inhibitors as drugs) 21 graduate students Contact time: 1.5 hours/year (Preparation time: ~15 h, including selecting papers to be discussed in a 1.5 hour breakout session along with questions to guide the discussion)
2006, 08	Research Chalk Talk, BCMP faculty
2012	BBS 230 (Analysis of Biological Literature) Section co-leader for discussion 8 graduate students Contact time 30 h/year (Preparation time: ~60 h)

Other Teaching/Advising:

2004	Harvard Center for Neurodegeneration and Repair (HCNR) Student & Faculty Journal Club. Article: Marambaud et al. A CBP binding transcriptional repressor produced by the PS1/e-cleavage of N-cadherin is inhibited by PS1 FAD mutations. Cell 2003, 114: 635-45. Student: Esther Becker. Faculty Comments: Michael S. Wolfe (Jan 13, 2004)
2005	Harvard Center for Neurodegeneration and Repair (HCNR) Student & Faculty Journal Club. Article: Singer et al. Targeting BACE1 with siRNAs ameliorates Alzheimer disease neuropathology in a transgenic model. Nat Neurosci 2005, 8: 1343-9 Postdoc: Sarah Luchansky. Faculty Comments: Michael S. Wolfe (Oct 10, 2005)
2009	Harvard Center for Neurodegeneration and Repair (HCNR) Student & Faculty Journal Club. Article: Ghosal et al. Alzheimer's disease-like pathological features in transgenic mice expressing the APP intracellular domain. PNAS 2009, 106: 18367-72. Postdoc: Morgan Martin. Faculty Comments: Michael S. Wolfe (Dec 8, 2009)
2010	Harvard NeuroDiscovery Center Student & Faculty Journal Club. Article: Gamma-secretase activating protein is a therapeutic target for Alzheimer's disease. Nature 2010,

467: 95-99. Postdoc: Amanda Krzysiak. Faculty Comments: Michael S. Wolfe (Oct 12, 2010).

2011 Harvard NeuroDiscovery Center Student & Faculty Journal Club. Article: Arc/Arg3.1 regulates an endosomal pathway essential for activity-dependent beta-amyloid generation. Cell 2011, 147: 615-628. Postdoc: Allen Chen. Faculty Comments: Michael S. Wolfe (Dec 13, 2011).

2012 Harvard NeuroDiscovery Center Student & Faculty Journal Club. Articles: Transynaptic spread of tau pathology in vivo. PLoS One 2012, 7: e31302 and Propagation of tau pathology in a model of early Alzheimer's disease. Neuron 2012, 73: 685-97. Postdoc: Se Hoon Choi. Faculty Comments: Michael S. Wolfe (Apr 10, 2012).

2005-12 One lecture each year on the biochemistry of Alzheimer's disease in an advanced undergraduate course on Protein Structure and Disease at Brandeis University.

Advising Responsibilities:

Undergraduate Thesis Advisor for Harvard Biology Students:

Jennifer Vandrovec. Thesis title: An *in vitro* assay for the proteolysis of Notch by γ-secretase, 2002
Ryan Shenning. Thesis title: Biochemistry of the γ-secretase complex: Assembly inhibition and subunit cross-linking, 2004
Gioacchino Curiale. Thesis title: Small molecule modulators of tau pre-mRNA splicing *in vivo*, 2005
Cathy Cheng. Thesis title: Synthesis and evaluation of helical peptide probes for signal peptide peptidase, a homolog of Alzheimer's disease-related presenilin: evidence for a substrate docking site, 2007
Jennifer Lee. Thesis title: The Role of Conserved Positively Charged Residues at the Membrane-Cytosol Interface of Presenilin in Processive Proteolysis, 2010

Pharmacy Student Advisor:

7 students/year; available for counseling; University of Tennessee, 1997-99

Predoctoral Trainees:

Past:

Chad L. Moore (Prior degree: B.S., Chemistry, Christian Brothers University, 1995)
Thesis Title: Synthesis and evaluation of difluoro ketone peptidomimetic inhibitors to investigate the intramembranous cleavage of amyloid precursor protein and Notch.
Years in Wolfe Lab: 1995-2000.
Ph.D., Medicinal Chemistry, University of Tennessee, 2000
Current position: Forensic Examiner, FBI Laboratory, US Department of Justice

Karen R. Mowrer (Prior degree: B.S., Biochemistry, Colorado State University, 2002)
Thesis title: Alternative splicing of BACE1 pre-mRNA and its implications for Alzheimer's disease
Years in Wolfe Lab: 2004-8
Ph.D., Biological Chemistry & Molecular Pharmacology, 2008
Current position: Legislative Affairs Officer, Federation of American Societies for Experimental Biology

Present

John Dickson (Prior degree: B.S., Chemistry, Furman University, 2006; MD-PhD student at HMS)
Thesis topic: Regulation of tau through its mRNA 3' untranslated region
Years in Wolfe Lab: 2008-

Marty Alyse Fernandez (Prior degree: B.S., Biochemistry, University of Florida, 2009)
Thesis topic: Regulation of proteolytic processing of APP by γ-secretase
Years in Wolfe Lab: 2010-

Catherine Hartman (Prior degree: B.A., Math, Duke University, 2010)

Thesis topic: A cellular model of tau alternative splicing and pathology
Years in Wolfe Lab: 2011-
Postdoctoral Trainees:

Past:

Rogers Harry-O'kuru (Prior degree: Ph.D., Chemistry, University of Memphis, 1988)
Project: Synthesis of 2'-substituted ribonucleosides as potential inhibitors of ribonucleotide reductase.
Years in Wolfe Lab: 1994-96
Current position: Research Scientist, USDA, Peoria, IL

Jui-Yi Tsai (Prior degree, Ph.D., Chemistry, Auburn University, 1998)
Project: Synthesis of peptidomimetic γ-secretase inhibitors
Years in Wolfe Lab: 1998-2000
Current position: Senior Scientist, Universal Display Corp., Ewing, NJ

William P. Esler (Prior degree: Ph.D., Biological Chemistry and Molecular Pharmacology, Harvard University, 1999)
Project: Inhibitor design, affinity labeling, purification and biochemical characterization of γ-secretase,
Years in Wolfe Lab: 1999-2002
Alzheimer's Association New Investigator Award (2000-03)
Current position: Senior Research Scientist, Pfizer Inc.

Jun Gao (Prior degree: Ph.D., Biochemistry, University of Kansas, 1998)
Project: Development of substrates for presenilinase, presenilin purification and proteolytic properties.
Years in Wolfe Lab: 2000-2003
NIH Postdoctoral Training Grant (Director: B. Yanker)
Current position: unknown

Chittaranjan Das (Prior degree: Ph.D., Molecular Biophysics, Indian Institute of Science, Bangalore, India, 2000)
Project: Design, synthesis, and evaluation of helical peptides as probes for γ-secretase.
Years in Wolfe Lab: 2000-2004
Current position: Assistant Professor, Department of Chemistry, Purdue University

Pancham Bakshi (Prior degree: Ph.D., Organic Chemistry, University of Dehli, India, 2000)
Project: Toward nonpeptide γ-secretase inhibitors
Years in Wolfe Lab: 2001-2004
Harvard Center for Neurodegeneration and Repair Core D Fellowship (2003)
Current position: Scientist II, Head of Medicinal Chemistry, Roskamp Institute, Sarasota, FL

Patrick Fraering (Prior degree: Ph.D., Biochemistry, University of Fribourg, Switzerland)
Project: Purification and biochemical characterization of γ-secretase
Years in Wolfe Lab: 2002-present
Fellowship from the Swiss National Science Foundation (2002-3)
Current Position: Assistant Professor, Swiss Federal Institute of Technology Centre (EPFL) in Lausanne

Frederic Bihel (Prior degree: Ph. D., Bioorganic Chemistry, Université Aix-Marseille II)
Project: Helical peptide probes for γ-secretase
Years in Wolfe Lab: 2003-2004
France Alzheimer and Fondation pour la Recherche Medicale (2003)
Current position: Associate Scientist, Faculté de Pharmacie de Strasbourg, CNRS (France's National Center of Scientific Research)

Michael J. Bowman (Prior degree: Ph.D., Chemistry, Purdue University, 2003)
Project: Solid-phase synthetic methods toward helical peptides
Years in Wolfe Lab: 2003-2004
Current position: unknown

Sinisa Urban (Prior degree: Ph.D., Developmental Biology, University of Cambridge)
Project: Biochemistry and inhibition of rhomboid, an intramembrane serine protease
Years in Wolfe Lab: 2003-5

Human Frontiers in Science Fellowship (2003-4); Harvard Society of Fellows (2004-; Burroughs-Welcome Career Development Award (2005-10)
Current Position: Associate Professor, Howard Hughes Medical Institute; Department of Molecular Biology and Genetics, Johns Hopkins University

Anna Kornilova (Prior degree: Ph.D., Chemistry, Bowling Green State University, Ohio, 2001)
Project: Understanding γ-secretase through affinity labeling and cysteine crosslinking.
Years in Wolfe Lab: 2001-6
Lefler Fellowship, Harvard Medical School (2003)
Current Position: Senior Research Biochemist, Merck & Co.

Ananda Kuppanna (Prior degree: Ph.D., Chemistry, Bangalore University, India, 2001)
Project: Helical peptide inhibitors for intramembrane proteases
Years in Wolfe Lab: 2005-6
Current Position: Research Chemist, Aurigene Discovery Technologies, Bangalore, India

Hanna Laudon (Prior degree: Ph.D., Neuroscience, Karolinska Institutet, Sweden, 2004)
Project: Mechanism of Alzheimer-causing presenilin mutations
Years in Wolfe Lab: 2005-6
Fellowship from the Wenner-Gren Foundation in Sweden (2006)
Current Position: Research Scientist, Bioarctic Neuroscience (Stockholm, Sweden)

Toru Sato (Prior degree: Ph.D., Biochemistry, University of Tokyo, 2004)
Project: Biochemistry of signal peptide peptidase, a presenilin homolog
Years in Wolfe Lab: 2004-2007
Research Fellowship, Uehara Memorial Foundation (2004)
Current Position: Research Scientist, Eisai Pharmaceuticals, UK

Pranab Maiti (Prior degree: Ph.D., Chemistry, Cambridge University, UK, 2003)
Project: Identifying new targets for Alzheimer's disease
Years in Wolfe Lab: 2005-7
Current Position: Group Leader, Jubilant Biosys, Bangalore, India

Christine Donahue (Prior degree: Ph.D., Biochemistry, University of Massachusetts Medical School, 2001)
Project: Targeting tau splicing for neurodegenerative diseases
Years in Wolfe Lab: 2005-7
Current Position: Manager, GlaxoSmithKline, Waltham, MA

Raquel Lieberman (Prior degree: Ph.D., Chemistry, Northwestern University, 2005)
Project: Structural studies on signal peptide peptidase
Years in Wolfe Lab: 2005-7
NIH National Research Service Award (2005-7)
Current Position: Assistant Professor, Department of Chemistry and Biochemistry, Georgia Institute of Technology

Pamela Osenkowski (Prior degree: Ph.D., Cancer Biology, Wayne State University, 2005)
Project: Structure and regulation of γ-secretase
Years in Wolfe Lab: 2005-9
NIH Postdoctoral Training Grant (Director: B. Yanker)
Current Position: Instructor, Loyola University

Saravanakumar Narayanan (Prior degree: Ph.D., Chemistry, Forschungsinstitut für Molekulare Pharmakologie, 2005)
Project: Expression and purification of signal peptide peptidase
Years in Wolfe Lab: 2005-10
Lefler Fellowship, Harvard Medical School (2006-8)
Current Position: Research Fellow, Harvard Medical School (Advisor: Gerhard Wagner)

Omar Quintero-Monzón (Prior degree: Ph.D., Biochemistry, Brandeis University, 2007)
Project: Mechanism of Alzheimer-causing presenilin mutations
Years in Wolfe Lab: 2007-2010
Current Position: Scientist I, Biogen-Idec

Eleanor Peacey (Prior degree: Ph.D., Neuroscience, King's College London, 2008)
Project: Tau mRNA splicing in Alzheimer's and related dementia's
Years in Wolfe Lab: 2009-2011
Current Position: Assay Development Scientist, Astra-Zeneca, U.K.

Jean-François Fisette (Prior degree: Ph.D., Microbiology, University of Sherbrooke, 2009)
Project: Regulation of β-secretase pre-mRNA splicing
Years in Wolfe Lab: 2009-2011
Current Position: Health Technology Assessment Specialist, Centre Hospitalier Universitaire de Sherbrooke, Canada

Morgan Martin (Prior degree: Ph.D. Microbiology & Immunology, University of British Columbia, 2008)
Project: Biochemistry of signal peptide peptidase
Years in Wolfe Lab: 2008-2011
Current Position: Postdoctoral fellow, University of British Columbia

Amanda Krzysiak (Prior degree: Ph.D. Medicinal Chemistry & Molecular Pharmacology, Purdue University, 2008)
Project: Substrate and inhibitor recognition by γ-secretase
Years in Wolfe Lab: 2008-12
Current Position: Assistant Professor, Bellarmine University, Louisville, KY

Present:

Yang Liu (Prior degree: Ph.D. Chemistry, Northeastern University, 2006)
Project: Designed agents for modulating tau splicing
Years in Wolfe Lab: 2007-

Rajeswari Edayathumangalam (Prior degree: Ph.D. Biochemistry, Colorado State University, 2005)
Project: Structure of γ-secretase
Years in Wolfe Lab: 2008-

Oliver Holmes, Ph.D. (Prior degree: Molecular Biology, University of Cambridge, 2008)
Project: Structure-function of γ-secretase
Years in Wolfe Lab: 2008-

Lilia Rodriguez (Prior degree: Ph.D., Cellular and Molecular Neuroscience, King's College London, 2010)
Project: Tau mRNA splicing in Alzheimer's and related dementia's
Years in Wolfe Lab: 2011-

Regional, National, and International Contributions:

Invited Presentations (Regional)

Johns Hopkins University, Department of Pharmacology and Molecular Sciences, Seminar: "*S*-Adenosyl-L-homocysteine Hydrolase as a Target for Antiviral Chemotherapy: Design and Synthesis of Carbocyclic Nucleoside Inhibitors" (1992).

University of Pennsylvania, Department of Pharmacology, Seminar: "*S*-Adenosyl-L-homocysteine Hydrolase as a Target for Antiviral Chemotherapy: Design and Synthesis of Carbocyclic Nucleoside Inhibitors" (1992).

University of Tennessee, Memphis, Department of Pharmaceutical Sciences, Seminar: "*S*-Adenosyl-L-homocysteine Hydrolase as a Target for Antiviral Chemotherapy: Design and Synthesis of Carbocyclic Nucleoside Inhibitors" (1993).

University of Illinois at Chicago, Department of Medicinal Chemistry, Seminar: “Chemistry, Cell Biology, and Drug Design: From Peptidomimetics to the Pineal” (1993).

University of Tennessee, Memphis, Department of Pharmaceutical Sciences, Seminar: “Serotonin *N*-Acetyl-transferase: Regulation and Properties of an Oscillating Enzyme” (1994).

University of Memphis, Department of Chemistry, Seminar: "Synthetic Methodology Toward Lactam-Based Dipeptidyl Analogues" (1995)

Union University, Department of Chemistry, Seminar: "Nucleoside Analogues as Chemotherapeutic Agents and Bio-organic Probes” (1996)

Christian Brothers University, Department of Chemistry, Memphis, TN, Seminar: "Nucleoside Analogues as Chemotherapeutic Agents and Bio-organic Probes" (1996)

Indiana University-Purdue University at Indianapolis, Department of Chemistry, Seminar: “Are γ-Secretases Transmembrane-Cleaving Proteases? Implications for the Molecular Mechanism of Alzheimer’s Disease” (1998)

University of Memphis, American Chemical Society Student Affiliate, Lecture: “Are γ-Secretases Transmembrane-Cleaving Proteases? Implications for the Molecular Mechanism of Alzheimer’s Disease” (1998)

University of Mississippi, Department of Medicinal Chemistry, Seminar: “Are γ-Secretases Transmembrane-Cleaving Proteases? Implications for the Molecular Mechanism of Alzheimer’s Disease” (1998)

Northeast Louisiana University, Divisions of Basic Pharmaceutical Sciences and Toxicology,Seminar: “Are γ-Secretases Transmembrane-Cleaving Proteases? Implications for the Molecular Mechanism of Alzheimer’s Disease” (1998)

Harvard Medical School, Center for Neurologic Diseases, Seminar: “Are γ-Secretases Transmembrane-Cleaving Proteases? Implications for the Molecular Mechanism of Alzheimer’s Disease” (1998)

Washington University in St. Louis, Alzheimer’s Disease Research Center, Seminar: “Are γ-Secretases Transmembrane-Cleaving Proteases? Implications for the Molecular Mechanism of Alzheimer’s Disease” (1999)

Merck and Co., Department of Biological Chemistry, Lecture: “Molecular Pieces in the Puzzle of Alzheimer’s Disease” (1999)

Du Pont Pharmaceutical Co., Department of Chemical Enzymology, Lecture: “Molecular Pieces in the Puzzle of Alzheimer’s Disease” (1999)

University of California, Irvine, Department of Chemistry, Lecture: “Molecular Pieces in the Puzzle of Alzheimer’s Disease” (1999)

University of Kansas, Department of Medicinal Chemistry, Lecture: “Molecular Pieces in the Puzzle of Alzheimer’s Disease” (1999)

Emory University, Program in Biochemistry, Cell and Molecular Biology, Symposium on Productive Degradation: The Role of Proteases in Development and Regulation. Lecture: “Looking Through a Glass Dimly: the Role of Presenilins in γ-Secretase Activity (2000)

Bristol-Meyers-Squibb Pharmaceutical Research Institute, Lecture: “In Search of γ-Secretase: Presenilin at the Cutting Edge” (2000)

Pfizer, Central Research Division, Lecture: “In Search of γ-Secretase: Presenilin at the Cutting Edge” (2000)

University of Tennessee, Memphis, Department of Pharmaceutical Sciences, Lecture: “Molecular Pieces in the Puzzle of Alzheimer’s Disease” (2001)

Northeastern University, Department of Pharmaceutical Sciences, Lecture: “Molecular Pieces in the Puzzle of Alzheimer’s Disease” (2001)

Mayo Clinic Jacksonville, Alzheimer’s and Parkinson’s Disease Seminar Series, Seminar: “Presenilins: Proteolysis from Womb to Tomb” (2001)

Trophos S.A., Marseilles, France, Lecture: “Molecular Probes for Alzheimer’s γ-Secretase” (2001)

Chiesi Farmaceutici S.p.A, Parma, Italy, Lecture: “Molecular Probes for Alzheimer’s γ-Secretase” (2001)

Boston University School of Medicine, Department of Pharmacology, Lecture: “Molecular Probes for Alzheimer’s γ-Secretase” (2001)

Locus Discovery, Norristown, PA, Lecture: “Presenilin, APP, and Notch: Proteolysis from Womb to Tomb” (2001)

Enanta Pharmaceuticals, Watertown, MA, Lecture: “Molecular Probes for Alzheimer’s γ-Secretase” (2001)

Sunesis Pharmaceuticals, South San Fransciso, CA, Lecture: “Presenilin, APP, and Notch: Proteolysis from Womb to Tomb” (2001)

Tufts University School of Medicine, Science Lecture Series in Psychiatry (Grand Rounds), “Molecular Pieces in the Puzzle of Alzheimer’s Disease (2001)

University of Michigan, Department of Cell & Developmental Biology, Lecture: “Presenilin/γ-Secretase: Protease for Life and Death (2002)

New York Academy of Sciences, Biochemical Pharmacology Discussion Group, New York, NY, Symposium on Regulated Intramembrane Proteolysis in Signaling and Disease, Lecture: “Identification and Biological Roles of γ-Secretase (2002)

University of California, San Diego, Neuroscience Program, Seminar: “γ-Secretase: Portrait of an Intramembrane Protease Complex” (2003)

University of Cambridge, UK, MRC Laboratory of Molecular Biology, Seminar: “γ-Secretase: Portrait of an Intramembrane Protease Complex” (2003)

MPM Capital, Scientific Advisory Board Retreat on The Brain, Newport, RI, Lecture: ”Therapeutic Strategies for Alzheimer’s Disease” (2003)

IBC Life Science Conference on Model Organisms in Drug Discovery, Boston, MA, Lecture: “Testing γ-Secretase Inhibitors for Alzheimer’s Disease in Developing Drosophila” (2003)

Tufts University, Department of Chemistry, Waltham, MA, Seminar: “Biochemistry and Inhibition of γ-Secretase” (2003)

Partners Program of Excellence in Alzheimer’s and Other Neurodegenerative Diseases, 7th annual colloquium, Boston, MA, Lecture: “Biochemistry and Inhibition, and Therapeutic Potential of γ-Secretase (2004)

University of Minnesota, Department of Medicinal Chemistry, Seminar: “Biochemistry and Inhibition of γ-Secretase” (2004)

The Scripps Research Institute, La Jolla, CA, Seminar: “Biochemistry and Inhibition of γ-Secretase (2004)

New York University, Department of Pharmacology, Seminar: “Biochemistry and Inhibition of γ-Secretase” (2004)

New York Academy of Sciences, Discussion Group on Neurodegeneration, New York, NY; speaker and organizer for session on “Chemical Biology of Neurodegenerative Diseases”, Lecture: “Chemical Biology of Alzheimer’s Disease” (2004)

Aventis Pharma, Paris France, Lecture: “Biochemistry and Inhibition of γ-Secretase” (2004)

Tufts Medical School, Department of Neuroscience, Boston, MA, Seminar: “Chemical Biomedicine & Neurodegeneration: Research in Pasteur’s Quadrant” (2004)

Forest Research Institute, Advisory Board Meeting: Evaluation of Disease-Modification Targets for Alzheimer’s Disease”, Jersey City, NJ, Lecture: “γ- and α-Secretase Modulators: Current Status” (2004)

Brandeis University, Department of Biochemistry, Seminar: “Biochemistry and Inhibition of γ-Secretase” (2004)

Karolinska Institutet, Huddinge, Sweden, Seminar: “Biochemistry and Inhibition of γ-Secretase” (2004)

University of Kansas, Lawrence, Kansas, Seminar: “Biochemistry and Inhibition of γ-Secretase” (2005)

University of Massachusetts Medical School, Program in Neuroscience, Worchester, MA, Seminar: “Biochemistry and Inhibition of γ-Secretase” (2005)

Katholieke Universiteit, Leuven, Belgium, Lecture: “Biochemistry and Inhibition of γ-Secretase” (2005)

University of Dublin, Dublin, Ireland, Lecture: “Biochemistry and Inhibition of γ-Secretase” (2005)

Ludwig-Maximillians-University, Munich, Germany, Lecture: “Biochemistry and Inhibition of γ-Secretase” (2005)

Boston VA Hospital, Harvard Medical School, Department of Neurology, Seminar: “Biochemistry and Inhibition of γ-Secretase” (2005)

Boston University, Genetics Program, Department of Medicine, Lecture: “Biochemistry and Inhibition of γ-Secretase” (2005)

Kansas City Area Life Sciences Research Day, Plenary Lecture: “Chemical Biology of Alzheimer’s Disease” (2005)

Gene Logic, Symposium on Neurodegeneration and Repair: Mechanisms and Assays for Drug Repositioning, Cambridge, MA, Lecture: “Neurodegeneration and Repair in Alzheimer’s Disease” (2005)

University of Colorado, Department of Chemistry, Seminar: “Biochemistry and Inhibition of Intramembrane Proteases” (2006)

Alzheimer’s Association Massachusetts Chapter, Lexington, MA, Panel Discussion: “On the Cutting Edge of Alzheimer’s Research: Searching for a Cure” (2006)

Harvard Center for Neurodegeneration and Repair (HCNR) Symposium on Neurodegenerative Diseases: From Mechanism to Medicine, Boston, MA, Lecture: “Targeting γ-Secretase for Alzheimer’s Disease” (2006)

Symposium on Translating Molecular Understanding into Disease-Modifying Therapeutics in Alzheimer’s Disease, Merck Research Laboratories-Boston, Lecture: “Selective Modulation of APP Cleavage by Certain Kinase Inhibitors” (2006)

Kyoto Pharmaceutical University, Department of Medicinal Chemistry, Kyoto, Japan, Seminar: “Biochemistry and Inhibition of Intramembrane Aspartyl Proteases: At the Interface of Chemistry, Biology, and Medicine” (2006)

University of Tokyo, Symposium on Neurodegenerative Disorders, Tokyo, Japan, Lecture: “Targeting γ-Secretase for Alzheimer’s Disease” (2006)

Mayo Clinic, Jacksonville, FL, Lecture: “Biochemistry and Inhibition of Intramembrane Aspartyl Proteases” (2006)

Massachusetts Chapter of the Alzheimer’s Association. Memory Walk Kick-off, Waltham, MA. Research Update: “Shutting Down Alzheimer’s” (2006)

University of the Sciences in Philadelphia. Ribbon cutting for new Science and Technology Center. Follow up panel discussion: “Shaping Science in the 21st Century: Foundations from the Past, Pillars for the Future” (2006)

New York Academy of Sciences, Biochemical Pharmacology Discussion Group, New York, NY, Symposium on Multiple Targets for Alzheimer’s Disease, Lecture: “Biochemistry of γ-Secretase, Presenilin, and Signal Peptide Peptidase” (2006)

Mount Sinai School of Medicine, New York, NY, Translational Neuroscience Seminar Series. Lecture title: “Presenilin Biochemistry and the Pathogenesis of Alzheimer's Disease” (2007)

University of Toronto, Center for Research on Neurologic Diseases, Diane Charlwood Memorial Lecture, Title: Presenilin Biochemistry and the Pathogenesis of Alzheimer's Disease (2007)

Elan Pharmaceuticals, So. San Francisco, CA, Seminar: γ-Secretase: Biochemistry, Mechanism, and Inhibition (2007)

University of California at Los Angeles, David Geffen School of Medicine, Grand Rounds: Presenilin Biochemistry and the Pathogenesis of Alzheimer's Disease (2007)

University of British Columbia, Department of Pharmaceutical Sciences, Seminar: Targeting γ-Secretase for Alzheimer’s Disease (2007)

Washington University in St. Louis, Department of Biochemistry, Seminar: Biochemistry and Inhibition of Intramembrane Aspartyl Proteases (2007)

Massachusetts Chapter of the Alzheimer’s Association. Annual Board Meeting, Boston, MA. Presentation: “Molecular Basis of Alzheimer’s Disease and Emerging Medicine” (2007)

Symposium on Understanding the Mechanisms of Action of γ-Secretase, sponsored by the Alzheimer’s Drug Discovery Foundation and Johnson & Johnson, Princeton, NJ. Presentation: Mechanism of γ-Secretase Inhibitors (2007)

Strategic Research Institute 3rd Annual CNS Diseases Congress, Boston, MA. Presentation: γ-Secretase Modulators for Alzheimer’s Disease (2007)

Massachusetts Chapter of the Alzheimer’s Association. Memory Walk Kick-off, Waltham, MA. Research Update: “The Road to Alzheimer Therapeutics: A Progress Report” (2007)

Cleveland Clinic, Department of Neurosciences, Seminar: Presenilin Biochemistry and the Pathogenesis of Alzheimer's Disease (2007)

Academy of Athens, Biomedical Research Foundation, Seminar: Presenilin Biochemistry and the Pathogenesis of Alzheimer's Disease (2007)

Boston University Alzheimer’s Disease Center, Seminar: Presenilin Biochemistry and the Pathogenesis of Alzheimer's Disease (2008)

University of Pennsylvania, Department of Pharmacology, Seminar: Membrane-Embedded Aspartyl Proteases in Biology and Medicine (2008)

MassGeneral Institute for Neurodegenerative Disease (MIND), Charlestown, MA. Seminar: Molecular Basis of Alzheimer's Disease and Therapeutic Strategies (2008)

Eli Lily and Co., Indianapolis, IN. Seminar: Biochemistry of γ-Secretase and Related Proteases (2008)

Massachusetts Chapter of the Alzheimer's Association. Annual Board Meeting, Boston, MA. Presentation: "Understanding Alzheimer's and the Road to Therapeutics" (2008)

University of Texas Southwestern Medical Center, Department of Neuroscience. Seminar: Presenilin Biochemistry and Alzheimer's Disease (2008)

McLean Hospital, Department of Psychiatry. Belmont, MA. Seminar: Molecular Basis of Alzheimer's Disease and Therapeutic Strategies (2008)

The Cooper Union for the Advancement of Science and Art, New York City, NY. Rudin Lecturer. The Science of Alzheimer's Disease: Prospects for Prevention and Treatment (2008)

Johns Hopkins University School of Medicine, Department of Molecular Biology and Genetics. Seminar: Presenilin Proteases in Alzheimer's Disease (2008)

University of Alabama at Birmingham, Alzheimer's Disease Research Center. Seminar: Presenilin Biochemistry and Alzheimer's Disease (2009)

Pfizer Inc., Groton, CT. Seminar: γ-Secretase: Biochemistry, Mechanism, and Inhibition (2009)

University of Chicago, Department of Neuroscience. Seminar: Splicing and Dicing in Alzheimer's Disease (2009)

Synta Pharmaceuticals Corp., Lexington, MA. Seminar: Targeting γ-Secretase: Chemical Biology and Medicinal Chemistry in Alzheimer's Disease (2009)

Massachusetts General Hospital, Charlestown, MA. Seminar: Spinning the Message: Regulating RNA in Alzheimer's and Related Dementias (2010)

Rhodes College, Memphis, TN. Lecture: Molecular Basis of Alzheimer's Disease and the Road to Therapeutics (2010)

Duquesne University, Division of Pharmaceutical Sciences, Pittsburgh, PA. Seminar: Gamma-Secretase in Biology and Medicine (2010)

University of Minnesota, Department of Medicinal Chemistry. Seminar: Splicing and Dicing in Alzheimer's and Related Dementias (2010)

University of Florida, Departments of Neuroscience and Pharmacology & Therapeutics. Seminar: Splicing and Dicing in Alzheimer's and Related Dementias (2010)

Care to Cure: Alzheimer's Association Conference for New Hampshire Families and Professionals. Concord, NH. Presentation: The Science of Alzheimer's Disease and the Road to Therapeutics (2010)

Vanderbilt University, Institute for Chemical Biology, Seminar: Splicing and Dicing in Alzheimer's and Related Dementias (2011)

Alzheimer Research Forum, Protein Ontology Meeting, University at Buffalo, Buffalo, NY (2011)

University of California at San Diego, Neurosciences Department. Seminar: Splicing and Dicing in Alzheimer's and Related Dementias (2012)

University of Alabama at Birmingham, Department of Neurology. Grand Rounds Seminar: Splicing and Dicing in Alzheimer's and Related Dementias (2012)

Tufts University School of Medicine, Program in Physiology and Pharmacology, Seminar: Splicing and Dicing in Alzheimer's and Related Dementias (2012)

Invited Presentations (National)

27th National Medicinal Chemistry Symposium, Plenary Speaker, Kansas City, MO, "Molecular Probes for Alzheimer's γ-Secretase" (2000)

American Society for Biochemistry and Molecular Biology, Annual Meeting, Orlando, FL, Symposium Lecture: "Molecular Probes for Alzheimer's γ-Secretase" (2001)

Fourth Annual Conference on Regenerative Medicine, speaker and chair for session on Alzheimer's disease, Washington, DC, Lecture: "Targeting γ-Secretase for Alzheimer's Disease" (2003)

American Chemical Society National Meeting, speaker and chair for session on inhibitors of Alzheimer secretases, Philadelphia, PA, Lecture: "Chemical Probes for γ-Secretase" (2004)

American Society of Pharmacology and Experimental Therapeutics annual meeting, San Diego, CA, Symposium Lecture: "Inhibition of γ-Secretase as a Therapeutic Objective in Alzheimer's Disease (2005)

Joint Steering Committee for Public Policy, Capitol Hill Day. Selected scientists spent the day visiting congressional offices to emphasize the importance of federal support for scientific and biomedical research (2005)

6th Annual Alzheimer's Disease Drug Discovery Conference, sponsored by the Institute for the Study of Aging, New York, NY, Lecture: "Targeting γ-Secretase" (2005)

Zenith Fellows Meeting, Alzheimer's Association, New York, NY, Presentation: "Targeting Amyloid for Alzheimer's Disease" (2006)

National Consortium of Specialized Secondary Schools in Mathematics, Science and Technology (NCSSSMST) Annual Conference, Philadelphia, PA. Keynote Lecture: "Interfacing Chemistry and Biology for Scientific and Biomedical Research: Solving the Puzzle of Alzheimer's Disease" (2007)

Alzheimer's Association Research Roundtable: Academic/Industry Interface for Alzheimer's Drug Discovery, Washington, D.C. Presentation: "Academic Medicinal Chemistry in Translational Research for Alzheimer's Disease" (2007)

Coalition for the Life Sciences, Capitol Hill Day. Selected scientists spent the day visiting congressional offices to emphasize the importance of federal support for scientific and biomedical research (2008)

Biophysical Society 53rd Annual Meeting, Boston, MA. Symposium Lecture. Title: Intramembrane Aspartyl Proteases: Structure, Mechanism and Inhibition (2009)

Federation for American Societies of Experimental Biology (FASEB) Summer Research Conference on Molecular Biophysics of Cellular Membranes. Session Chair and Speaker. Lecture title: Structure, Mechanism and Inhibition of γ-Secretase (2010)

Invited Presentations (International)

Strategic Research Institute 3rd Internat'l Meeting on Neurodegeneration. Princeton, NJ, Lecture: "Molecular Pieces in the Puzzle of Alzheimer's Disease" (1999)

Ninth Meeting of the International Study Group on the Pharmacology of Memory Disorders Associated with Aging. Zurich, Switzerland, Symposium lecture: "Toward the Characterization and Identification of γ-Secretases Using Transition-State Analogue Inhibitors" (2000)

Sixth International Stockholm/Springfield Symposium on Advances in Alzheimer's Therapy, Stockholm, Sweden. Symposium lecture: "Looking Through a Glass Dimly: the Role of Presenilins in γ-Secretase Activity (2000)

7th Internat'l Conference on Alzheimer's Disease and Related Disorders (ICAD), Washington, DC. Symposium Lecture: "Biochemistry and Identity of γ-Secretase" (2000)

Fondation IPSEN, Notch from Neurodevelopment to Neurodegeneration, Paris, France, Symposium Lecture: "Presenilin, APP, and Notch: Proteolysis from Womb to Tomb" (2001)

Strategic Research Institute 4th Internat'l Meeting on Neurodegeneration. Princeton, NJ, Symposium Lecture: "Molecular Probes for Alzheimer's γ-Secretase" (2001)

International Conference on Protease Inhibitors, Friesing, Germany, Symposium Lecture: "Lessons from Gamma-Secretase/Presenilin Inhibitors in vitro and in vivo" (2001)

16th International Kinin Conference, Charleston, SC, Plenary Speaker, "APP, Notch, and Presenilins: Molecular Pieces in the Puzzle of Alzheimer's Disease" (2002)

Gordon Conference of Hormonal and Neural Peptide Biosynthesis, Colby-Sawyer College, NH, Symposium Lecturer: "Identification and Inhibition of Alzheimer's γ-Secretase" (2002)

8th Internat'l Conf. on Alzheimer's Disease and Related Disorders (ICAD), Stockholm, Sweden, Symposium Lecture: "Inhibitors of the Presenilin/γ-Secretase Complex: Biological Tools and Therapeutic Potential" (2002)

Keystone Symposium on Membrane Proteins: Structure and Mechanism, Taos, NM, Lecture: "γ-Secretase: Portrait of an Intramembrane Protease Complex" (2003)

Horizon Conference, sponsored by the Nature Publishing Group, "Signaling Scissors: New Perspectives on Proteases", session leader on intramembrane proteases, Palazzo Argaza, Italy (2003)

International Congress on Aspartate Proteases and Inhibitors, Kyoto, Japan, Lecture: "Biochemistry and Inhibition of γ-Secretase (2003)

Gordon Research Conference on Proteases, Colby-Sawyer College, NH, Lecture: "Biochemistry and Inhibition of γ-Secretase" (2004)

Alzheimer's Association International Conference on Prevention of Dementia. Speaker at pre-conference tutorial on the amyloid hypothesis and therapeutic intervention. Washington, D.C. Lecture: "Inhibition of γ-Secretase as a Therapeutic Objective in Alzheimer's Disease" (2005)

International Society for Proteolysis, 4th General Meeting, Organizer and Chair for Session on "Membrane-Associated Proteolysis and Signal Transduction", Quebec, Canada (2005)

3rd Takeda Science Foundation Symposium on PharmaSciences: On the Frontiers of Neuro-PharmaSciences: Molecular Pathology and Drug Action, Tokyo, Japan, Lecture: "γ-Secretase: Biochemistry and Therapeutic Potential as a Target for Alzheimer's Disease" (2005)

20th International Congress of Biochemistry and Molecular Biology, Kyoto, Japan, Symposium Lecture: "Biochemistry and Inhibition of γ-Secretase" (2006)

Gordon Research Conference on Proprotein Processing, Trafficking & Secretase, Colby-Sawyer College, NH, Lecture: "Molecular Probes for γ-Secretase" (2006)

Gordon Research Conference on Proteolytic Enzymes & Their Inhibitors, Colby-Sawyer College, NH, Lecture: "Structure, Function and Inhibition of γ-Secretase" (2006)

10th Internat'l Conf. on Alzheimer's Disease and Related Disorders (ICAD), Madrid, Spain, Plenary Lecture: "Biochemistry of γ-Secretase and Its Potential as a Therapeutic Target" (2006)

Biomarkers in Plasma and CSF to Support Anti-Amyloid Therapies. Ancillary symposium to the 10th Internat'l Conf. on Alzheimer's Disease and Related Disorders, Madrid, Spain. Presentation: "Modulating γ-Secretase for Alzheimer's Disease" (2006)

7th International Conference on Alzheimer's Disease Drug Discovery, sponsored by the Institute for the Study of Aging, New York, NY, Symposium Lecture: "Targeting γ-Secretase and Beyond" (2006)

Alzheimer 100 Meeting (commemorating the 100th anniversary of Alois Alzheimer's report on the disease that bears his name), Tübingen, Germany, Lecture: "Translating γ-Secretase Modulators into Alzheimer Therapeutics" (2006)

Conference on Regulated Intramembrane Proteolysis, Schloß Ringberg, Germany; Organizer, Session Chair and Lecturer: "Structure, Mechanism and Inhibition of Intramembrane Aspartyl Proteases (2006)

8th International Conference on Alzheimer's Disease Drug Discovery, sponsored by the Institute for the Study of Aging, New York, NY. Session Chair, Symposium Lecture: "Selective Amyloid-Lowering Agents" (2007)

International Society for Proteolysis, 5th General Meeting, Organizer and Chair for Session on Intramembrane Proteolysis, Patras, Greece (2007)

Keystone Symposium on Alzheimer's Disease, Keystone, CO, Lecture title: "Biochemistry of γ-Secretase and Presenilin-like Proteases" (2008)

Gordon Research Conference on Enzymes, Coenzymes and Metabolic Pathways, University of New England, Biddeford, Maine (2008). Lecture title: "Intramembrane Aspartyl Proteases"

6th Asan Medical Center/Partners Harvard Medical International Symposium. "Present and Future of Neuroscience: From Molecules to Human Disease". Seoul, South Korea (2009). Lecture: "Amyloid and Tau Production in Alzheimer's and Related Dementias".

10th International Conference on Alzheimer's Disease Drug Discovery, sponsored by the Alzheimer Drug Discovery Foundation, Jersey City, NJ. Session Chair and Speaker: "Discovery of Potent Notch-Sparing γ-Secretase Inhibitors" (2009)

International Society for Proteolysis, 6th General Meeting, Surfers Paradise, Australia (2009). Plenary Lecture: Title: Structure, Mechanism and Inhibition of γ-Secretase.

International Conference on Alzheimer's Disease and Related Disorders (ICAD) 2010, Honolulu, HI. Symposium Lecture: "Splicing and Dicing in APP Processing: Targeting Proteases and mRNAs that Regulate Aβ Production" (2010)

11th International Conference on Alzheimer's Disease Drug Discovery, sponsored by the Alzheimer Drug Discovery Foundation, Jersey City, NJ. Session Chair and Speaker: "Targeting Tau Pre-mRNA for Frontotemporal Dementia and Related Disorders" (2010)

7th International Winter Conference on Alzheimer's Disease, Zürs, Austria. Symposium presentation: "Targeting Tau Pre-mRNA for Frontotemporal Dementia and Related Disorders" (2010)

International Society for Proteolysis, 7th General Meeting, San Diego, CA. Plenary Lecture: Title: Regulation of γ-Secretase in the Production of the Amyloid β-Protein of Alzheimer's Disease: Mutations and Microenvironment (2011).

Alzheimer's Association International Conference (AAIC) 2012, Vancouver, Canada. Session presenter and co-chair: "Targeting Tau Alternative mRNA Splicing for Dementia" (2012)

Part III: Bibliography

Original Articles:

1. Wolfe MS, Borcherding DR, Borchardt RT. A 9-Step Enantiospecific Synthesis of (-)-Aristeromycin from D-Ribonic Acid γ-Lactone. Tetrahedron Lett. 1989;30:1453-6.

2. Paisley SD, Wolfe MS, Borchardt RT. Oxidation of Neplanocin A to the Corresponding 3'-Keto-Cyclopentenyl Derivative by Adenosylhomocysteine Hydrolase. J. Med. Chem. 1989;32:1415-8.

3. Wolfe MS, Anderson BL, Borcherding DR, Borchardt RT. Enantiospecific Syntheses of Aristeromycin and Neplanocin A. J. Org.Chem. 1990;55:4712-7.

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Dissertation:

1990 Carbocyclic Nucleosides as Inhibitors of S-Adenosyl-L-Homocysteine Hydrolase: Design and Synthesis of Potential Antiviral Agents

Patents:

(Hydroxyethyl)ureas as inhibitors of Alzheimer's beta-amyloid production.
Inventors: M. S. Wolfe and D. J. Selkoe.
U.S. Patent No. 6,696,488

Helical Peptidomimetics
Inventor: M. S. Wolfe
U.S. Patent No. 6,846,805

Helical Peptidomimetics with Enhanced Activity
Inventor: M. S. Wolfe
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