BIOGRAPHICAL SKETCH

NAME P. Jeffrey Conn	POSITION TITLE Lee E. Limbird Professor of Pharmacology Director, Vanderbilt Program in Drug Discovery
eRA COMMONS USER NAME connpj	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Lee University, Cleveland, TN	BS	1981	Psychology/Biology
University of Cincinnati, Cincinnati, OH	None	1982	Physiological Psych.
Vanderbilt University, Nashville, TN	Ph.D.	1986	Pharmacology
Yale University	Postdoc	1988	Neurophysiology

A. PERSONAL STATEMENT

The primary focus of the proposed research is to develop a detailed understanding of the cellular and molecular mechanisms involved in regulating chemical and electrical signaling in the central nervous system (CNS). Such changes in neuronal function are often brought about by neuromodulators acting on G protein-coupled receptors and ion channels and play important roles in all normal physiological processes in the brain and are critical for development of a variety of brain diseases. Additionally, I focus major effort on discovery of novel small molecule ligands for specific neurotransmitter receptors and neurotransmitter transporters that allow us to probe these pathways in brain slices and in vivo. I am especially interested in metabotropic glutamate receptors and muscarinic acetylcholine receptors and in regulation of these receptors in the nervous system by small molecules that act as allosteric modulators. These studies are providing advances in developing novel treatments for schizophrenia, Parkinson's disease, and other CNS disorders and my experience in these areas has prepared me for the role of principal investigator on the proposed research.

B. POSITIONS AND HONORS

Professional Experience

1987 - 1988 Visiting Lecturer, Yale College, Yale Univ. New Haven, CT
1988 - 1994 Assistant Professor, Dept. of Pharmacology, Emory University, Atlanta, GA
1984 - 1999 Associate Professor, Dept. of Pharmacology, Emory University, Atlanta, GA
1999 - 2001 Professor, Dept. of Pharmacology, Emory University, Atlanta, GA
2000 - 2003 Senior Director and Head, Department of Neuroscience, Merck Research Laboratories, West Point, PA
2003 - Present Lee E. Limbird Professor, Department of Pharmacology, Vanderbilt University, Nashville, TN
2003 - Present Director, Vanderbilt Program in Drug Discovery, Vanderbilt University

Editorial Positions

Editorial Boards: SYNAPSE ('94 – '04); Neuroscience Net ('96 – '02), J. Neurochem. ('98 - present); Current Drug Targets, CNS & Neurological Disorders ('00-present), Letters in Drug Design & Discovery ('02 - present), Current Med. Chem, ('03–present), Neurobiol. of Disease ('04–present); Guest Editor: Pharmacology, Biochem. & Behavior ('02), Current Drug Targets, CNS & Neurol. Disorders (2002); Current Neuropharmacol, (2004); Associate Editor: Molecular Pharmacology ('95-'00); Journal of Neurochemistry ('05-present); Regional Editor, North America: Current Neuropharmacology ('02-present); and Editor in Chief: Molecular Pharmacology (2006-present).

Review Positions

ISI 100 Most Highly Cited Scientists in Pharmacology and Toxicology ('93 – '03); Member, multiple Special Emphasis Panels & Ad Hoc member NLS Study Section II, NIH-NINDS ('94-'04); Program Committee, Society for Neuroscience ('97-'00); NARSAD Independent Investigator Award ('98); Member, NIH Brain Disorders and

Review Positions, continued

Clinical - 2 Study Section (‘98-‘00); Member American College of Neuropsychopharmacology (ACNP) ('99-present); Executive Committee, American Society for Pharmacology and Experimental Therapeutics (ASPET) Neuropharmacology Division (‘01-’03; ’05-present); NIMH National Advisory Mental Health Council (NAMHC) (‘03); American College of Neuropsychopharmacology (ACNP) Liaison Committee ('03-present); ASPET Award Committee (’04–’07); Expert Consultant, Compound Selection Committee, Treatment Units for Research on Neurocognition and Schizophrenia (TURNS) (’04 – present); Consultant, NIH NINDS Parkinson’s Disease Research Summit (’05); Chair Elect/Chair, ASPET Neuropharmacology Div. (’06 – ’08); Steering Committee, NIH Molecular Libraries Screening Centers Network (’10-present).

Awards

2004 NARSAD Essel Investigator, Distinguished Investigator Award
2007 ASPET-Astellas Award in Translational Pharmacology
2007 Pharmacia - ASPET Award for Experimental Therapeutics
2007 Charles R. Park Award for Basic Research Revealing Insights into Physiology and Pathophysiology
2008 Lee University Distinguished Alumnus of the Year
2008 PhRMA Foundation Award for Excellence in Pharmacology and Toxicology

Scientific Advisory Boards

2004	-	2005	InVitrogen
2004	-	2006	Precient Neuropharma
2004	-	2008	Addex Pharmaceuticals
2005	-	Present	Michael J Fox Foundation
2005	-	Present	Dystonia Research Foundation
2006	-	2008	AstraZeneca
2006	-	2008	Cephalon Inc.
2006	-	Present	Seaside Therapeutics
2006	-	Present	Cure Dystonia Initiative Advisory Council
2007	-	2008	Eyeforpharma CNS Drugs
2007	-	2008	Hoffman La Roche
2007	-	Present	NeuroOP Inc

C. REPRESENTATIVE PUBLICATIONS (representative publications from **205** total publications)

1. Hemstapat, K., de Paulis, T., Chen, Y., Brady, A.E., Grover, V.K., Alagille, D., Tamagnan, G.D., **Conn**, P. J. (2006) A novel class of positive allosteric modulators of metabotropic glutamate receptor subtype 1 interact with a site distinct from that of negative allosteric modulators. Mol. Pharmacol. 70:616-26.
2. Hemstapat, K., Da Costa, H., Nong, Y., Brady, A.E.,, Luo, Q., Niswender, C.M., Tamagnan, G.D., **Conn**, P.J. (2007) A novel family of potent negative allosteric modulators of group II metabotropic glutamate receptors. J. Pharmacol. Exp. Ther. 322:254-64.
3. Chen, Y., Nong, Y., Goudet, C., Hemstapat, K., de Paulis, T., Pin, J., and **Conn**, P.J., (2007) Interaction of novel positive allosteric modulators of metabotropic glutamate receptor 5 with the negative allosteric antagonist site is required for potentiation of receptor responses. Mol Pharmacol. 71:1389-98.
4. Shirey, J.K., Xiang, Z., Orton, D., Brady, A.E., Johnson, K.A., Williams, R., Ayala, J.E., Rodriguez, A.L., Wess, J., Weaver, D., Niswender, C.M., **Conn**, P.J. (2008) An allosteric potentiator of M4 mAChR modulates hippocampal synaptic transmission. Nat Chem. Biol. 4:42-50. PMC Journal – In Process.
5. Jones, C.K., Brady, A., Davis, A., Xiang, Z., Bubser, M., Tantawy, M., Kane, A., Bridges, T., Kennedy, J.P., Peterson, T.E., Baldwin, R., Kessler, R., Deutch, A.Y., Levey, A., Lindsley, C., and **Conn**, P.J. (2008) Selective allosteric activation of the M1 muscarinic acetylcholine receptor produces antipsychotic-like activity and disease modifying potential for Alzheimer’s Disease. J. Neurosci. 28:10422-33. PMC18842902.
6. Chen, Y., Goudet, C., Pin, J.P **Conn**, P.J. (2008) N-{4-Chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2yl)methyl]phenyl}-2 hydroxybenzamide (CPPHA) acts through a novel site as a positive allosteric modulator of group 1 metabotropic glutamate receptors. Mol Pharmacol. 73:909-18. PMC18056795.
7. Niswender, C., Johnson, K., Weaver, C.D., Jones, C.K., Luo, Q., Rodridguez, A., Marlo, J., de Paulis, T., Thompson, A., Days, E., Nalywajko, T., Austin, C., Williams, M.B., Ayala, J., Williams, R., Lindsley, C.W., and **Conn**, P.J. (2008) Discovery, characterization, and antiparkinsonian effect of novel positive allosteric modulators of metabotropic glutamate receptor 4. Mol. Pharmacol. 74:1345-58. PMC18664603.

Representative Publications, continued

8. Marlo, J., Niswender, C., Days, E., Bridges, T., Xiang, Y., Rodriguez, A., Shirey, J., Brady, A., Nalywajko, T., Luo, Q., Austin, C., Williams, M., Kim, K., Williams, R., Orton, D., Brown, A., Lindsley, C.W., Weaver, D., **Conn**, P.J. (2008) Discovery and characterization of novel allosteric potentiators of M1 muscarinic receptors reveals multiple modes of activity. Mol. Pharmacol 75:577-88. PMC2684909.
9. Engers, D., Niswender, C., Weaver, D., Jadhav, S., Menon, U., Zamorano, R., **Conn**, P.J., Lindsley, C.W., and Hopkins, C. (2009) Synthesis and evaluation of a series of heterobiarylamides that are centrally penetrant metabotropic glutamate receptor 4 (mGluR4) positive allosteric modulators (PAMs). J. Med. Chem. 52:4115-18. PMC Journal – In Process.
10. Sharma, S., Kedrowski, J., Rook, J., Smith, R.,L., Jones, C.K., Rodriguez, A., **Conn**, P.J., and Lindsley, C.W. (2009) Discovery of Molecular Switches that modulate modes, of mGluR5 Pharmacology In Vitro and In Vivo within a series of functionalized, regioisomeric 2- and 5- (Phenylethynyl) pyrimidines". J. Med. Chem 52:4103-06. PMC Journal – In Process.
11. Sheffler, D., Williams, R., Bridges, T., Xiang, Z., Kane, A., Byun, N., Jadhav, S., Mock, M., Zheng, F., Lewis, L., Jones, C.K., Niswender, C., Weaver, C.D., Lindsley, C.W., and **Conn**, P.J. (2009) A novel selective muscarinic acetylcholine receptor subtype 1 antagonist reduces seizures without impairing hippocampus-dependent learning. Mol Pharmacol 76:356-68.
12. Shirey, J., Brady, A., Davis, A., Bridges, T., Kennedy, J., Jadhav, S., Menon, U., Watson, M., Christian, E., Doherty, J., Quirk, M., Snyder, D., Levey, A., Nicolle, M, Lindsley, W., and **Conn**, P.J. (2009) A selective allosteric potentiator of the M1 muscarinic acetylcholine receptor increases activity of medial prefrontal cortical neurons and can restore impairments to reversal learning. J Neurosci 29:14271-86. PMC Journal – In Process
13. Ayala, J., Chen, Y., Banko, J., Sheffler, D., Williams, R., Telk, A., Watson, N., Xiang, Z., Zhang, Y., Jones, P., Lindsley, C.W., Olive, M., and **Conn**, P.J., (2009) mGluR5 PAMs facilitate LTP and LTD induction Neuropsychopharmacology 34:2057-71. PMC Journal – In Process
14. **Conn**, P.J., Christopoulos, A., Lindsley, C.W. (2009) Allosteric Modulators of GPCRs as a Novel Approach for Treatment of CNS Disorders. *Nature Review Drug Discov.* 8:41-54. PMC Journal – In Process
15. Hackler, E., Byun, N., Jones, C.K., Williams, J., Baheza, R., Sengupta, S., Grier, M., Avison, M., **Conn**, P.J., and Gore, J. (2010) Selective potentiation of the metabotropic glutamate receptor subtype 2 blocks phencyclidine-induced hyperlocomotion and brain activation. Neuroscience (in press). PMC Journal – In Process.

D. RESEARCH SUPPORT

Ongoing

R01 MH062646 Conn (PI) 02/15/2001 – 01/31/2011
NIH/NIMH
Regulation of Signaling by mGluR5
This project is focused on evaluating the physiological effects of allosteric modulators of mGluR5 in the hippocampus and potential antipsychotic and cognition-enhancing effects of these agents.

R01 MH073676 Conn (PI) 01/01/06 – 12/31/2010
NIH/NIMH
Muscarinic receptor activators as novel antipsychotic agents
This project is focused on evaluating the physiological effects of allosteric modulators of muscarinic recepors in the hippocampus and prefrontal cortex and evaluating potential antipsychotic and cognition-enhancing effects of these agents.

R01MH074953 Conn (PI) 06/01/2006 – 05/31/2011
NIH/NIMH
Functional effects of mGluR2 potentiators in the CNS
This project is focused on evaluating the physiological effects of mGluR2 allosteric potentiator in the prefrontal cortex and effects of these compounds in animal models of schizophrenia.

Ongoing Research Support, continued

Michael J. Fox LEAPS — Conn (PI) — 12/01/07-12/31/11
Michael J. Fox Foundation
Discovery of mGluR4 potentiators for symptomatic and disease-modifying treatment of PD
This project is focused on chemical optimization of novel potentiators of the mGluR4 receptor for the treatment of Parkinson's Disease.

VUMC34998 — Conn (PI) — 12/09/2008-12/09/2011
Johnson & Johnson
Johnson & Johnson Industry Sponsored Contract
This project is focused on discovery and optimization on novel compounds that can enter clinical development for treatment of schizophrenia.

R01 NS031373 — Conn (PI) — 07/15/10-06/30/2015
NIH/NINDS
Functions of Metabotropic glutamate receptor subtypes
The major goals of this project are to determine the cellular localization and physiological roles of multiple metabotropic glutamate receptor subtypes in the rat hippocampus.

U01 MH087965 — Jones (PI) — 02/19/2010-12/31/2014
NIH/NIMH
Vanderbilt NCDDDG for Discovery of Novel Treatments for Schizophrenia
The studies proposed in this application are focused on discovery and optimization of novel compounds for treatment of schizophrenia. The primary focus is on optimization of inhibitors of the glycine transporter GlyT1 and allosteric activators of the M1 muscarinic receptor to a point where they are suitable for clinical development.
Role on the project: Co-Investigator

1P50 NS071669 — Conn (PI) — 09/30/2010-08/31/2015
NIH/Subcontract with Emory University
Circuitry to therapy: Regulation of basal ganglia and antiparkinsonian efforts of muscarinic agents.
Role on the project: Subcontract PI

1R01 MH087989 — Conn (PI) — 09/30/2010-08/31/2015
NIH/Subcontract with University of California, San Diego
Group II mGluR antagonists and negative modulators in depression
This is a subcontract in which we will evaluate the activity of novel compounds designed to inhibit metabotropic glutamate receptors by measuring their effects on receptors expressed in cell lines. These compounds will be synthesized and further tested in animal models by our collaborators.
Role on the project: Subcontract PI

Completed

VUMC33842 — Conn (PI) — 11/01/2007-10/31/2010
Seaside Therapeutics
Discovery of Novel mGluR5 Allosteric Antagonists
The objective of this program is to develop an orally bioavailable drug candidate and backup compounds suitable for entry into preclinical and clinical development for treatment of Fragile X syndrome and other disorders.