

Michael J. Schell

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EDUCATION:

Ph.D. Neuroscience. The Johns Hopkins University School of Medicine. Nov. 1996

M.A. Science Writing. The Johns Hopkins University, Baltimore. June 1989

B.S. Biochemistry. Indiana University, Bloomington. May 1984

RESEARCH EXPERIENCE:

- **February 2005 to present.** Assistant Professor. Uniformed Services University, Dept. of Pharmacology. *Current reserch focuses on the mechanisms that control the shape of the actin cytoskeleton in dendritic spines in response to physiological and patho-physiological synaptic activity. Also investigating metabotropic glutamate receptor trafficking and the cell biology of peroxisomes in neurons and glia.*
- **October 2001- Feb 2005.** The Royal Society Robert and Joan Case Fellow for Brain Research. University of Cambridge, Dept. of Pharmacology. *Studied the relationship between the actin cytoskeleton and inositol tetrakisphosphate formation in dendritic spines.*
- **2001.** Senior Research Associate. University of Cambridge, Dept. of Pharmacology.
- **1999-2000.** Burroughs-Wellcome Fund Hitchings-Elion Fellow. University of Cambridge, Dept. of Pharmacology.
- **1997-1998.** Postdoctoral Fellow. University of Cambridge, Dept. of Pharmacology, in the laboratory of Professor Robin F. Irvine, FRS. *Studied the cellular and molecular neuroscience of a putative inositol tetrakisphosphate receptor protein, GAPI^{IP4BP}.*
- **1992-1996.** Graduate student. Johns Hopkins School of Medicine, Dept. of Neuroscience. Ph.D thesis work in the laboratory of Solomon H. Snyder, M.D. **Ph.D Thesis:** *“Localization and functions of endogenous D-amino acids in brain.”*
- **1987-1988; 1990-1991.** Research technician for Ann L. Hubbard, Ph.D. Johns Hopkins School of Medicine, Dept. Cell Biology and Anatomy. *Studied protein trafficking in polarized epithelial cells in vivo.*
- **1989.** Student and research assistant of Professor Horace Freeland Judson, Dept. of Writing Seminars, Johns Hopkins University. **Master’s thesis:** *“A soft and melancholy glow: the limbic system, drug abuse, and synesthesia”.* Also assisted Professor Judson (author of “The eighth day of creation”) in gathering background research for his book writing.
- **1984-1987.** Research technician for Theodore G. Gabig, M.D. Indiana University Medical School, Division of Hematology/Oncology. *Studied the G-protein activation of phagocyte superoxide production in a cell-free system.*

AWARDS:

- Research Starter Grant from the PhRMA Foundation (2007-2009).
- Merck Educational Assistance Graduate Award. Awarded jointly to my graduate student, Samantha-Lloyd Burton (2003-2006).
- Royal Society Robert and Joan Case Fellowship for Brain Research (2001-2006)
- Burroughs-Wellcome Fund Hitchings-Elion Fellowship (1998-2000)
- NIMH NRSA postdoctoral fellowship (1996-1998)
- Neuroscience Training Program NIMH predoctoral fellowship (1991-1994)
- Johns Hopkins University Scholarship in Science and Writing
- Edward A. Mellinger Educational Scholarship

ONGOING RESEARCH SUPPORT:

G175MT Pharmacology Research Starter Grant. Schell (PI) 1/1/07-12/31/08
Source: PhRMA Foundation
“PPAR-targeted regulation of peroxisome and mitochondrial function in brain cells”
ANNUAL DIRECT COSTS: \$30,000
Goal is to understand the mechanisms by which PPAR-targeted drugs influence organelle function and number in neurons and glia.

G175LZ Research grant. Schell (PI) 3/01/07-05/31/08
Source: USUHS Comprehensive Neuroscience Program
“Nervous system damage prevention and class 1 metabotropic glutamate receptors”
ANNUAL DIRECT COSTS: \$87,000
Goal is to understand the molecular mechanisms that underlie the anti-epileptic effects of blocking glutamate receptors coupled to the production of inositol trisphosphate.

RO75NX Competitive standard grant Schell (PI) 2/1/08-8/30/10
Source: USUHS Intramural
“Synaptic structure of dendritic spine actin during pathology and hypothermia”
ANNUAL DIRECT COSTS: \$20,000
Goal is to learn how the pharmaceutical manipulation of actin in dendritic spines affects neuronal survival.

1 S10 RR022601-01A1. Shared equipment grant. Giam (PI) 4/2008
Source: NIH
“Carl Zeiss LSM 510 Confocal Inverted Microscope System”
DIRECT COSTS: \$390,988
Funds for the purchase of a two-photon microscope for NIH supported researchers at USUHS.

COMPLETED RESEARCH SUPPORT:

5 R21 CA113506-02 Exploratory/Development Grant. Schell (PI) 1/26/06-12/31/07
Source: NIH/NCI
“Nutriceutical Inhibition of Neoplastic HIF”
ANNUAL DIRECT COSTS: \$86,000
Goal was to lower expression of hypoxia inducible factor (HIF) using ascorbate and amino acid nutrients for the purpose of reducing tumor growth in a model of head and neck cancer.

RO75LN Startup funds. Schell (PI) 2/1/05-9/30/07
Source: USUHS Intramural
“Calcium regulation of actin dynamics in dendritic spines”

ANNUAL DIRECT COSTS: \$50,000

Goal was to characterize how Ca^{2+} signals in dendritic spines regulate F-actin structure.

GM175LM Hitchings-Elion Fellowship Schell (PI)

2/1/05-1/31/06

Burroughs-Wellcome Fund

Brain calcium homeostasis: Functional roles of GAP1-IP4BP

ANNUAL DIRECT COSTS: \$50,000

Goal was to understand the signaling role of a putative IP_4 receptor in brain

SELECTED INVITED TALKS: *(from a total of 17)*

“Structure, regulation and dynamics of IP_3 3-kinase in dendritic spines.” Research Seminar at the Dept. of Biology, Catholic University of America, Washington, DC March 12, 2007.

"Dynamics of IP_3 3-kinase in dendritic spines." Gordon Research Conference on Calcium Signaling, Mt. Holyoke, MA. July 8, 2003

“Evolution and synaptic targeting of inositol trisphosphate 3-kinases.” British Calcium Meeting, University of Leicester, April 18, 2002.

“Modulating hippocampal calcium: Roles of IP_4 binding proteins.” European forum for neuroscience satellite symposium: Calcium signalling in the nervous system. Berlin, Germany, June 25, 1998

“D-Amino acids and the role of glia in brain function.” Cambridge Biological Computation Group one day symposium: "Recent stimulating theories in molecular neuroscience" Cambridge, UK. November 7, 1997

“D-Serine, a glial-derived modulator of NMDA receptors.” NIH Glia Club, Bethesda, MD. October 11, 1995.

“Endogenous D-serine in brain: Role in modulating NMDA receptors.” Center for Molecular Neurobiology, Hamburg, Germany. September 25, 1995.

TEACHING EXPERIENCE:

- Laboratory demonstrator in Pharmacology, University of Cambridge
- Teaching assistant for Medical School Neuroanatomy, Johns Hopkins School of Medicine
- Writing workshop instructor, Johns Hopkins University Dept. Writing Seminars.
- I have supervised and trained 18 undergraduates in laboratory research.

GRADUATE STUDENTS SUPERVISED:

Samantha Lloyd-Burton, my first graduate student, recently graduated from the University of Cambridge with a PhD in Pharmacology PhD. Her project involved the regulation of Ca^{2+} signals in neurons by the enzyme IP_3 3-kinase, focusing on how the enzyme itself is regulated by the cytoskeleton, calmodulin, and Ca^{2+} . Her manuscript describing a portion of her Ph.D work was recently accepted to the JBC.

Megan Hershfield has completed her qualifying examinations in Neuroscience Graduate program at USUHS. Megan is studying the cell biology of peroxisomes in brain cells.

GRADUATE THESIS COMMITTEES:

Nader Halim, MCB program (Aug 2006-2007). Thesis title: "Regulation of brain glucose metabolic patterns by protein phosphorylation and drug therapy"
Shuijn He, Neuroscience program (Sept 2006-)
Jeremy Henriques, Neuroscience program (July 2006-)
Young Lee, MCB program (June 2007-)

ASPET SUMMER UNDERGRADUATE RESEARCH PROGRAM: I chair and organize the Departmental Summer Undergraduate Research program, sponsored by ASPET.

Students supervised:

Catherine Njathi, College of Notre Dame (June-August 2005)
Meeta Desai, Mary Baldwin College (June-August 2006)
Pragnesh Mistry, Univ. of Maryland (June 2007-June 2008)

OTHER USU COMMITTEES:

BIC imaging committee (Aug 2006-)
Graduate Education Committee (July 2007-)

AD HOC REVIEWER: Biochim Biophys Acta, Brain Res, Eur. J. Neurosci., J. Comp. Neurol., J. Neurosci., Life Sci., Neurosci. Lett., Proc. Nat. Acad. Sci., USA, Glia, Molec. Psychiatry.

GRADUATE LECTURES:

April 14, 2005. "Learning, memory, and disease at the postsynapse: Focus on dendritic spines." To "Neurobiology of Disease" class.
May 16, 2006: "Synaptogenesis" to "Developmental Neuroscience class."
March 5, 2007: "Cytoskeleton I" to Cell Biology class
March 7, 2007: "Cytoskeleton II" to Cell Biology class.

GRADUATE SUPERVISION:

I organize and tutor the student historical presentations for the Introduction to Neuroscience class, Sept-Nov each year. I meet individually twice with each student and help them develop a professional Powerpoint presentation on a topic in the history of neuroscience, which is presented in an afternoon public seminar.

MEDICAL PHARM LECTURES:

Jan 18, 2006: Acetylcholinesterase inhibitors
Feb 14, 2006: Stimulants
Mar 1, 2006: Thromolytics and antiplatelet drugs
Jan 17, 2007: Acetylcholinesterase inhibitors
Feb 7, 2007: Stimulants
Feb 27, 2007: Pharmacology of primary hemostasis
Feb 28, 2007: Pharmacology of secondary hemostasis
Jan 22, 2008: Acetylcholinesterase inhibitors
Feb 15, 2008: Stimulants
Mar 31, 2008: Antiplatelet, anticoagulant and thrombolytic drugs (2 lectures)

SOCIETY MEMBERSHIPS:

Society for Neuroscience (1994-present)
American Society of Cell Biology (2003-present)
ASPET, (2005-present)

VOLUNTEER:

March 2005: Talked to Jr. HS students in Washington about the brain during The Society of Neuroscience "Brain awareness week"

REFEREED PUBLICATIONS (33 peer reviewed publications):

Lloyd-Burton SM, Yu JC, Irvine RF, and Schell MJ (2007). Regulation of Ins(1,4,5)P₃ 3-kinases by calcium and localization in cells. **J. Biol Chem.** 282:9526-9535

Schell MJ and Irvine RF (2006). Calcium-triggered exit of F-actin and IP₃ 3-kinase A from dendritic spines is rapid and reversible. **Eur. J. Neurosci.** 24:2491-2503

Irvine RF, Lloyd-Burton S, Yu J, Letcher AJ, and Schell MJ (2006). The Regulation and Function of Inositol 1,4,5-trisphosphate 3-kinases. **Adv. Enzyme Regulation** 46:314-323.

Chalmers M, Schell MJ, and Thorn P (2006). Agonist-evoked inositol trisphosphate receptor clustering is not dependent on changes to the structure of the endoplasmic reticulum. **Biochem J.** 394:57-66.

Yu JC, Lloyd-Burton SM, Irvine RF, Schell MJ (2005). Regulation of the localisation and activity of inositol 1,4,5-trisphosphate 3-kinase B in intact cells by proteolysis. **Biochem J.** 392:435-441.

Brough D, Schell MJ, and Irvine RF (2005). Agonist-induced regulation of mitochondrial and endoplasmic reticulum motility. **Biochem J.** 392:291-297.

Young KW, Billups D, Nelson CP, Johnston N, Willets JM, Schell MJ, Challis RAJ, and Nahorski SR (2005). Muscarinic acetylcholine receptor activation enhances hippocampal neuron excitability and potentiates synaptically evoked Ca²⁺ signals via phosphatidylinositol 4,5-bisphosphate depletion. **Mol Cell Neurosci** 30:48-57

Gonzalez B, Schell MJ, Letcher AJ, Veprintsev DV, Irvine RF, and Williams RL (2004). Structure of a human inositol 1,4,5-trisphosphate 3-kinase: Substrate binding reveals why it is not a phosphoinositide 3-kinase. **Mol Cell** 15:689-701

Schell MJ (2004). The NMDA receptor glycine site and D-serine metabolism: An evolutionary perspective. **Phil. Trans. R. Soc. Lond. B** 359:943-964.

Kyttälä A, Ihrke G, Vesa J, Schell MJ, and Luzio JP (2004). Two motifs target Batten disease protein CLN3 to lysosomes in transfected non-neuronal and neuronal cells. **Mol Biol Cell** 15:1313-1323.

Nash MS, Schell MJ, Atkinson PJ, Johnston NR, Nahorski SR, and Challis, RAJ (2002). Determinants of metabotropic glutamate receptor-5-mediated Ca²⁺ and inositol 1,4,5-trisphosphate oscillation frequency: Receptor density versus agonist concentration. **J. Biol Chem.** 277:35947-35960.

Kidd JF, Pilkington MF, Schell MJ, Fogarty KE, Skepper JN, Taylor CW, and Thorn, P

- (2002). Paclitaxel affects cytosolic calcium signals by opening the mitochondrial permeability transition pore. **J. Biol Chem.** 277:6504-6510.
- Schell MJ, Erneux C, and Irvine RF (2001). Inositol (1,4,5)-trisphosphate 3-kinase A associates with F-actin and dendritic spines via its N-Terminus. **J. Biol Chem.** 276:37537-37546.
- Irvine RF and Schell MJ (2001). Back in the water: The return of the inositol phosphates. **Nature Rev. Cell Mol. Biol** 2:327-338.
- Schell MJ, Letcher AJ, Brearley CA, Biber J, Murer H, and Irvine RF (1999). PiUS (Pi-uptake stimulator) is an inositol hexakisphosphate kinase. **FEBS Lett.** 461:169-172.
- Irvine RF, McNulty TJ, and Schell MJ (1999). Inositol (1,3,4,5)-tetrakisphosphate as a second messenger--a special role in neurons? **Chem. Phys. Lipids** 98:49-57.
- Koizumi S, Bootman MD, Bobanovic L, Schell MJ, Berridge MJ, and Lipp P (1999). Characterization of elementary Ca²⁺ release signals in NGF-differentiated PC-12 cells and hippocampal neurons. **Neuron** 22:125-137.
- Cooper DMF, Schell MJ, Thorn P, and Irvine RF (1998). Regulation of adenylyl cyclase by membrane potential. **J. Biol. Chem.** 273:27703-27707.
- Eliasson MJL, Blackshaw S, Schell MJ, and Snyder SH (1997). Neuronal nitric oxide synthase alternatively spliced forms: Prominent functional localizations in the brain. **Proc. Natl. Acad. Sci., USA** 94:3396-3401.
- Schell MJ, Cooper OB, and Snyder SH (1997). D-Aspartate localizations imply neuronal and neuroendocrine roles. **Proc. Natl. Acad. Sci., USA** 94:2013-2018.
- Schell MJ, Brady RO Jr., Molliver ME, and Snyder SH (1997). D-Serine as a neuromodulator: Regional and developmental localizations in rat brain glia resemble NMDA receptors. **J. Neurosci.** 17:1604-1615
- Sabatini DM, Pierchala BA, Barrow RK, Schell MJ, and Snyder SH (1995). The rapamycin and FKBP12 target (RAFT1) displays phosphatidylinositol 4-kinase activity. **J. Biol. Chem** 270:20875-20878.
- Schell MJ, Molliver ME, and Snyder SH (1995). D-Serine, an endogenous synaptic modulator: Localization to astrocytes and glutamate-stimulated release. **Proc. Natl. Acad. Sci., USA** 92:3948-3952.
- Dinerman JL, Dawson TM, Schell MJ, Snowmann A, and Snyder SH (1994). Endothelial nitric oxide synthase localized to hippocampal pyramidal cells: Implications for synaptic plasticity. **Proc. Natl. Acad. Sci., USA** 91:4214-4218.
- Maurice M, Schell MJ, Lardeux B, and Hubbard AL (1994). Biosynthesis and intracellular transport of a bile canalicular plasma membrane protein: Studies in vivo and in the perfused rat liver. **Hepatology** 19:648-655.
- Schell MJ, Danoff SK, and Ross CA (1993). Alternate splicing of the inositol 1,4,5-trisphosphate receptor in brain and peripheral tissues. **Molec. Brain Res.** 17:212-216.
- Scott L, Schell MJ, and Hubbard AL (1993). Isolation of plasma membrane sheets and plasma membrane domains from rat liver. *In: Methods in Mol. Biol.*, J.M. Graham and J.A. Higgins, Eds., 19:59-69.

Schell MJ, Maurice M, Stieger B, and Hubbard AL (1992). 5' Nucleotidase is sorted to the apical domain of hepatocytes via an indirect route. **J. Cell Biol.** 119:1173-1182.

Ross CA, Danoff,SK, Schell MJ, Snyder SH, and Ullrich A (1992). Three additional inositol 1,4,5-triphosphate receptors: Molecular cloning and differential localization in brain and peripheral tissues. **Proc. Natl. Acad. Sci. USA** 89:4265-4269.

Margolis RN, Schell MJ, Taylor SI, and Hubbard AL (1990). Hepatocyte plasma membrane ecto-ATPase (pp120/HA4) is a substrate for tyrosine kinase activity of the insulin receptor. **Biochem. Biophys. Res. Comm.** 166:562-566.

Gabig TG, English D, Akard LP, and Schell MJ (1987). Regulation of neutrophil NADPH oxidase activation in a cell-free system by guanine nucleotides and fluoride: Evidence for participation of a pertussis and cholera toxin-insensitive G protein. **J. Biol. Chem.** 262:1685-1690.

Parkinson JF, Akard LP, Schell MJ, and Gabig TG (1987). Cell-free activation of phagocyte NADPH oxidase: Tissue and differentiation-specific expression of cytosolic cofactor activity. **Biochem. Biophys. Res. Comm.** 145:1198-1204,

English D, Schell MJ, Siakotos A, and Gabig TG (1986). Reversible activation of the neutrophil superoxide generating system by hexachlorocyclohexane: Correlation with effects on a subcellular superoxide-generating fraction. **J. Immunol.** 137:283-290.

BOOK CHAPTERS:

Letcher AJ, Schell MJ, and Irvine RF (2008). A femtomole-sensitivity mass assay for inositol hexakisphosphate. *In: Methods in Inositide Research.* C. Barker, ed. Humana Press (*in press*).

Schell MJ (2006). Immunohistochemistry for D-serine in Brain. *In: D-Amino Acids: A New Frontier in Amino Acid and Protein Research -Practical Methods and Protocols.* R. Konno et al., Eds. Nova Science Publishers (Hauppauge, NY).

SELECTED RECENT ABSTRACTS: (from a total of 22)

Wu H and Schell MJ. Mechanism of Inositol Trisphosphate 3-kinase A-induced Alterations in Dendritic Spine F-actin. American Society of Cell Biology Annual Meeting, Washington, DC. Dec 4, 2007

Wu H, Lloyd-Burton SM, and Schell MJ. Microstructure of inositol trisphosphate signaling components in dendritic spines revealed by deconvolution light microscopy. Society for Neuroscience Annual Meeting, San Diego, CA. Nov 4, 2007.

Lloyd-Burton SM, Yu JCH, Irvine RF, and Schell MJ. Roles and regulation of Ins(1,4,5)P₃ 3-kinase A in hippocampal neurons. Society for Neuroscience Annual Meeting, Washington, DC. Nov 14, 2005.

MANUSCRIPTS SUMMITTED:

Halim ND, McFate T, Okagaki P, Korotchkina LG, Patel MS, Jeoung MH, Harris RA, Schell MJ, and Verma A. (2007). Phosphorylation status of pyruvate dehydrogenase distinguishes metabolic phenotypes of rat cerebral cortical astrocytes and neurons

McFate T, Mohyeldin A, Lu H, Thakar J, Henriques J, Wu H, Schell MJ, Zhou S, Califano JA, Jeoung NH, Harris R, and Verma A. (2007) Pyruvate dehydrogenase complex controls metabolic and malignant phenotype in cancer cells.

MANUSCRIPT IN PREPARATION:

Schell MJ, Letcher AJ, and Irvine RF. Molecular evolution of inositol (1,4,5)P₃ 3-kinases.