

**Medical Student Summer Research Program (MSSRP) and Research Thesis Program (RTP): Mentor Information**

**1) Research description (maximum 1 page):**

a) General Description: My research involves the use of two-photon fluorescence microscopy for studying cell physiology in living brain slices. In particular we are investigating the following: (1) the migratory behavior of neural stem cells in transgenic mice (see *J. Comp. Neurol.* 505: 190-208, 2007), and (2) the electrical properties of mitochondria in neurons in mouse brain slices (*Biophysical Society Abstract* No. 1522, 2007). Learning how to influence the migratory behavior of neural stem cells holds promise as a therapeutic strategy for repair of damaged brains. Understanding the normal and pathogenic properties of mitochondria in situ may provide insight into the pathophysiology of certain neurological diseases including Parkinson's Disease.

b) Potential Student Projects: I am looking for 1-2 students who are interested in learning how we use infrared lasers, advanced microscopic techniques, and digital imaging to study stem cell migration and mitochondrial function in brain slices. I will help each student design a project utilizing these techniques that can be accomplished in the allotted time. Previous MSSRP students in my lab have won awards for their projects (see below).

**2) Cover letter explaining the reasons for your interest in becoming a mentor**

I enjoy working directly with medical students, and I have had good experiences with students in this program. The program is a good fit for my research.

**3) Current Biosketch - attached**

**4) Trainees over the past 5 years (undergraduate, medical or graduate students; post-doctoral fellows)**

Eric Yang – MSSRP, 2002 – awarded Julie Namkung Memorial Research Fellowship Prize for his project titled “Physical and Biological Testing of Multiphoton Microscope”

Chris Chu – MSSRP, 2004 – awarded \$500 for one of the outstanding posters at MSSRP Poster Day for his project titled “Classification of Nestin-Expressing, Migrating Cells in Mouse Brain Slices”

**Research area (check all that apply):**

- Basic Science
- Translational Science
- Clinical Science
- Other

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.

Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Philip Edward Hockberger		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME Hockberger			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Western Illinois University, Macomb, IL	B.A.	1972	Chemistry
University of Illinois, Champaign-Urbana, IL	Ph.D.	1982	Neuroscience
AT&T Bell Laboratories, Murray Hill, NJ	Postdoc	1982-1987	Molecular Biophysics

**Positions and Honors.****Positions**

- 1987 – 1993 Assistant Professor, Dept. of Physiology, Northwestern University (NU),  
Feinberg School of Medicine (FSM), Chicago, IL
- 1993 – Associate Professor (tenured), Dept. of Physiology, NU-FSM
- 1995 – 2000 Director, Laser-Based Microscopy and Digital Imaging Facility, NU-FSM
- 2002 – Multiphoton Core Advisor, NU-FSM

**Honors and Awards**

- 1978 – 1980 National Research Service Award, National Institute of Mental Health
- 1982 – 1984 Postdoctoral Fellowship, National Institutes of Health
- 1988 Visiting Research Fellowship, Max Planck Institute, Martinsreid,  
FIRST Award, National Institutes of Health  
New Investigator Award, Whitaker Foundation  
Special Opportunity Award, Whitaker Foundation
- 1995, 1998 Visiting Research Fellowship, University of Erlangen-Nürnberg, Germany
- 1997, 1998 National Advisory Committee, Integrated Microscopy Resource, Univ. of Wisconsin
- 2002, 2005 Visiting Research Fellowship, University of Bonn, Germany

**Selected peer-reviewed publications.****Spectroscopy and Imaging of Small Molecules (Ca<sup>2+</sup>, pH, H<sub>2</sub>O<sub>2</sub>) in Living Cells**

- Hockberger, P. and Connor, J.A. (1983). Intracellular calcium measurements using arsenazo III during cyclic AMP injections into molluscan neurons. Science 219: 869-871
- Connor, J.A. and Hockberger, P.E. (1984). Intracellular pH changes induced by injection of cyclic nucleotides into gastropod neurons. J. Physiology (Lond.) 354: 163-172
- Connor, J.A., Tseng, H.-Y. and Hockberger, P.E. (1987). Depolarization and transmitter induced changes in intracellular Ca<sup>2+</sup> of rat cerebellar granule cells in explant cultures. J. Neuroscience 7: 1384-1400
- Connor, J.A., Wadman, W., Hockberger, P. and Wong, R. (1988). Sustained dendritic gradients of Ca<sup>2+</sup> induced by excitatory amino acids in CA1 hippocampal neurons. Science 240: 649-653
- Hockberger, P.E., Tseng, H.-Y. and Connor, J.A. (1989) Fura-2 measurements of cultured rat Purkinje neurons show dendritic localization of Ca<sup>2+</sup> influx. J. Neuroscience 9: 890-909
- Sabeh, F., Hockberger, P.E. and Sayeed, M.M. (1998) Signaling mechanisms of elevated neutrophil O<sub>2</sub><sup>-</sup> generation after burn injury. Am. J. Physiology 274: R476-R485
- Choudhry, M., Hockberger, P.E. and Sayeed, M. (1999) PGE<sub>2</sub> suppresses mitogen-induced Ca<sup>2+</sup>

- mobilization in T cells. Am. J. Physiology 277: R1741-R1748
- Hockberger, P.E., Skimina, T.A., Centonze, V.E., Lavin, C., Chu, S., Dadras, S., Reddy, J.K. and White, J.G. (1999) Activation of flavin-containing oxidases underlies light-induced H<sub>2</sub>O<sub>2</sub> production in mammalian cells. Proc. Natl. Acad. Sci. (USA), 96: 6255-6250.
- Ahmed, M.S., Hung, W.-Y., Zu, J.S., Hockberger, P.E. and Siddique, T. (2000) Increased reactive oxygen species in familial amyotrophic lateral sclerosis with mutations in SOD1. J. Neurol. Sci. 176:88-94
- Tian, X., Kai, L., Hockberger, P.E., Wokosin, D. and Surmeier, D.J. (submitted) Membrane depolarization induced L-type calcium channels dependent spine loss in striatopallidal medium spiny neurons.

### Membrane Biophysics

- Connor, J.A. and Hockberger, P.E. (1984). A novel membrane sodium current induced by injection of cyclic nucleotides into gastropod neurons. J. Physiology (Lond.) 354:139-162
- Hockberger, P. and Connor, J.A. (1984). Alteration of calcium conductances and outward current by cAMP in neurons of *Limax maximus*. Cell. Mol. Neurobiology 4: 319-338
- Hockberger, P. and Swandulla, D. (1987). Direct ion channel gating: a new function for intracellular messengers. Cell. Mol. Neurobiology 7: 229-236
- Hockberger, P.E., Tseng, H.-Y., and Connor, J.A. (1987). Immunocytochemical and electrophysiological differentiation of rat cerebellar granule cells in explant cultures. J. Neuroscience 7: 1370-1383
- Hockberger, P.E., Tseng, H.-Y. and Connor, J.A. (1989) Development of rat cerebellar Purkinje cells: electrophysiological properties following acute isolation and long-term culture. J. Neuroscience 9: 867-889
- Hockberger, P., Toselli, M., Swandulla, D. and Lux, H.D. (1989) A diacylglycerol analogue reduces neuronal Ca<sup>2+</sup> currents independently of protein kinase C activation. Nature 338: 340-342
- Hyndman, A.G., Hockberger, P.E., Zeevalk, G.D. and Connor, J.A. (1991) Transferrin can alter physiological properties of retinal neurons. Brain Res. 561: 318-323
- Nam, S.C. and Hockberger, P.E. (1992) Divalent ions from stainless steel hypodermic needles reduce neuronal calcium currents. European J. Physiology 420: 106-108
- Hockberger, P.E. and Nam, S.C. (1994) High-voltage-activated calcium current in developing neurons is insensitive to nifedipine. European J. Physiology 426: 402-411
- Yuen, G.L., Hockberger, P.E. and Houk, J.C. (1995) Bistability in cerebellar Purkinje cell dendrites modelled with high-threshold calcium and delayed rectifier potassium channels. Biol. Cybern. 73:375-388
- Nam, S.G. and Hockberger, P.E. (1997) Analysis of spontaneous electrical activity in acutely isolated Purkinje neurons from postnatal rats. J. Neurobiology 33: 18-32
- Bhattacharyya, B., Lee, E., Krupin, D., Hockberger, P.E. and Krupin, T. (2002) Isoproterenol modulation of maxi-K<sup>+</sup> channel in nonpigmented ciliary epithelial cells through a G-protein gated pathway. Current Eye Research 24: 173-181

### Cell Migration

- Kleinfeld, D., Kahler, K. and Hockberger, P.E. (1988). Controlled outgrowth of dissociated neurons on patterned substrates. J. Neuroscience 8: 4098-4120
- Soekarno, A., Lom, B. and Hockberger, P.E. (1993) Pathfinding by neuroblastoma cells in culture is directed by preferential adhesion to positively-charged surfaces. NeuroImage 1: 129 - 144
- Lom, B., Healy, K.E. and Hockberger, P.E. (1993) A versatile technique for patterning biomaterials onto glass substrates. J. Neurosci. Methods 50: 385-397
- Healy, K.E., Lom, B. and Hockberger, P.E. (1994) Spatial distribution of mammalian cells dictated by material surface chemistry. Biotech. Bioeng. 43: 792-800
- Healy, K.E., Thomas, C.H., Reznia, A., Kim, J.E., McKeown, P.J., Lom, B. and Hockberger, P.E. (1996) Kinetics of bone cell organization and mineralization on materials with patterned surface chemistry. Biomaterials 17:195-208
- Lom, B. and Hockberger, P.E. (1997) Is laminin-1 a guidance cue for cerebellar granule cell migration? J. Neurobiology 33: 72-84
- Nam, S.C., et al. (2007) Dynamic features of postnatal subventricular zone motility: a 2-photon time-lapse study. J. Comp. Neurology 505: 190-208.

## Photobiology

- Hockberger, P.E., Skimina, T.A., Centonze, V.E., Lavin, C., Chu, S., Dadras, S., Reddy, J.K. and White, J.G. (1999) Activation of flavin-containing oxidases underlies light-induced H<sub>2</sub>O<sub>2</sub> production in mammalian cells. Proc. Natl. Acad. Sci. (USA), 96: 6255-6250.
- Hockberger, P.E. (2000) The discovery of the damaging effect of sunlight on bacteria. J. Photochem. Photobiol.B. Biol. 58: 185-191
- Hockberger, P.E. (2002) A history of ultraviolet photobiology for humans, animals and microorganisms. Photochem. Photobiol. 76: 561-579

## Research Support.

### Ongoing

- |           |                       |                   |
|-----------|-----------------------|-------------------|
| 1. R01    | Szele, F. (PI)        | 1/15/05 – 1/14/10 |
| NIH/NINDS | Hockberger, P. (Co-I) |                   |

### Subventricular Zone Cell Migration After Injury

The specific aims are to study the migratory behavior of stem cell in mouse brain in vivo and in vitro following brain injury. Dr. Hockberger is responsible for directing the multiphoton videomicroscopic studies of stem cells in brain slices from transgenic mice expressing eGFP-tagged proteins (e.g., nestin, GAD, Dcx, GFAP).

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|-----------|-----------------------|---------------------|
| 2. P30    | Surmeier, J. (PI)     | 05/01/06 – 04/30/12 |
| NIH/NINDS | Hockberger, P. (Co-I) |                     |

### Interdepartmental Two-Photon Imaging Center

The specific aims of this proposal are to characterize, optimize and extend the capabilities of our existing 2P imaging workstations with electrophysiology and molecular uncaging; to create additional 2P imaging workstations for other investigators at NU needing these capabilities; to provide technical support and infrastructure that will ensure the safe, efficient and productive operation of the cores; and to create an internet-based distribution point for hardware and software development.

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|------------------------|-----------------------|---------------------|
| 3. NETRP               | Surmeier, J. (PI)     | 12/01/06 – 11/30/08 |
| Department of the Army | Hockberger, P. (Co-I) |                     |

### Calcium Homeostasis and Mitochondrial Dysfunction in DA Neurons of the Substantia Nigra Compacta

The specific aims are to compare the impact of Ca loading during autonomous pacemaking on mitochondrial function in SNc DA neurons in normal and mutant mice harboring PD-related genetic changes. In addition, we will determine the impact of synaptically evoked elevations in cytosolic Ca on mitochondrial function in SNc neurons, and whether reliance upon Cav1.3 Ca channels renders SNc neurons more prone to degenerative changes following exposure to mitochondria toxins.