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NAME OF SPONSOR (CO-SPONSOR) Michael Kerry O'Banion, M.D., Ph.D.		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME MKOBANION			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University of Illinois, Urbana	B.S.	1980	Biology
University of Illinois, Urbana	Ph.D.	1987	Microbiology
University of Illinois, Urbana	M.D.	1987	

**A. Positions and Honors.**

- 1987-1990 **Postdoctoral Fellow**, Depts. of Medicine and Biochemistry, University of Rochester School of Medicine
- 1990-1991 **Instructor and Fellow**, Depts. of Medicine and Biochemistry, University of Rochester School of Medicine
- 1991-1997 **Assistant Professor**, Dept. of Neurology and Dept. of Neurobiology and Anatomy, University of Rochester School of Medicine
- 1997- **Associate Professor**, Dept. of Neurology and Dept. of Neurobiology and Anatomy, University of Rochester School of Medicine (tenured March, 2002)
- 2001- **Director**, University of Rochester M.D./Ph.D. Training Program
- 2001-2005 **Member**, NIH Study Section BDCN-4 (CNBT-1 as of Fall, 2003)

**Honors and Awards**

- Graduated summa cum laude, 1980
- Alpha Omega Alpha (Honorary Medical Society), 1984
- NIH Endocrine Training Grant Fellow, 1987-1989
- Wilmot Cancer Research Fellow, 1988-1991
- New York State Health Research Council's Diabetes Fellow, 1990-1991
- George W. Corner Dean's Teaching Scholar, 1996-1999

**B. Selected peer-reviewed publications (in chronological order, from over 60).**

- O'Banion, M.K., H.B. Sadowski, V. Winn, and D. A. Young. 1991. A serum- and glucocorticoid-regulated 4 kb mRNA encodes a cyclooxygenase-related protein. *J. Biol. Chem.* 266:23261-23267.
- O'Banion, M.K., V.D. Winn, and D.A. Young. 1992. cDNA cloning and functional activity of a glucocorticoid-regulated inflammatory cyclooxygenase (griPGHS). *Proc. Natl. Acad. Sci. USA* 89:4888-4892.
- O'Banion, M.K., D.A. Young, and M.C. Bohn. 1994. Corticosterone responsive mRNAs in primary astrocytes. *Mol. Brain Res.* 22:57-68.
- O'Banion, M.K., J. Dusel, J.C. Chang, M.D. Kaplan, and P.D. Coleman. 1996. Interleukin-1 $\beta$  induces prostaglandin G/H synthase-2 (cyclooxygenase-2) in primary murine astrocyte cultures. *J. Neurochem.* 66:2532-2540.
- Chang, J.W., P.D. Coleman, and M.K. O'Banion. 1996. Prostaglandin G/H synthase-2 (cyclooxygenase-2) mRNA expression is decreased in Alzheimer's disease. *Neurobiol. Aging.* 17:801-808.
- Kaplan, M.D., J.A. Olschowka, and M.K. O'Banion. 1997. Cyclooxygenase-1 behaves as a delayed-response gene in PC12 cells differentiated with NGF. *J. Biol. Chem.* 272:18534-18537.
- Huang, T.L. and M.K. O'Banion. 1998. Interleukin-1 $\beta$  and tumor necrosis factor- $\alpha$  suppress dexamethasone induction of glutamine synthetase in primary mouse astrocytes. *J. Neurochem.* 71:1436-1442.
- O'Banion, M.K. 1999. Cyclooxygenase-2: Molecular biology, pharmacology and neurobiology. *Crit. Rev. Neurobiol.* 13:45-82.

- Kyrkanides, S., J.A. Olschowka, J.P. Williams, J.T. Hansen, and M.K. O'Banion. 1999. TNF $\alpha$  and IL-1 $\beta$  mediate ICAM-1 induction via microglia astrocyte interaction in CNS radiation injury. *J. Neuroimmunol.* 95:95-106.
- Yermakova, A., J. Rollins, L.M. Callahan, J. Rogers, and M.K. O'Banion. 1999. Cyclooxygenase-1 in human Alzheimer's and control brain: Quantitative analysis of expression by microglia and CA3 hippocampal neurons. *J. Neuropathol. Exp. Neurol.* 58:1135-1146.
- Yermakova, A.V., and M.K. O'Banion. 2001. Downregulation of neuronal cyclooxygenase-2 expression in end stage Alzheimer's disease. *Neurobiol. Aging.* 22:823-836.
- Kyrkanides, S., M.K. O'Banion, P.E. Whiteley, J.C. Daeschner, J.A. Olschowka. 2001. Enhanced glial activation and expression of specific CNS inflammation-related molecules in aged versus young rats following cortical stab injury. *J. Neuroimmunol.* 119: 269-277.
- Heneka, M.T., V. Gavrilyuk, L. Dumitrescu, M.K. O'Banion, J.C. Daeschner, E. Galea, T. Klockgether, and D.L. Feinstein. 2002. Noradrenergic depletion potentiates  $\beta$ -amyloid induced neuroinflammation in the frontal cortex: implications for Alzheimers disease. *J. Neurosci.* 22:2434-2442.
- Kyrkanides, S., A.H. Moore, J.A. Olschowka, J.C. Daeschner, J.P. Williams, J.T. Hansen and M. K. O'Banion. 2002. Cyclooxygenase-2 modulates brain inflammation-related gene expression in CNS radiation injury. *Mol. Brain Res.* 104:159-169.
- Hurley, S.D., M.K. O'Banion, D.D. Song, F.S. Arana, J.A. Olschowka and S.N. Haber. 2003. Microglial response is poorly correlated with neurodegeneration following low dose MPTP-administration in monkeys. *Exp. Neurol.* 184:659-668.
- Moore, A.H., J.A. Olschowka, J.P. Williams, S.L. Paige and M.K. O'Banion. 2004. Radiation-induced edema is dependent on cyclooxygenase-2 activity in mouse brain. *Radiat. Res.* 161:153-160.
- Moore, A.H., J.A. Olschowka and M.K. O'Banion. 2004. Cyclooxygenase-2 activity mediates expression of membrane- and cytosolic-associated prostaglandin E<sub>2</sub> synthases following intracerebral administration of IL-1 $\beta$ . *J. Neuroimmunol.* 148:32-40.
- Moore, A.H., J.A. Olschowka, J.P. Williams, P. Okunieff, and M.K. O'Banion. 2005. Regulation of prostaglandin E<sub>2</sub> synthesis after brain irradiation. *Int. J. Rad. Oncol. Biol. Phys.* 62:267-272.
- Lai, Y.-C., S.S. Shaftel, J.H. Miller, R.H. Tallents, Y. Chang, C.A. Pinkert, J.A. Olschowka, I.M. Dickerson, J.E. Puzas, M.K. O'Banion, S. Kyrkanides. 2006. Intra-articular induction of IL-1 $\beta$  expression in the adult mouse results in TMJ pathology, dysfunction and pain. *Arthritis Rheumat.* 54:1184-1197.
- Joseph, S.A., E. Lynd-Balta, M.K. O'Banion, R.M. Rappold, J. Daeschner, A. Allen, and J. Padowski. 2006. Enhanced cyclooxygenase-2 expression in olfactory-limbic forebrain following kainate-induced seizures. *Neuroscience* 140:1051-1065.
- Maida, M.E., S.D. Hurley, J. Daeschner, A.H. Moore, and M.K. O'Banion. 2006. Cytosolic PGE<sub>2</sub> synthase expression is decreased in discrete cortical regions in psychiatric disease. *Brain Res.* 1103:164-172.
- Kyrkanides, S., P.M. Fiorentino, Y. Gan, Y-C. Lai, S.S. Shaftel, J.E. Puzas, M.G. Piacino, M.K. O'Banion, and R.H. Tallents. 2007.  $\mu$ -opioid receptor induction in the temporomandibular joint ameliorates arthritic pain and joint pathology in the Col1-IL-1 $\beta$ <sup>XAT</sup> mouse model of arthritis. *Arthritis Rheumat.* 56:2038-2048.
- Shaftel, S.S., S. Kyrkanides, J.A. Olschowka, J.H. Miller, R.E. Johnson, and M.K. O'Banion. 2007. Sustained hippocampal IL-1 $\beta$  overexpression mediates chronic neuroinflammation and ameliorates Alzheimer's plaque pathology. *J. Clin. Invest.* 117:1595-1604.
- Brouxhon, S, S. Kyrkanides, M.K. O'Banion, R. Johnson, D.A. Pearce, G.M. Centrola, J.N. Miller, K.H. McGrath, B. Erdle, G. Scott, S. Schneider, J. vanBuskirk, and A.P. Pentland. 2007. Sequential downregulation of E-cadherin with squamous cell carcinoma progression: loss of E-cadherin via a prostaglandin E<sub>2</sub>-EP2 dependent mechanism. *Cancer Res.* 67:7654-7664.
- Shaftel, S. S., T. J. Carlson, J. A. Olschowka, S. B. Matousek, S. Kyrkanides, and M. K. O'Banion. 2007. Chronic IL-1 $\beta$  expression in mouse brain leads to leukocyte infiltration and neutrophil independent blood-brain barrier permeability without overt neurodegeneration. *J. Neuroscience* 27:9301-9309.
- Fiorentino, P. M., R. H. Tallents, J. H. Miller, S. M. Brouxhon, M. K. O'Banion, J. E. Puzas, and S. Kyrkanides. 2008. Spinal IL-1 $\beta$  in arthritis and joint pain. *Arthritis Rheumat.* In Press.
- Zhong, Z., R. Deane, Z. Ali, M. Parisi, Y. Shapovalov, M. K. O'Banion, K. Stojanovic, A. Sagare, S. Boillee, D. W. Cleveland, and B. V. Zlokovic. 2008. ALS-causing SOD-1 mutants generate vascular changes prior to motor neuron degeneration. *Nat. Neurosci.* March 16 [Epub ahead of print].

## C. Research Support

### Current

“Neuroinflammation in CNS Radiation Injury: IL-1 and COX-2”

Principal Investigator: M. Kerry O'Banion, M.D., Ph.D.

Agency: NCI

Type: RO1 (CA114587) Period: February 01, 2005 to January 30, 2010

The goals of this project are to test the hypothesis that neuroinflammation following brain radiation is dependent, at least in part, on an IL-1/COX-2 dependent pathway.

“Interleukin-1: A Mediator of Neuroinflammation and Alzheimer's Neuropathogenesis”

Principal Investigator: M. Kerry O'Banion, M.D., Ph.D.

Agency: NIA

Type: RO1 (AG030149) Period: April 01, 2007 – March 30, 2011

The aims of this study are to examine the effects of IL-1 expression and repression in mouse models of Alzheimer's disease using a newly developed transgenic mouse that models chronic, localized neuroinflammation.

“HZE Radiation Effects on Neuroinflammation: Role of COX-2”

Principal Investigator: M. Kerry O'Banion, M.D., Ph.D.

Agency: NASA Space Radiation Biology Program

Type: Individual Investigator Period: May 15, 2004 to June 01, 2008

The aims of this study are to examine indices of neuroinflammation in mouse brain following high-energy <sup>56</sup>Fe ion irradiation at the NASA Space Radiation Laboratory at Brookhaven National Laboratories.

“Low Dose Ionizing Radiation and HZE Particle Effects on Adult Hippocampal Neurogenesis: A Sensitive Indicator of CNS Microenvironmental Changes” Principal Investigator: M. Kerry O'Banion, M.D., Ph.D.

Agency DOE/NASA

Type: Individual Investigator (DE-FG02-07ER64338) Period: July 01, 2007 – June 30, 2010

The goal of this proposal is to determine a lower dose for gamma and HZE radiation effects on inhibiting hippocampal neurogenesis in adult mice. A second goal is to perform microarray analysis of gene expression patterns at such doses.

“Does peripheral localized chronic inflammation predispose to neurodegeneration?”

Principal Investigator: Stephanos Kyrkanides, DDS, Ph.D.

Agency: NIA

Type: R21 (AG028325) Period: July 01, 2006 to June 30, 2008

The goal of this project is to determine whether arthritis contributes to the development of Alzheimer's disease.  
Role in Project: Investigator

“Joint degeneration: Somatic mosaic analysis in a transgenic mouse”

Principal Investigator: Stephanos Kyrkanides, DDS, Ph.D.

Agency: DRC

Type: R21 (DE017765) Period: July 15, 2006 to July 14, 2008

The goal of this project is to determine the effects of temporomandibular joint disease on brain inflammation.  
Role in Project: Investigator

Medical Scientist Training Program (Training Grant)

Principal Investigator: M. Kerry O'Banion, M.D., Ph.D.

Agency: NIGMS

Type: T32 (GM07356) Period: July 01, 2004 to June 30, 2009

The aim of this grant is to provide rigorous training for preparation of future physician scientists holding the M.D. and Ph.D. degrees.

**"Training in Neuroinflammation and Glial Cell Biology" (Training Grant)**

Principal Investigator: M. Kerry O'Banion, M.D., Ph.D.

Agency: NINDS

Type: T32 (NS051152) Period: July 01, 2005 to June 30, 2010

The goal of this proposal is to provide rigorous training for 2 pre and 2 postdoctoral fellows with faculty examining the roles of neuroinflammation and glial cells in neurological disease.

**Pending:**

**"CNS and Systemic Effects of Radiation Combined with Traumatic Brain Injury"**

Principal Investigators: M. Kerry O'Banion, M.D., Ph.D. and John Olschowka, Ph.D. (Multiple PI)

Agency: NIAID

Type: R21/33 AI080550 Period: TBD

The goal of this project is to establish a model of traumatic brain injury combined with radiation to explore possible synergies in local CNS, pulmonary and systemic cytokine cascades and tissue damage.

**"Neuroinflammation and Glial ROS in Methamphetamine Neurotoxicity" PHS RO1. Role: Principal Principal**

Investigators: M. Kerry O'Banion, M.D., Ph.D. and Lisa Opanashuk, Ph.D. (Multiple PI)

Agency: NIDA

Type: R01 DA026009 Period: TBD

The goal of this project is to explore the contribution of neuroinflammation to nigrostriatal neurotoxicity in a mouse model of binge methamphetamine exposure.

**Past (3 years):**

**"IL-1 in Neurodegeneration: Development of a New Model"**

Principal Investigator: M. Kerry O'Banion, M.D., Ph.D.

Agency: NINDS

Type R21 (NS048522) Period: April 01, 2004 to March 31, 2006 (no-cost extension to March 31, 2007).

The aims of this study were to: 1) construct and test vectors for regulated expression of IL-1 $\beta$  and IL-1ra in mouse astrocytes; 2) generate and test transgenic mice harboring these vectors; 3) carry out a pilot study of IL-1 and IL-1ra effects in double transgenic mice with AD pathology.

**"IL-1 Induced Mediators of CNS Inflammation and AD: PGE<sub>2</sub>"**

Principal Investigator: M. Kerry O'Banion, M.D., Ph.D.

Agency NINDS

Type: RO1 (NS33553, Continuation-year 12) Period: September 30, 2003 to July 31, 2007

The aims of this project are to: 1) characterize the role of PGE synthases in elaboration of PGE<sub>2</sub> following an inflammatory stimulus; 2) determine the functions of EP receptors in acute models of neuroinflammation; 3) explore the role of PGE<sub>2</sub> in a chronic model of neuroinflammation and in APP transgenic mice.

**"Collaborative Multiple Sclerosis Research Center Award"**

Principal Investigator: Benjamin M. Segal, M.D.

Agency: National Multiple Sclerosis Society

Type: Center Award Period: April 01, 2006 to July 31, 2007

The primary objective of this grant is to support and facilitate collaborations and educational activities on MS related topics across scientific disciplines.

Role in Project: Leader, Project 1 "Modulation of the IL-23/IL-1 Axis in Autoimmune Demyelination"