BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **MILLER, Richard Joel**

eRA COMMONS USER NAME (credential, e.g., agency login): **rjm821**

POSITION TITLE: **Alfred Newton Richards Professor of Pharmacology**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
The University of Bristol (UK)	BSc (Ist Class)	06/1972	Biochemistry
The University of Cambridge (UK)	PhD	05/1975	Neuropharmacology

A. PERSONAL STATEMENT

Dr. Richard Miller has had over 40 years of experience in research in the field of neuropharmacology, particularly the study of analgesic drugs and their mechanism of action including work on endorphins and opioid receptors, voltage dependent calcium channels and inflammatory cytokines. He has been continuously funded by the NIH for over 40 years during which time he has received two MERIT awards and a Guggenheim fellowship. Dr. Miller has previously trained 44 graduate students and 50 postdoctoral fellows as well as numerous undergraduate and medical students seeking research experience. He has also acted as a mentor for students receiving NRSA and K08 awards. Dr. Miller is currently enjoying working on the molecular and cellular basis of pain in association with osteoarthritis and other musculoskeletal diseases.

B. POSITIONS

Professor in Department of Psychiatry (secondary,2018-present)
Professor in Department of Medical Humanities and Bioethics (secondary, 2014-present)
Alfred Newton Richards Professor of Pharmacology (2005-Present)
Professor in Department of Molecular Pharmacology and Biological Chemistry (now Department of Pharmacology), Northwestern University (2001-Present)
William Mabie Professor of Neuroscience (1995-2001)
Professor in Department of Pharmacological and Physiological Sciences and Committee on Neurobiology - University of Chicago (1981-1995)
Associate Professor - University of Chicago (1980-1981)
Assistant Professor - University of Chicago (1976-1980)
Post-Doctoral Research at Burroughs Wellcome Labs, North Carolina, with Dr. P. Cuatrecasas (1975-1976)
Tutor in Biochemistry and Pharmacology, St. John's and Trinity Colleges, University of Cambridge (1972-1975)

C. CONTRIBUTIONS TO SCIENCE

Dr. Miller has published 512 scientific articles (Google h-index 131) and four books on the subjects of neuropharmacology, genetics and animal welfare. He also publishes a blog : see richardjmiller.org) *A list of Dr. Miller's publications can be viewed through PubMed at MyNCBI using this URL- https://www.scholars.northwestern.edu/en/persons/richard-j-miller/publications/.*
Contributions to science relevant to this application are explained below.

- **The effects of antipsychotic drugs on dopamine receptors**

Dr. Miller was one of the first people to demonstrate that antipsychotic drugs acted directly as antagonists of dopamine receptors using a biochemical system. He elucidated the structure activity relationships for agonists acting at what eventually became known as the D1 dopamine receptor and also showed how the metabolites of antipsychotic drugs could participate in the actions of these drugs. Importantly, Dr. Miller provided the original evidence that atypical antipsychotic drugs such as clozapine could act on receptors in addition to dopamine receptors by demonstrating that they had strong antimuscarinic activity and that this property might help to explain their lack of extrapyramidal side effects.

Miller, R.J. and Hiley, C.R. (1974). Antimuscarinic properties of neuroleptics and drug-induced parkinsonism. *Nature.* 248: 596-597.

Miller, R.J., Horn, A.S., Iversen, L.L. and Pinder, R. (1974). Effects of dopamine-like drugs on rat striatal adenyl cyclase have implications for CNS dopamine receptor topography. *Nature.* 250: 238-241.

Miller, R.J. and Kelly, P.H. (1975). Dopamine-like effects of cholera toxin in the central nervous system. *Nature.* 255: 163-166.

Iversen, L.L., Rogawski, M.J. and **Miller, R.J.** (1976). Comparison of the effects of neuroleptic drugs on pre- and postsynaptic dopaminergic mechanisms in the rat striatum. *Molec. Pharmacol.* 12: 251-262.

- **Identification of endorphins and other neuropeptides and their distribution and actions in the brain and gut.**

Dr Miller published one of the first descriptions of the distribution of the enkephalins using antibodies that he raised. He also used radiolabelled endorphins to map the interaction of drugs with opioid receptors and the structural basis for the actions of the enkephalins in particular. Dr Miller established the effects of endorphins and other neuropeptides on the epithelium of the gut.

Rossier, J., Battenberg, E., Bayon, A., **Miller, R.J.**, Guillemin, R. and Bloom, F. (1979). Hypothalamic enkephalin neurones may regulate the neurohypophysis. *Nature.* 277: 653-655.

Manning, D., Snyder, S.H., Kachur, J.F., **Miller, R.J.** and Field, M. (1982). Bradykinin receptor-mediated chloride secretion in intestinal function. *Nature.* 299; 256-259

Forsberg, E.J. and **Miller, R.J.** (1982). Cholinergic regulation of enterochromaffin cells in the rabbit duodenum. *Science.* 217: 355-356

Musch, M.W., **Miller, R.J.**, Field, M. and Siegel, M.I. (1982). Stimulation of colonic secretion by lipoxygenase metabolites of arachidonic acid. *Science.* 217: 1255-1256.

- **Identification of the different types of voltage dependent calcium channels.**

Dr Miller's laboratory was one of the first to define the properties of the different types of voltage dependent calcium channels and to define their roles in the regulation of neurotransmitter release. He was the first to identify and clone the $Ca_V2.3$ channel. Dr. Miller established the regulation of calcium channels by receptors as a mechanism of presynaptic inhibition. Dr. Miller was the first to demonstrate the calcium permeability of AMPA receptors. Dr Miller's laboratory was the first to define the combined roles of calcium buffers including binding proteins, ryanodine receptors and mitochondria in defining the regulation of neuronal calcium signaling using combined voltage clamp and calcium imaging techniques. Dr Miller's laboratory helped to establish how glutamate regulated intraneuronal calcium signaling in the context of excitotoxicity.

Miller, R.J. (1987). Multiple calcium channels and neuronal function. *Science.* 235: 46-52.

Hirning, L.D., Thayer, S.A., **Miller, R.J.,** Fox, A.P., McCleskey, E.W. and Tsien, R.W. (1988). Dominant role of N-type calcium channels in evoked release of norepinephrine from rat sympathetic neurones. *Science.* 239: 57-61.

Scholz, K.P. and **Miller, R.J.** (1992). Inhibition of quantal transmitter release in the absence of calcium influx by a G-protein-linked adenosine receptor at hippocampal synapses. *Neuron.* 8: 1139-1150.

Toth, P.T., Bindokas, V., Bleakman, D., Colmers, W.F. and **Miller, R.J.** (1993). Mechanism of presynaptic inhibition by neuropeptide Y at sympathetic nerve terminals. *Nature.* 364: 635-639

- **Inflammatory cytokine signaling in the nervous system**

Dr Miller's laboratory discovered the expression of chemokine receptors in the nervous system. He then helped to define the role of chemokine signaling in the regulation of neural stem cells both during development and in the adult nervous system. Dr Miller has helped to establish the role of inflammatory cytokine signaling in the control of neurogenesis in the context of diseases such as HIV-1 dementia, multiple sclerosis and stroke.

Meucci, O., Fatatis, A., Simen, A., Bushell, T.J., Gray, P.W. and **Miller, R.J.** (1998). Chemokines regulate hippocampal neuronal signalling and gp120 neurotoxicity. *Proc. Natl. Acad. Sci. USA.* 95: 14500-14505.

Lu, M.L., Grove, E.A. and **Miller, R.J.** (2002). Abnormal development of the hippocamapal dentate gyrus in mice lacking the CXCR4 chemokine receptors. *Proc. Natl. Acad Sci. USA.* 99: 7090-7095.

Bhattacharyya, B., Banisadr, G., Jung, H.S., Ren, D.J., Cranshaw, D.G., Zou, Y.R. and **Miller, R.J.** (2008). The chemokine SDF-1 is a neurotransmitter that regulates neurotransmission in the adult dentate gyrus stem cell niche. *J. Neurosci.* 28: 6720-6730

Haldipur,P., Gillies, G.S., Janson, O.K., Chizhikov, V.V., Mithal, D.S., **Miller, R.J.,** and Millen, K.J. (2015) Mesenchymal Foxc1 acts through SDF1α-Cxcr4 signaling in radial glial cells to drive embryonic cerebellar growth *Elife.* 2014 Dec 16;4. doi: 10.7554/eLife.03962

- **Inflammatory cytokines in the development of pain**

Dr. Miller's laboratory has also investigated the role of chemokine signaling in the peripheral nervous system,particularly with respect to the development of the sensory neuron hyperexcitability that underlies neuropathic pain. Dr. Miller and his colleagues have demonstrated that chemokines can be produced by sensory nociceptors .Dr. Miller has helped to support the hypothesis that the activation of the innate immune system can produce inflammatory cytokines that help to promote neuronal hyperexcitability and have demonstrated the participation of such events in models of osteoarthritis and diabetic neuropathy.

White, F.A., Jung, H.S. and **Miller, R.J.** (2007). Chemokines as integrators of pain and inflammation. *Proc. Natl. Acad. Sci. USA.* 104: 20151-20158

Jung, H.S., Bhangoo, S., Banisadr, G., Freitag, C., White, F.A. and **Miller, R.J.** (2009). Visualization of chemokine receptor activation *in vivo* reveals peripheral activation of CCR2 receptors in states of neuropathic pain. *J. Neurosci.* 29: 8051-8062.

Miller RE, Tran PB, Das R, Ghoreishi-Haack N, **Miller RJ** and Malfait AM (2012) CCR2 chemokine receptor signaling mediates persistent pain in a mouse model of osteoarthritis *Proc.Natl.Acad.Sci.USA.* 109: 20602-20607

Lim, K., Hyun, Y.M., Lambert-Emo, K., Capece, T., Bae, S., **Miller, R.J.**, Topham, D.J. and Kim, M. (2015). Neutrophil trails guide influenza-specific $CD8^+$ T cells in the airways. *Science.* 4;349(6252):aaa4352. doi: 10.1126/science.aaa4352. PMID: 26339033.