Lynn A. Raymond - Presidential Lecturer

Professor, Department of Psychiatry,
University of British Columbia

Title of Presentation: **Mechanisms and neuroprotective strategies in neurodegeneration: Huntington disease can lead the way**

Dr. Lynn Raymond's research aims to understand how specific neurons are targeted for degeneration in Huntington's disease. Her laboratory is specifically interested in the role specific glutamate receptors, called the NMDA receptors, play in this process. NMDA receptors also play a key role in neuroplasticity during development and in activity-dependent modifications in the adult brain that may contribute to learning and memory. A major focus of Dr. Raymond's laboratory is to elucidate the mechanisms regulating NMDA receptor function.

Honors (selected)

2010	Huntington Society of Canada/INMHA Prize for Research Excellence
2005	Killam Research Prize, Senior Scientist, Univ. of B.C.
2003	Lieberman Award, Hereditary Disease Foundation
2003-08	Investigator Award, Canadian Institutes of Health Research
2003-08	Senior Scholar Award, Michael Smith Foundation for Health Research
2001	Elected Member, American Neurological Association
1995,1998	James A. and Donna-Mae Moore Award for Research in Neurodegenerative Disorders
1994-99	Scholar Award, Medical Research Council of Canada
1991-94	Clinician Scientist Development Award, NIH
1980-86	Medical Scientist Training Program, NIH

Selected peer-review publications (chronological order)

1. Zeron, M.M., Hansson, O., Chen, N., Wellington, C.L., Leavitt, B.R., Brundin, P., Hayden, M.R., **Raymond, L.A.** (2002) Increased sensitivity to N-methyl-D-aspartate receptor-mediated excitotoxicity in a mouse model of Huntington's disease. *Neuron*, 33:849-860.
2. Li, B., Chen, N., Luo, T., Otsu, Y., Murphy, T.H., **Raymond, L.A.** (2002) Differential regulation of synaptic and extrasynaptic NMDA receptors by calcium and tyrosine phosphorylation. *Nature Neuroscience*, 5:833-834.
3. Li, B., Otsu, Y., Murphy, T.H., **Raymond, L.A**. (2003) Developmental decrease in NMDA receptor desensitization associated with shift to synapse and interaction with PSD-95. *Journal of Neuroscience*, 23:11244-11254.
4. Graham, R.K., Deng, Y., Slow, E.J., Bissada, N., Lu, G., Pearson, P., Bertram, L., Shehadeh, J., Murphy, Z., Warby, S., Roy, S., Wellington, C.L., Leavitt, B.R., **Raymond, L.A**., Nicholson, D.W., Hayden, M.R. (2006) Cleavage at the caspase-6 site in huntingtin is required for motor dysfunction, neurodegeneration and excitotoxicity in Huntington Disease. *Cell*, 125:1179-1191.
5. Cowan, C.M., **Raymond, L.A**. (2006) Selective neuronal degeneration in Huntington's disease. *Current Topics in Developmental Biology*, 75:25-71.
6. Fan, M.M.Y., **Raymond, L.A.** (2007) N-methyl-D-aspartate (NMDA) receptor function and excitotoxicity in Huntington's disease. *Progress in Neurobiology*, 81:272-293.
7. Fan, M.M.Y., Fernandes, H.B., Zhang, L.Y.J., Hayden, M.R., **Raymond, L.A.** (2007) Altered NMDA Receptor Trafficking in a YAC Transgenic Mouse Model of Huntington's Disease. *J Neuroscience*, 27: 3768-3779.
8. Fernandes, H.B., Baimbridge, K.G., Church, J., Hayden, M.R., **Raymond, L.A**. (2007) Mitochondrial sensitivity and altered calcium handling underlie enhanced NMDA-induced apoptosis in YAC128 model of Huntington's disease. *Journal of Neuroscience*, 27(50):13614-13623.
9. Milnerwood, A.J., **Raymond, L.A**. (2007) Corticostriatal synaptic function in mouse models of Huntington's disease:Early effects of huntingtin repeat length and protein load. *J Physiology*, 585:817-831.
10. Sornarajah, L., Vasuta, O., Zhang, L., Sutton, C., Li, B., El-Husseini, A., **Raymond, L.A**. (2008) NMDA receptor desensitization regulated by direct binding to PDZ1-2 domains of PSD-95. *Journal of Neurophysiology*, 99(6):3052-62.
11. Cowan, C.M., Fan, M.M.Y., Fan, J., Shehadeh, J., Zhang, L.Y.J., Graham, R.K., Hayden, M.R., **Raymond, L.A**. (2008) Chronically elevated calpain activity in YAC transgenic Huntington disease mouse model: Impact on NMDA receptor function and toxicity. *Journal of Neuroscience*, 28(48):12725-35.
12. Fan, J., Cowan, C.M., Zhang, L., Hayden, M.R., **Raymond, L.A.** (2009) Interaction of postsynaptic density protein-95 with N-methyl-D-aspartate receptors influences

excitotoxicity in the YAC mouse model of Huntington's disease. *Journal of Neuroscience*, 29(35):10928-10938.

13. Milnerwood AJ, Gladding CM, Pouladi MA, Kaufmann AM, Hines RM, Boyd JD, Ko RWY, Vasuta OC, Graham RK, Hayden MR, Murphy TM, **Raymond LA.** (2010) Early increase in extrasynaptic NMDA receptor signalling and expression contributes to phenotype onset in Huntington's disease mice. *Neuron*, 65(2):178-190.
14. Graham RK, Deng Y, Carroll J, Vaid K, Cowan C, Pouladi MA, Metzler M, Bissada N, Liu L, Faull R, Gray M, Yang XW, **Raymond LA,** Hayden MR. (2010) Cleavage at the 586aa caspase-6 site in mutant huntingtin influences caspase-6 activation in vivo. *Journal of Neuroscience*, 30:15019-15029.
15. Milnerwood AJ and **Raymond LA.** (2010) Early synaptic pathophysiology in neurodegeneration: Insights from Huntington's disease. *Trends in Neuroscience*, 33:513-523.
16. Fan J, Vasuta OC, Zhang LYJ, Wang L, George A, **Raymond LA**. (2010) N-Methyl-D-Aspartate receptor subunit- and neuronal-type dependence of excitotoxic signaling through postsynaptic density 95. *Journal of Neurochemistry*, 115:1045-1056.
17. Tapia L, Milnerwood A, Guo A, Mills F, Yoshida E, Vasuta C, Mackenzie IR, **Raymond L**, Cynader M, Jia W, Bamji SX. (2011) Progranulin deficiency decreases gross neural connectivity but enhances transmission at individual synapses. *Journal of Neuroscience*, 31:11126-11132.
18. Gladding CM and **Raymond LA**. (2011) Mechanisms underlying NMDA receptor synaptic/extrasynaptic distribution and function. *Molecular Cellular Neuroscience*, 48:308-320.
19. **Raymond LA,** André VM, Cepeda C, Gladding CM, Milnerwood AJ, Levine MS. (2011) Pathophysiology of Huntington's disease: time-dependent alterations in synaptic and receptor function. *Neuroscience*, 198:252-273.
20. Fan J, Gladding CM, Wang L, Zhang LYJ, Kaufman AM, Milnerwood AJ, **Raymond LA.** (2012) P38 MAPK is involved in enhanced NMDA receptor-dependent excitotoxicity in YAC transgenic mouse model of Huntington disease. *Neurobiology of Disease*, 45:999-1009.
21. Kaufman AM*, Milnerwood AJ*, Sepers M, Coquinco A, She K, Wang L, Lee H, Craig AM, Cynader M, **Raymond LA**. (2012) Opposing roles of synaptic and extrasynaptic NMDA receptor signaling in co-cultured striatal and cortical neurons. *Journal of Neuroscience*, 32:3992-4003.
22. Gladding CM, Sepers MD, Xu J, Zhang LYJ, Milnerwood AJ, Lombroso PJ, **Raymond LA**. (2012) Calpain and Striatal-Enriched Tyrosine Phosphatase (STEP) activation contribute to extrasynaptic NMDA receptor localization in a Huntington's disease mouse model. *Human Molecular Genetics*, 21:3739-3752.
23. Milnerwood AJ, Kaufman AM, Sepers MD, Gladding CM, Zhang L, Wang L, Fan J, Coquinco A, Qiao JY, Lee H, Wang YT, Cynader M, **Raymond LA**. (2012) Mitigation of augmented extrasynaptic NMDAR signaling in cortico-striatal co-cultures from Huntington's disease mice. *Neurobiology of Disease,*48:40-51.