Miles Ingram

2015/11/2

Final Project Proposal

**Introduction**

The transport protein p11(S100A10) has been linked both to depression and addiction[[1]](#endnote-1) [[2]](#endnote-2)[[3]](#endnote-3). While its connection to depression has been suggested to be as a result of moving the 5-HT1b to the cell surface­­­­­­­­ 1, its mechanism of action in addiction is still somewhat unclear. However it has been shown that selectively eliminating p11 in D2 expressing medium spiny neurons (MSNs), but not in D1 expressing MSNs 2 does what?. Additionally prenatally stressed rats have been shown to have both higher nicotine CPP scores, but also an increase in D2 receptor mRNA[[4]](#endnote-4). Taken together this suggests that p11 may be acting upon D2 receptors in the Nac, though the exact mechanism is unclear. For this project I want to first model the expression of D2 receptors and firing of neurons in the Nac, and then model different ways p11 could be effecting D2 receptor expression and how that could effect firing rates. The ultimate goal would be to test these models against experimental data gathered at a later date. Clearly state your hypothesis. How do D2 receptors themselves affect the firing of Nac neurons?

**Methods**

I intend to run simulations in the program Neuron ([www.neuron.yale.edu](http://www.neuron.yale.edu) ). Neuron is an open source simulation environment designed specifically for simulating neurons. I will first simulate the firing and D2 expression levels of a Nac neuron, I will then introduce p11 as an element and simulate various effects p11 could be having. Such as? I will then attempt to categorize what effects on firing rates different actions of p11 are having. Hopefully I will be able to attempt to confirm one of these models at a later date.

**Expected Outcomes and Significance**

Based on the studies cited in the introduction, I suspect that p11 is likely reducing the numbers of D2 receptors at the cell surface. How would this affect cell firing (*i.e.,* what would change in the outcome of your model in one that includes p11 and one that does not). This project will provide me with a model to attempt to confirm in my keystone. If I can determine how p11 is working in addiction I would hope to move on to an animal model and search for pharmacological targets for the treatment of addiction.

General comments:

* Be careful of jargon. Pretend I am not a neuroscientist and you are submitting this to someone outside your field (this is most often the case in science…).
* All acronyms **must** be defined the first time they are used.

References

1. Per Svenningsson, Paul Greengard, p11 (S100A10) — an inducible adaptor protein that modulates neuronal functions, Current Opinion in Pharmacology, Volume 7, Issue 1, February 2007, Pages 27-32, ISSN 1471-4892, http://dx.doi.org/10.1016/j.coph.2006.10.001. [↑](#endnote-ref-1)
2. Margarita Arango-Lievano, Justin T. Schwarz, Mary Vernov, Matthew B. Wilkinson, Kathryn Bradbury, Akira Feliz, Roberta Marongiu, Yaroslav Gelfand, Jennifer Warner-Schmidt, Eric J. Nestler, Paul Greengard, Scott J. Russo, Michael G. Kaplitt, Cell-Type Specific Expression of p11 Controls Cocaine Reward, Biological Psychiatry, Volume 76, Issue 10, 15 November 2014, Pages 794-801, ISSN 0006-3223, http://dx.doi.org/10.1016/j.biopsych.2014.02.012.

   (http://www.sciencedirect.com/science/article/pii/S0006322314001073) [↑](#endnote-ref-2)
3. Jennifer L. Warner-Schmidt, Emily Y. Chen, Xiaoqun Zhang, John J. Marshall, Alexei Morozov, Per Svenningsson, Paul Greengard, A Role for p11 in the Antidepressant Action of Brain-Derived Neurotrophic Factor, Biological Psychiatry, Volume 68, Issue 6, 15 September 2010, Pages 528-535, ISSN 0006-3223, http://dx.doi.org/10.1016/j.biopsych.2010.04.029.

   (http://www.sciencedirect.com/science/article/pii/S0006322310004233) [↑](#endnote-ref-3)
4. N. Said, S. Lakehayli, M. El Khachibi, M. El Ouahli, S. Nadifi, F. Hakkou, A. Tazi, Prenatal stress induces vulnerability to nicotine addiction and alters D2 receptors’ expression in the nucleus accumbens in adult rats, Neuroscience, Volume 304, 24 September 2015, Pages 279-285, ISSN 0306-4522, http://dx.doi.org/10.1016/j.neuroscience.2015.07.029.

   (http://www.sciencedirect.com/science/article/pii/S0306452215006430) [↑](#endnote-ref-4)