Project Title:

High-Throughput profiling of Purkinje neuron dendrites during memory formation and neuronal stress

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Background and purpose

Protein synthesis in neuronal cells is necessary for the formation of long-term memory. In neurons, translation occurs not only in the soma but also distally within dendrites [Davis 1987]. There is mounting evidence that this local protein synthesis beneath or within dendritic spines responds to neural stimulation by altering spine morphology and molecular signal processing, thus resulting in synaptic plasticity [Bramham 2007]. An analysis of the dendritic transcriptome and proteome can therefore be expected to lead to novel insights into the molecular basis of long-term memory formation and storage.

Although the de novo synthesis of protein in distal dendrites has received increased recognition as a key event in physiological processes such as development and plasticity/memory as well as in disease such as mental retardation [Bramham 2007], our current knowledge is still limited to a handful of genes. It is therefore clear that until we clarify the fundamental mechanisms controlling mRNA targeting and translation in neurons, the goal of understanding how our brain works and stores information will remain out of reach. To fill this knowledge gap, we propose a breakthrough experimental approach by identifying all the genes specifically expressed in the cell-body, cytosol and dendrites of a specific type of neuron (Purkinje cell). We also aim to identify the proteins undergoing translation in the three compartments and correlate their abundance with that of the mRNA, with the goal of identifying regulatory sequences (and in the long-term, with also with epigenetic modifications) that are regulating translation efficacy.

Why no jobs have been executed

For this project, I use published software as well as not-yet-published software developed inside OSC. The published software has proven difficult to install on RICC (cufflinks pipeline), and some of the OSC-internal software is only available to me in binary form, the source code is not available to me. However these binaries do not execute on RICC.

Therefore I have not actually executed the computations on RICC. However, during fiscal year 2013 my project will enter a new phase with new experimental data, and I would like to make another attempt at installing the relevant code on RICC.

I am using D2S through my RICC account for important back-up of data.

For these reasons I would like to re-apply for a quick use account, because although I have not used RICC for actual computation, I plan on doing so as soon as I can the relevant code to run.

So far the project has not led to publications, but I expect at least two major publications to arise out of my project during the fiscal years 2013 and 2014.