EVENT ABSTRACT Back to Event

Gene expression analysis and metabolic optimization in cortical fast-spiking interneurons

Andrea Hasenstaub*, Terrence J. Sejnowski and Ed Callaway

The neocortex contains a wealth of neuronal subtypes, distinctive in their locations, anatomy, connectivity, and physiology. Among these, the parvalbumin-positive fast-spiking interneurons are of particular interest for their role in regulating or timing neuronal activity in the healthy neocortex, and for the clear association between their structural and functional abnormalities and neuropsychiatric disorders such as schizophrenia. These neurons are uniquely identifiable by their high activity levels, narrow action potentials, lack of spike-frequency adaptation, and high expression of the calcium binding protein parvalbumin. As well, a variety of theoretical, anatomical, and functional studies have suggested that the activity of these neurons is peculiarly metabolically expensive. Is gene expression in fast-spiking interneurons altered or optimized to accommodate high metabolic demand?

We investigated this question by applying information theory to the analysis of previously collected microarray data (Sugino and Hempel et al). This technique identifies the genes that are most informative regarding whether or not a sample was collected from neurons of a given type. This analysis complements that provided by more common statistical techniques, which either identify genes that are dramatically over- or under-expressed compared to the entire sample (i.e. t-test) or identify genes that are differentially expressed across the entire dataset, irrespective of in which cell type the gene is distinctively expressed (i.e. simple ANOVA).

To identify the functions of these maximally informative genes, we queried gene ontology databases to determine which annotations were overrepresented among our gene set. We then used NIH-developed software (DAVID) to identify functional clusters among these annotations, and finally classified these clusters according to their roles in neuronal function (signal transduction, synaptic transmission, and so on). Each step of this analysis (from the identification of informative genes to the classification of overrepresented functions) was checked for significance using Monte Carlo and/or bootstrap techniques, and our cluster classification algorithm was validated by an unbiased reviewer.

We found that each studied subtype of cortical neuron was characterized by the significant differential expression of hundreds or thousands of genes. In four of the five types of neuron studied, the most informative genes were predominantly related to cell structure, synaptic transmission, and signal transduction, and to a lesser extent to ion channel expression and electrophysiology. However, among the genes whose expression levels best distinguished fast-spiking cells from their neighbors, genes related to energy generation, including genes related to lactate-pyruvate conversion, the electron transport chain, mitochondrial structure, and other aspects of cellular respiration, were dramatically and significantly overrepresented, as were ion channel genes.

Thus, we conclude that neocortical fast-spiking interneurons, in addition to being electrophysiologically unique, are also distinctive in their expression of genes related to energy generation and metabolism. We propose that these alterations in metabolic gene expression are an adaptation associated with the unusually high energy consumption required to sustain activity in networks of fast-spiking interneurons. In addition, we suggest that information theoretic techniques provide a valuable alternative to standard statistical techniques for the identification of genes of interest in microarray data.

Conference: Computational and systems neuroscience 2009, Salt Lake City, UT, USA, 26 Feb - 3 Mar, 2009.

Presentation Type: Poster Presentation

Topic: Poster Presentations

Citation: Hasenstaub A, Sejnowski TJ and Callaway E (2009). Gene expression analysis and metabolic optimization in cortical fast-spiking interneurons. *Front. Syst. Neurosci. Conference Abstract: Computational and systems neuroscience 2009.* doi: 10.3389/conf.neuro.06.2009.03.175

Received: 03 Feb 2009; **Published Online:** 03 Feb 2009.

* **Correspondence:** Andrea Hasenstaub, andrea@salk.edu