Docket #: S01-257

fosGFP Mouse: A Novel Transgenic Mouse for Identifying Subsets of Activated Cells

The fosGFP Mouse was created to address a fundamental question in neuroscience and physiology: following a behavioral task or exposure to a drug, what are the changes in physiological properties of activated neurons and cells?

The fosGFP Mouse enables identification of cells that are functionally activated by a stimulus. This identification can be done without destroying cell viability. The fosGFP Mouse enables, for instance, identification of neurons that are functionally activated by administration of a drug.

Stage of Research:
The Barth Lab has visualized functionally activated GPF-labeled neurons in vivo in an array of brain areas, including hypothalamus, somatosensory cortex, and olfactory bulb. Transgene expression in the fosGFP mouse validates what has been observed by other laboratories for cfos expression by fos immunohistochemistry or in situ hybridization. Concluded and ongoing experiments include: a) induction of fosGFP mice in a variety of experimental protocols and b) recording from activated subsets of cells after behavioral and pharmacological manipulations of the mice.

Applications

- **Analyzing neural activation caused by a stimulus, including:**
- 1) Identifying which subsets of neurons are activated by administration of a drug
- 2) Quantifying the level of neural activation caused by a drug
- 3) Analyzing a drug's neural activation over time

- 4) Visualizing neural activation caused by depression, anger, pain or other emotional stimuli
- 5) Indentifying drugs that penetrate the blood/brain barrier
- **Identifying activation without immunochemisty:** The fosGFP Mouse can be used to identify cfos-expressing cells without immunohistochemistry. This simplifies the procedure for examining cfos induction in that tissue does not require fixation, block, primary or secondary antibody application, or any washes. It allows a much higher throughput for examination of cfos expression patterns under a variety of experimental conditions.
- **Using DNA microarrays to generate expression profiles of labeled cells:** cfosGFP labeled cells could be used with microdissection to look at expression profiles of labeled cells using DNA microarrays. An advantage over current technology here is it does not require you to fix or permeablize the tissue to find "activated" cell, processes which decrease the amount of mRNA that you can recover from a cell.

Advantages

- Detecting GFP expression in vivo without additional manipulation (e.g. fixation, dye administration).
- Performing live-cell assays on subset of activated cells.
- Examining in vivo the electorphysiological properties of neurons.
- Previously neuroscientists have been able to identify an *area* of the brain that may have been activated by a stimulus, but they were unable to isolate the particular subset of cells that are directly involved in mediating the behavior or the "memory." The fosGFP Mouse enables direct identification of this subset of cells without killing the cells. Thus, the electrophysiological properties of the neuron can be examined and other in vivo properties of the cell (for example, its response to a pharmacological compound) can be assayed.

Patents

- Published Application: 20040031065

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