Docket #: S16-125

Activity-dependent expression system for labeling and optogenetic control of neuronal circuits

Researchers in Prof. Karl Deisseroth's laboratory have engineered versatile, virus-based constructs that are driven by neuronal activity to either label or optogenetically control those active neurons. These vectors can be administered to any brain region where they function to express desired proteins in neurons that are active during distinct experiences of freely moving animals. The expression system utilizes a minimal c-fos-based promoter packaged into AAV particles and designed to specifically drive protein synthesis in active neurons in a variety of mammalian species. Downstream, the time-locked activity is translated into sustained gene expression, which can then facilitate either imaging of complex cell activity or optogenetic control of cell responses.

Stage of Research
The inventors used this tool in mice to visualize wiring (axonal projections) and molecular features in the prefrontal cortex associated with distinct behavioral experiences. They identified brain-wide projection patterns and discovered unique and unexpected cell responses.

Applications

- **Optogenetics** - expression cassettes for activity-dependent opsin expression
- **Neuronal circuit imaging** - expression cassettes for activity dependent Cre recombinase activity designed to insert and express genes for visualizing neurons

Advantages

- **Activity-dependent gene expression** - optogenetic control of specific populations of neurons selected by experience
- **Direct administration to any brain region** - viral constructs can be administered via direct stereotaxic microinjection to neurons in any part of the brain in a range of wild-type mammalian species or in animal models of disease
- **Long-range cellular resolution** - labeling neurons through this system can reveal the number, location and cell-type of neurons capable of modulating specific behaviors, including circuit connections through axon projections
- Identifies or controls activity in **awake, behaving animals**

Publications

- Ye L, Allen WE, Thompson KR, Tian Q, Hsueh B, Ramakrishnan C, Wang A-C, Jennings JH, Adhikari A, Halpern CH, Witten IB, Barth AL, Luo L, McNab, JA, Deisseroth K. Wiring and Molecular Features of Prefrontal Ensembles Representing Distinct Experiences *Cell.* 2016.
- Stanford research shows that different brain cells process positive and negative experiences. *Stanford Report* May 26, 2016

Patents

- Published Application: WO2017205395
- Published Application: 20200318079

Innovators

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