Docket #: S13-389

ASAP1 and ASAP2: Fluorescent voltage sensor with fast kinetics for imaging high-frequency neuronal electrical activity

Researchers in Dr. Michael Lin's lab have developed a fluorescent voltage sensor for non-invasive optical monitoring of electrical events in living cells *in vitro* and *in vivo*. A longstanding goal of neuroscience has been the accurate optical reporting of electrical activity in genetically defined neuronal populations. Fluorescent voltage sensors offer a promising approach to this as they allow a set of neurons in a region to be genetically defined and simultaneously visualized without the need for chemical access. However, existing sensors have limitations such as slow kinetics and suboptimal fluorescence responses that hinder their ability to accurately sense the range of neuronal activity. To overcome these limitations, the inventors have developed a voltage sensor named Allosteric Sensor for Action Potentials 1 (ASAP1). ASAP1 has sufficient brightness, dynamic range and kinetics to detect neuronal activity ranging from subthreshold potentials to rapid trains of action potentials.

Stage of Research

The inventors have shown that ASAP1 is able to discriminate between subthreshold voltage changes, single action potentials, and closely spaced action potentials in neurons in culture and in brain slices.

Ongoing Research

Sensor development and optimization are ongoing.

Applications

- **Drug development**
  - High throughput screening of agents targeting ion channels
  - Screen for drugs for cardiac applications, including drugs that affect the cardiomyocyte excitation/contraction cycle
- **Research**
  - Study genetically defined neural circuits in normal and diseased states
  - Measure membrane potential of any excitable cell

Advantages

- Large response - fluorescence change in response to action potentials is 83% larger than its closest competitor
- Fast kinetics
- Bright
- Sensitive
- Can be used in vitro and in vivo
- Uses standard optical equipment
- General purpose sensor
  - Detect and count action potentials alone or in trains
  - Detect subthreshold voltage changes

Publications

- St-Pierre F, Marshall JD, Yang Y, Gong Y, Schnitzer MJ, Lin MZ, High-fidelity optical reporting of neuronal electrical activity with an ultrafast fluorescent voltage sensor, Nature Neuroscience, published online April 22, 2014.
- Amy J Lam, François St-Pierre, Yiyang Gong, Jesse D Marshall, Paula J Cranfill, Michelle A Baird, Michael R McKeown, Jörg Wiedenmann, Michael W Davidson, Mark J Schnitzer, Roger Y Tsien & Michael Z Lin, Improving FRET dynamic range with bright green and red fluorescent proteins, Nature Methods, Oct. 2012, (9)10: 1005-1012.

Patents

- Published Application: 20150132774

- Issued: 9,606,100 (USA)

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