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Light Activated Inducers of GPCR Activity for Screening Novel Therapeutics

Researchers in Dr. Karl Deisseroth's laboratory at Stanford University have developed a novel suite of genetically-encodable, optically-activated modulators of second messengers (such as cAMP and IP3). This technology could be used for light-activated drug screening for compounds that target G-protein coupled receptors (GPCR's).

Traditional chemical-based methods for modulating cAMP are too slow to study activity in the physiological time scales (such as those seen in nervous or cardiac tissue). This new optical approach is ideally suited for fast modulation. This method also eliminates the waste inherent in chemical techniques. In addition, the technology itself has the potential for therapeutic uses in cAMP-related disease such as ADHD and cardiac channelopathies.

Stage of Research
The inventors have optimized protein expression, attached fluorescent proteins for visualization, and optimized the modality for studying downstream effects. They have shown that they can visualize optically-evoked cAMP regulation of targeted ion channels by transfecting cells with both the cAMP-inducer and the cAMP-targeted cation channel and visualizing resultant activity using Ca++-sensitive dyes.

In addition, the inventors have confirmed that the optical proteins are active in intact neural tissue without supplementation of exogenous cofactors, and can be used to determine millisecond scale kinetics of neuromodulatory GPCR activation. They have also found that when used in awake, behaving animals the optical proteins can be activated to induce reward in a place preference paradigm.

Applications

- **Drug screening** - for novel compounds that target GPCRs
- **Therapeutic** - for modulating cAMP in conditions such as ADHD and cardiac channelopathies
- **Research** - for studying GPCR activity in cardiac and nervous tissue

Advantages

- **Fast** - can be used to observe effects in millisecond time scale seen in physiological conditions
- **Low cost** - light activation does not create the waste inherent in chemically-based approaches

Publications

- Published PCT Application: PCT/US2009/045611

Patents

- Published Application: WO2009148946
- Published Application: 20110112179
- Published Application: 20130331441
- Published Application: 20150218547
- Published Application: 20170081388
- Issued: 8,729,040 (USA)
- Issued: 8,962,589 (USA)

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