A fast, sensitive optical indicator for membrane potential in cells

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Technology description

Summary

Dr. Adam Cohen and colleagues have developed a novel protein-based indicator of cell membrane voltage with the potential to revolutionize the field of electrophysiology. Membrane potential plays a crucial role in biological processes such as nerve impulse transmission, mitochondrial and bacterial ATP production, and membrane transport. Currently, the only way to measure the voltage across a cell membrane in real time involves placing electrical probes on both sides of the membrane. This technique is slow, painstaking, and limited to large cells without cell walls, and it often damages or kills the cells. An optical indicator of membrane potential is highly desirable, but current candidates are either not sensitive enough, too slow, or toxic and difficult to install in the cell. Thus, the Cohen lab's fast, sensitive, nontoxic, genetically encoded optical indicator represents a major breakthrough for electrophysiology.

The PROPS voltage indicator is expected to have a major impact on a wide variety of scientific and commercial applications. PROPS will enable, for the first time, the direct measurement of electrical activity in bacterial and mitochondrial membranes. Most bacteria are too small for electrophysiological measurements via physical probes, and thus their electrical properties are almost entirely unknown. Understanding bacterial electrophysiology could have far-reaching implications for medical, industrial and ecological applications. Likewise, PROPS has the potential to tremendously advance our understanding of the equally inaccessible mitochondrial membrane, which in turn may shed new light on disorders such as diabetes, cancer, neurodegenerative disease and aging. Other important applications of PROPS include drug discovery screens for ion-channel modulators, which are used to treat neurodegenerative, psychiatric, metabolic, and cardiac disorders, as well as real-time in vivo imaging of neuronal activity.

Advantages

The indicator developed by Dr. Cohen et al is a modified form of microbial rhodopsin called

Proteorhodopsin Optical Proton Sensor (PROPS). In the wild, proteorhodopsin harnesses absorbed sunlight in order to establish a voltage across the bacterial cell membrane. In PROPS, this mechanism has been reversed, resulting in an indicator which emits light in response to a membrane voltage. PROPS is a hundred times more sensitive to voltage than any other protein-based voltage indicator currently available, and can respond to changes in membrane potential within 4 milliseconds. The Cohen lab has incorporated the gene for PROPS into constructs optimized for expression in both bacterial and eukaryotic cells (including human cells), and the indicator can be targeted to specific cell types, or even specific cellular structures. PROPS has a number of other highly advantageous properties: it is very photostable, fluoresces in the cell-friendly red spectrum, and can be incorporated into other measurement techniques, such as spectral shift FRET, Optical Lock-In Imaging, Raman spectroscopy, and Second Harmonic Generation image.

Institution

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