Localized bioprobes for electrophysiology

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Technology description

MARKETS ADDRESSED:

Ion channels currently represent a less well charted territory of druggable targets than cell-surface receptors and enzymes, but this is changing. The electrophysiological techniques traditionally used to study ion-channel activity (one-cell, one-pipette patch clamping) are too slow for screening drug candidates, but some companies are finding ways to adapt and automate these techniques. One factor driving this development is the requirement by the regulatory authorities that all drugs must be tested for possible effects on a cardiac potassium channel (the hERG channel), which can cause cardiac arrhythmia. Compounds with adverse effects need to be weeded out as early as possible in the drug-discovery process.

Patch clamp has been an essential tool in the study of ion channels. Drug discovery, however often requires high throughput methods given the large number of compounds in compound libraries that must be screened. Conventional patch clamp has the following disadvantages: chemical invasive, mechanical invasive and high impedance. In addition, it remains a low efficiency technique such that even a skilled patch clamper can record data from only 20-30 cells during an 8-hour work day. In response to this major limitation, several companies have developed automated patch clamp systems that can record from hundreds to thousands of cells a day. However, it's only suitable for recording from cell lines with stable, high expression of the ion channel of interest. In addition, it lacks protocol flexibility for academic applications. Researchers in the laboratory of Charles M. Lieber have developed a free-standing nanoscale field effect transistors enabled by designed kinked nanowire structures. It can achieve point-like three-dimensional sensing and recording, and monitor intracellular potential change inside single cells.

INNOVATIONS & ADVANTAGES:

Nanoelectronic devices offer substantial potential for interrogating biological systems, although nearly all work has focused on planar device designs. The inventors have overcome this limitation through synthetic integration of a nanoscale field effect transistor (nanoFET) device at the tip of an acuteangle kinked silicon nanowire, where nanoscale connections are made by the arms of the kinked nanostructure and remote multilayer interconnects allow three-dimensional (3D) probe presentation. The acute-angle probe geometry was designed and synthesized by controlling cis versus trans crystal conformations between adjacent kinks, and the nanoFET was localized through modulation doping. 3D nanoFET probes exhibited conductance and sensitivity in aqueous solution independent of large

mechanical deflections, and demonstrated high pH sensitivity. Additionally, 3D nanoprobes modified with phospholipid bilayers can enter single cells to allow robust recording of intracellular potentials.

Advantages

The invention has the following advantages:
It's easy to use compared to conventional patch clamp.
Its tip size is much smaller and can reach places where current technology cannot.
Current patch clamp tip is about 2um.
The reported nano-FET is about 80 nm.
Their recent fabrication in the lab is of 15 nm.
In addition, it's chemical and mechanical non-invasive.
Last but not least, it provides more flexibility for academic users than automated patch clamp technology.

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