Drug Discovery & Development

High-Speed On-Chip Patch-Clamping Technique for High Throughput Drug Screening Applications

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Inventors: Robert Blick, Hua Qin

The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing a patch-clamp system that enables real-time tracking of ion channel activity.

Overview

A cell membrane is made up of lipid bilayers that include ion channels for controlling the flow of ions into and out of the cell. Certain ion channels open in response to signaling molecules, including naturally occurring signaling molecules and some drug molecules. During drug development, it is necessary to determine the effects of drugs on ion channels to avoid adverse effects or create a positive therapeutic effect for the treatment of ion-channel related diseases.

Analysis of ion channel response often is performed with a patch-clamping technique. An electrical connection is made across the cell membrane, and then small current changes across the membrane can be used to trace the flow of ions through the channel. A tight electrical seal between the cell wall and pipette is needed so the small amount of ionic current can be measured.

High throughput drug screening requires the measurement of many ion channels. But traditional methods using single micropipette tips are inefficient and tedious. To address this shortfall, on-chip patch clamping methods offer parallel processing of multiple cells by using a plate with an array of holes, each of which accepts a cell. However, these patch-clamping methods lack the sensitivity to measure rapid changes in the ionic transport in real-time due to poor electrical characteristics. A need exists for improved devices and methods with greater data acquisition speed and resolution.

The Invention

UW-Madison researchers have developed a high frequency patch-clamp system that quickly and accurately measures changes in ion channels. The system uses a “tank circuit” to analyze the impedance of the membrane at high frequency. This circuit design is reliable and is commonly used in high impedance devices. It improves sensitivity by rapidly detecting small current changes in the ion channels.

The tank circuit is fabricated on the top of a glass/quartz chip with an array of apertures. A whole cell, bi-lipid membrane or single ion channel within a membrane is positioned over an aperture, and opposing electrodes are placed on opposite sides of the cell membrane. Then a high frequency electrical signal is applied to the electrodes to provide a connection between the electrodes and the cell membrane. The effects of chemical signals on ion channels may be observed in real-time via the impedance changes across the cell membrane. These impedance changes can be measured easily by monitoring the resonance of the tank circuit.

Applications

- High throughput drug screening for ion channel activity

Key Benefits

- Allows changes in ion activity to be measured in real-time
- Uses an alternating current measurement technique to improve sensitivity of ion channel measurements
- Direct current measurements also may be used.
- Provides enhanced bandwidth of up to 500 MHz
- Integrates easily into automated equipment
- Allows parallel processing of multiple cells
- Does not require manipulation of freestanding electrodes during the patch-clamping process
- Allows waveguide-like electrodes to provide a high frequency response
- Eliminates need for a high resistance seal

Tech Fields

- Drug Discovery & Development : Preclinical testing

For current licensing status, please contact Jennifer Gottwald at jennifer@warf.org or 608-960-9854