Stable HERG Expressing Cells

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Technology description

Summary
Vanderbilt researchers have designed a cell line with stable expression of the human heart potassium channel, HERG. This cell line has robust and very consistent cell-to-cell HERG activity without detectable endogenous ionic currents, making it ideal to use in preclinical drug screening.
Investment Needed
No investment is needed, as these cells have been generated and validated for high and stable expression of HERG. Vanderbilt will license these cell lines non-exclusively.
Current Competitive Product(s)
Stable HERG expressing lines in HEK-293 cells are available but have problems including endogenous ionic currents and highly variable cell-to-cell expression levels. Commercially available CHO cell lines also exist, but some may be limited by low or inconsistent cell-to-cell channel expression. In some circumstances, the currently available cell lines may be suboptimal for research and certain preclinical drug screening programs.
Description
The human heart potassium channel, HERG, is critically important for repolarizing the myocardium following action potentials. Genetic mutations in HERG lead to the congenital long-QT syndrome and may also predispose patients to drug-induced or acquired long-QT syndrome. Inadvertent HERG block by a variety of drugs can cause adverse events including potentially fatal cardiac arrhythmia. In fact, block of the HERG channel is such a common and serious potential side effect of many drugs that the regulatory authorities issued recommendations for the establishment of cardiac safety testing during preclinical drug development that include screening for HERG blocking activity.
The standard approach to screen HERG for drug block utilizes mam- malian cell lines that stably express the channel. The most widely used stable HERG cell lines have been established using HEK-293 cells. However, these cells can exhibit endogenous ionic currents and in practice, the HERG expression is a high variable from cell to cell. Vanderbilt researchers have overcome these drawbacks and developed HERG stably expressed in Chinese hamster ovary (CHO-K1) cells using a novel transposon-mediated system coupled with a high throughput fluorescent assay in order to select clonal lines exhibited high expression levels. The selected cell lines were then validated using manual patch clamp recording (see figure below).

Advantages

These cells offer several advantages over existing cell lines including:
Improved background with lower endogenous ionic current
Highly consistent cell-to-cell HERG expression
High level of HERG functional expression

Institution

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