



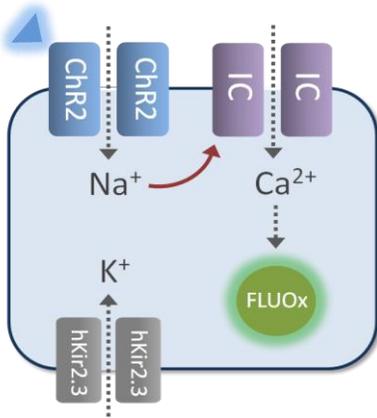
Cell-Based Optogenetic Assays

Axxam (Italy) has developed a new assay technology for functional cell-based HTS of voltage-gated ion channels. Utilizing optogenetics, this unique technology has a number of advantages over conventional methods, including physiologically-close assay conditions; channel activation is triggered by blue light, avoiding artificial depolarization methods such as high KCl concentration conditions. The assays are fluorescence-based and highly suited for HTS applications.

Key Advantages

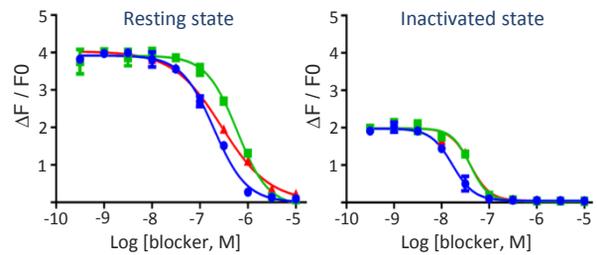
- Assay under physiologically-close conditions
- Screen against the resting or inactivated state
- Assays validated using patch clamp
- Results correlate well with high K⁺ protocols
- Homogenous assay format
- Works with standard HTS instrumentation

How the System Works



Example of an optogenetics cell line. The ion channel of interest (IC) is over-expressed, in addition to Channelrhodopsin-2 (ChR2), and an inward K⁺ rectifier (hKir2.3). Blue light stimulation of ChR2 leads to a Na⁺ influx, causing IC activation. The resulting Ca²⁺ influx is detected by Ca²⁺ sensitive FLUOx dye. Following closure of ChR2 and IC, hKir2.3 activity helps to restore the membrane potential to resting levels.

Case Study



Evaluation of known state dependent blockers in an optogenetic cell line expressing hCaV1.3 (Isradipine, Nimodipine and Nifedipine; circles, squares and triangles respectively). For resting state evaluation, cells were pre-incubated with compound and stimulated with blue light. For inactivated state evaluation, hCaV1.3 was inactivated by blue light stimulation, followed by compound addition. 10 minutes later the cells again stimulated with blue light. All three compounds clearly show greater affinity for the inactivated state of hCaV1.3, and the IC₅₀ values show good correlation to the literature.

Custom Assay Development

Axxam offers construction of Optogenetic cell lines as a contract research service. Cell lines can be transferred to the client or used as part of contract research studies at Axxam. Time to delivery of a new assay in a 384 well plate-adapted format can be as little as 4 months. Depending on the target. Please contact us for further information.