

CARDIOTOXICITY

Overview

- Some approved drugs have been withdrawn from the market because of deaths linked to heart ion channel blockage.
- hERG testing for drug candidates is a crucial element of drug development. Some of all lead compounds show some level of hERG related toxicity. Inhibition of the hERG current causes QT interval prolongation. Regulatory agencies (FDA and EMEA) require hERG/IKr pre-clinical safety data as part of any investigational new drug submission.
- The Nav 1.5 channel contributes to phase 0. Drugs or toxins that increase late INA tend to prolong the action potential and refractoriness.
- The Cav1.2 channel regulates the phase 2 o plateau; drugs that modify the behaviour of these channels have a significant impact on heart function.

Protocols

Fundación MEDINA offers analyses of compound effects on cardiac ion channels involved in the different phases of the action potential: hERG, Nav1.5 and Cav1.2.

Instruments

FLIPR (Molecular Devices)
VIPR (AURORA)
Manual Patch Clamp

Analysis methods

Fluorescence based cell
Electrophysiology

Cell lines

CHO hERG
HEK hERG
HEK Nav1.5
HEK Cav1.2

Test compounds

Fundación MEDINA offers different dilution patterns :
2 concentration points
6 concentration points
10 concentration points
All compounds will be tested per triplicate

Data reports

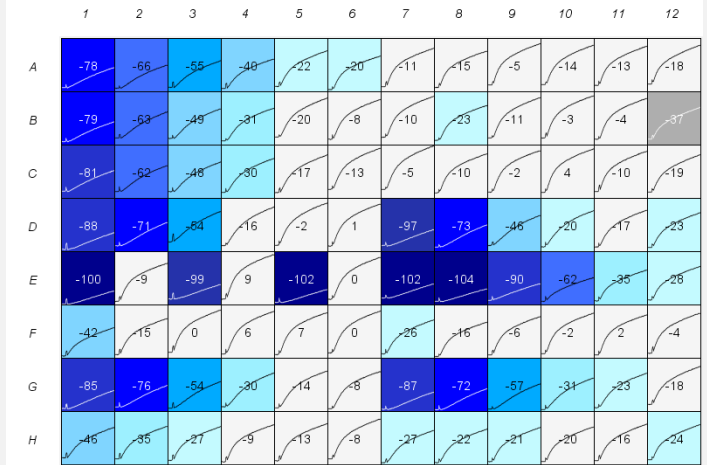
%Inh, dose-response curve, IC50.



MEDINA offers robust assays to determine drug's effects on cardiac ion channels :

High-throughput fluorescence ion channel

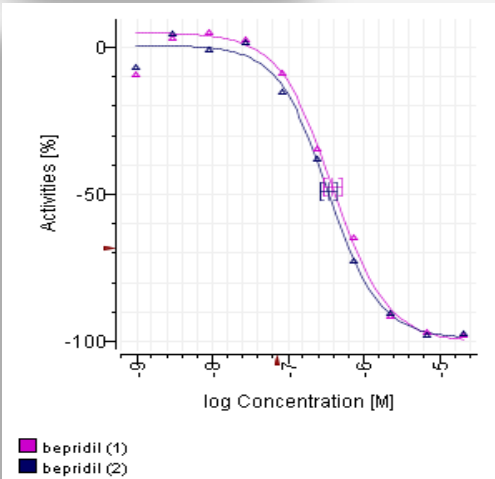
Fluorescence based cell assays are based on the measurement of dyes , which respond to the behavior of the channel or the flux ion.



Genedata Screener®

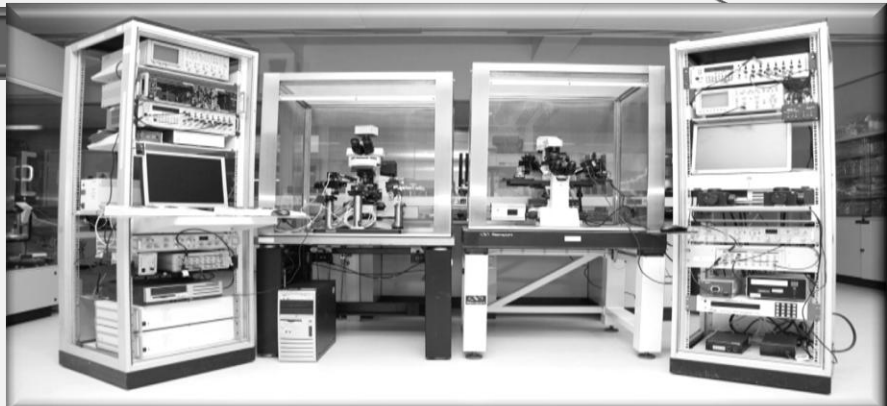
These assays have been validated with a large number of standards and were used as reference model in a pharmaceutical company.

All of the data are produced and analyzed in a high quality control environment.



Manual Patch Clamp

More definitive and confirmative investigation of cardiac ion channel can be done using traditional Patch Clamp.



To find out more contact us
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