

Cardiac Toxicity Assessment

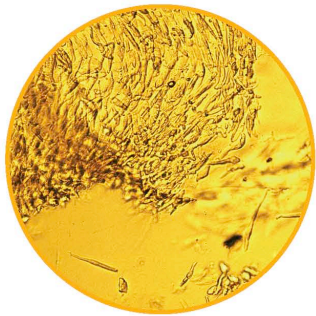
hERG & NaV1.5 ion channel studies



One of the major reasons for withdrawal of a drug from the market has been the risk of drug induced sudden cardiac death resulting from prolongation of the QT interval in the heart. Often this is the result of unintended blockade of the hERG potassium ion channel, or associated cardiac ion channels by the drug.



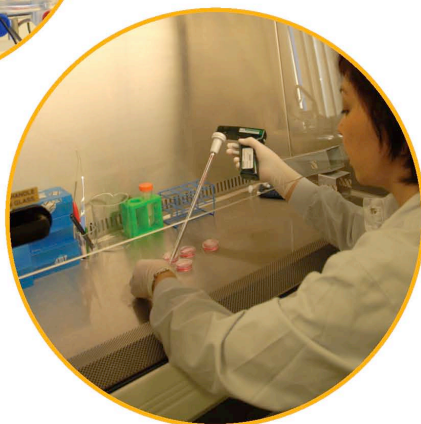
This has led FDA and EMEA regulators to require a data package showing drug effects on hERG as an indicator of the potential of the drug to induce abnormal cardiac events.



Early evaluation of the effects of drugs on cardiac ion channels is a critical screen that allows investigators to determine the potential for abnormal cardiac events in later stage trials, eliminating toxic compounds at the early stages of drug development. At ICBC we use two assays; a wild type hERG K⁺ channel assay and a wild type NaV1.5 channel assay, both ion channels being stably transfected into human embryonic kidney cells (HEK293). All recordings are taken using the gold standard manual whole cell patch clamp technique and can be conducted at room temperature or 37°C.



Studies can also be tailored to client needs. Generally, a 5-point dose response curve is constructed, using industry standard protocols and a full report is given which includes all protocols and estimated IC₅₀ values. Expert consultation is available as part of the service. All data remains the property of the client and is treated under confidentiality.



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Panel A shows the recording protocol employed to study hERG. Panel B shows a typical record from a dose response for 5 concentrations of the known hERG channel antagonist Cisapride. The summary data for 6 cells is shown in panel C. Plotted are the mean normalised current amplitude \pm SEM for each drug concentration. In this example Cisapride shows an IC_{50} of 7 ± 1 nM. All experiments were conducted at ICBC and all data shown here is proprietary to ICBC.

