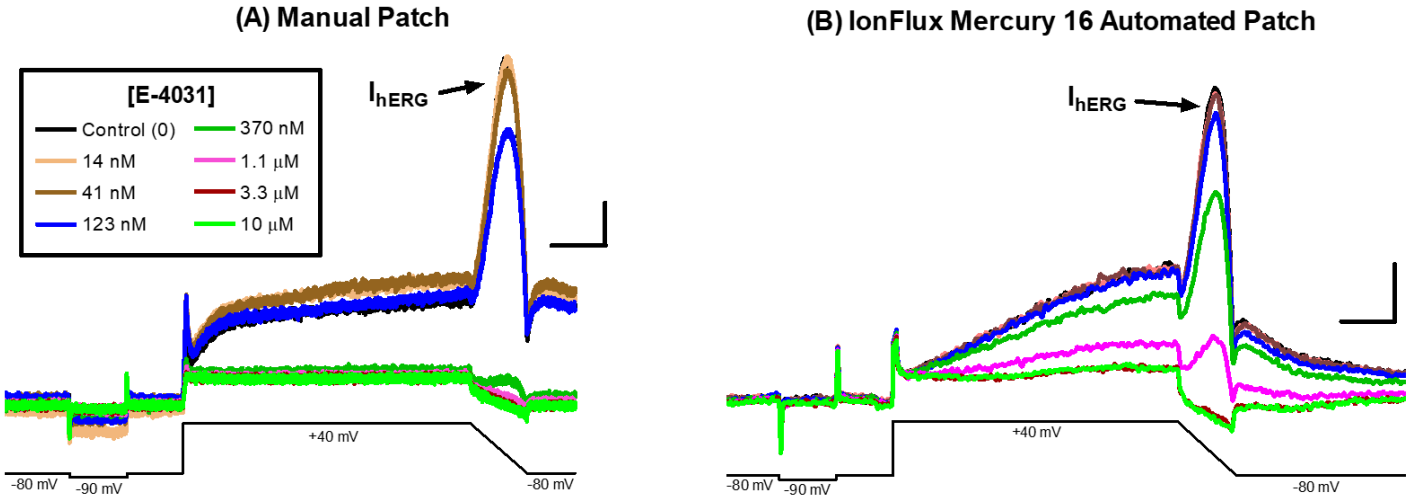
hERG Patch Clamp Assay – Cardiac Safety Panel

Functional hERG Whole Cell Manual and Automated Patch Clamp Assays for compound screening and profiling

Target Overview	
Overview	hERG ion channel is a voltage-gated potassium channel that is expressed in the heart and the nervous system. It regulates the flow of potassium ions in the form of a rapidly activating, delayed rectifier cardiac current, which plays an essential role in the generation of the ventricular action potential. Inhibiting hERG channel activity by small molecules or mutations can lead to long QT syndrome; the prolongation of the QT segment can lead to the development of life-threatening arrhythmias. For this reason, regulatory bodies such as the FDA and EMA, mandate that molecules be tested against hERG to identify possible cardiac liability.
Target	hERG ion channel
HGNC Reference	KCNH2
Synonyms	Kv11.1, HERG, erg1
Protein	Potassium voltage-gated channel, subfamily H (eag-related), member 2

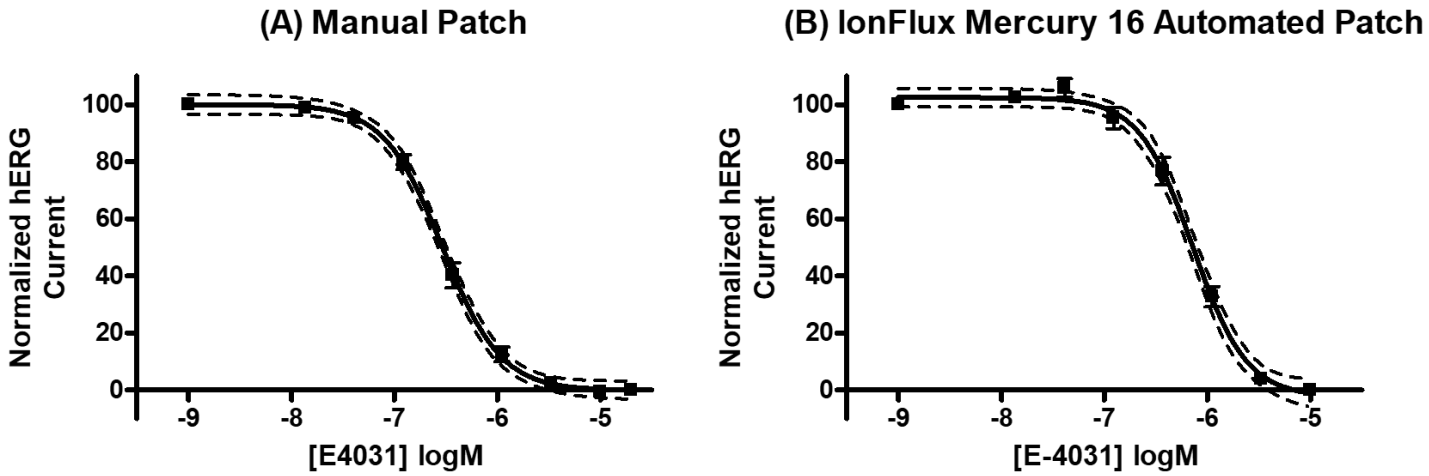
Assay Properties	
Properties	·Compound profiling against the voltage-gated potassium channel hERG to evaluate potential cardiac liability ·Manual Patch Clamp; Automated Patch Clamp with IonFlux Mercury 16 system ·Full positive control concentration-response curve (CRC) in every assay ·Single concentration profiling and full CRCs (6 pt. curves; n=3 cells)
Target Expression	CHO cell-expressed human potassium voltage-gated channel, subfamily H (eag-related), member 2 (hERG) ion channel
Assay Format	Whole cell manual and automated patch clamp formats
Readout	Current
Reference Compound IC50s	**Compounds** **IC50 (nM)** E-4031 294 nM (manual patch); 724 nM (IonFlux automated patch)
Scientific Information:	Q12809 (https://www.uniprot.org/uniprotkb/Q12809/entry)
Screening Location	Malvern, PA, USA
Further Information	More information can be found on our website In Vitro Safety Screening Services.

hERG Current Recordings ± E-4031



Exemplar traces of hERG current (I_{hERG}) elicited from one CHO hERG DUO cell using (A) manual patch and (B) the IonFlux Mercury 16 automated patch system. I_{hERG} measured at peak elicited by a ramp step from +40 mV to -80 mV and inhibited in concentration-dependent manner by E 4031. Voltage protocol is shown below the traces. Capacitance transients are truncated for clarity. Scale bars: 100 pA, 100 ms.

E-4031 IC_{50} Data for hERG



Concentration-dependent effect of E 4031 on normalized hERG current recorded using (A) manual patch and (B) IonFlux Mercury 16 automated patch system. hERG current normalized to current in the absence of E-4031. Sigmoid fit (solid line) parameters (95% confidence intervals – dashed lines): manual patch (n=23, 6 independent preparations): IC_{50}=294 nM (260 to 332 nM), Hill Slope=-1.53 (-1.78 to -1.28); automated patch (n=28, 7 independent preparations): IC_{50}=724 nM (624 to 841 nM), Hill slope=−1.67 (2.03 to 1.32).