

# OCP Ltd

## Specialists in cardiac research

With over 20 years experience in academic research within the University we can offer a wide range of contract research services using a variety of cardiac preparations that include:

- ♥ Repolarisation assays in Purkinje fibres
- ♥ Repolarisation assays in ventricular myocytes
- ♥ Voltage-clamp studies of specific ion currents in single ventricular myocytes.
- ♥ hERG channel assay (expressed in HEK293 cells)
- ♥ Native  $I_{Kr}$  channel assay in cardiac myocytes
- ♥ Papillary muscle preparations
- ♥ Atrial muscle preparations
- ♥ Isolated Langendorff heart preparations.

### An individual approach

We encourage a personalised approach to each study. Close consultation with clients means that all protocols are carefully designed and validated by scientists at OCP Ltd for each project. With this approach OCP Ltd can devise the best experimental design tailored to the client's individual needs.

\* hERG tails currents were recorded in collaboration with the Department of Pharmacology, University of Oxford.

Visit us at  
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Oxford Cardiac Pharmacology Ltd

*Setting standards for the investigation of drug effects on cardiac tissue*



## Fulfilling your specific research needs

### Safety Pharmacology

- ♥ Repolarisation assays  
(Purkinje fibre, ventricular myocyte)
- ♥ hERG channel assays  
(hERG / HEK293 cells, native  $I_{Kr}$ )

### Drug Development

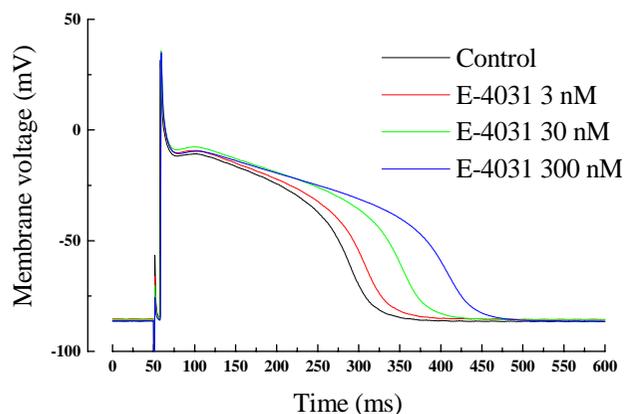
- ♥ Ion Channel assays  
( $I_{Ca}$ ,  $I_{Kr}$ ,  $I_{Ks}$ ,  $I_{Na}$ )

OCP Ltd are specialists in cardiac research with particular expertise in the types of tests that are now required by drug regulatory authorities to assess the potential of new human pharmaceuticals to cause delayed ventricular repolarisation.

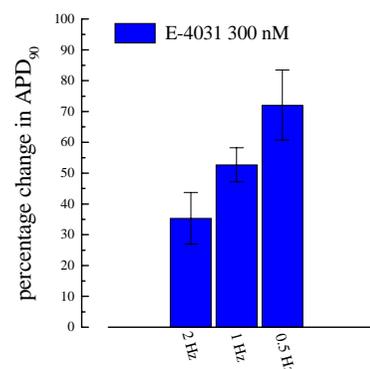
## In vitro repolarisation assays

Prolongation of the QT interval and subsequent increased risk of arrhythmia is caused by the prolongation of the action potential. Repolarisation assays are conducted in either **isolated Purkinje fibres** or in **single ventricular myocytes**.

### Purkinje Fibre Effect of E-4031 on APD



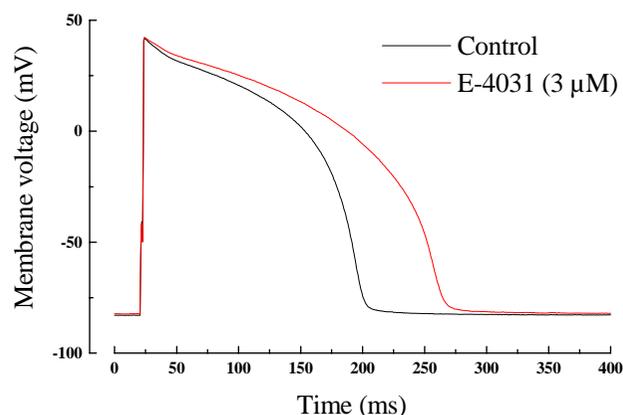
### Reverse use dependence E-4031 on APD



OCP Ltd provides the industry standard *in vitro* ventricular repolarisation assay in Purkinje fibres. Comparator compounds such as E-4031 are routinely used in conjunction with test compounds in assays. A range of stimulation frequencies are used to assess possible reverse use dependence of test compounds.

## In vitro repolarisation assays

### Single Ventricular Myocytes Effect of E-4031 on APD



### Advantages of ventricular myocyte assays

- ♥ AP changes reveal possible actions on many potential ion channel targets
- ♥ Effects can be tested on a variety of ionic channels in normal cardiac environment
- ♥ Greater drug access
- ♥ More cost effective than Purkinje fibre preparations.

### Electrophysiological measurement

Cardiac action potentials are recorded from Purkinje fibres or single ventricular myocytes, using conventional electrophysiological techniques.

### Action potential parameters recorded include:

- ♥ Maximum Rate of Depolarisation (MRD)
- ♥ Upstroke Amplitude (UA)
- ♥ Action Potential Duration at 50 % and 90 % repolarisation (APD<sub>50</sub> & APD<sub>90</sub>)
- ♥ Measurements are made at  $\sim 35 \pm 1^\circ\text{C}$ .

## In vitro hERG channel assays

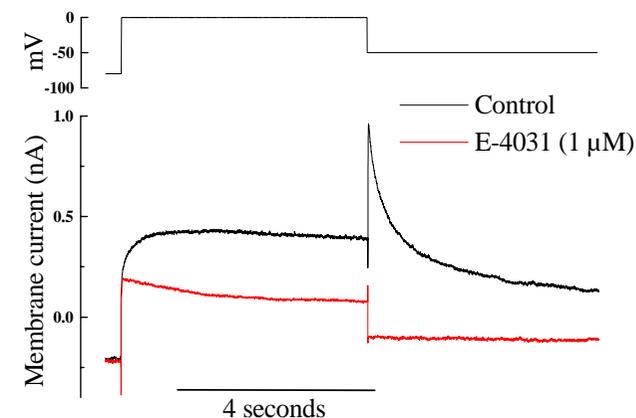
### hERG Channel Assays

Most pharmaceuticals associated with torsade de pointes inhibit the rapidly-activating delayed rectifier current,  $I_{Kr}$ . Therefore particular attention to assays for  $I_{Kr}$  is prudent for assessing risk of QT interval prolongation.

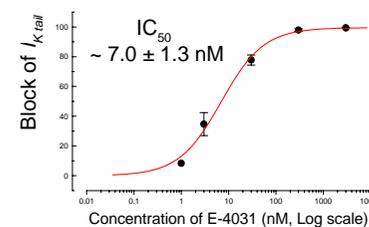
- ♥ hERG expressed in HEK 293 cells
- ♥ Native  $I_{Kr}$  expressed in ventricular myocytes

### hERG expressed in HEK 293 cells

- ♥ Single concentration studies (3 cells)\*



- ♥ Determination of IC<sub>50</sub> values



- ♥ Control comparator compounds used
- ♥ Time control studies if required.