The QPatch™ technology has been developed to significantly increase throughput in ion channel drug screening. It is based on planar glass-coated silicon chips with micro-etched patch-clamp holes. Extra- and intracellular Ringer solutions are applied by miniature flow channels, which ensure laminar flow and short fluid exchange times (<100 ms). The walls of the flow channels are coated with non-polymer materials (glass and silicon) to minimize problems with non-specific binding of ‘sticky’ compounds.

Below is shown the QPatch-16, the first instrument based on the QPatch technology. It runs 16 parallel whole-cell patch-clamp experiments simultaneously with success rates of 50-80%. Cells are maintained in growth medium in an outboard cell storage facility for up to 4 hours until shortly before an experiment. At that time they are automatically lifted in a miniature centrifuge, washed, and reseated in Ringer’s solution before being applied to the patch-clamp tips.

We have determined the IC50 values for 32 hERG channel blockers in a blind test and made a comparison with IC50 values obtained in conventional manual patch-clamp.

MATERIALS AND METHODS

CELL CULTURE

The cell lines were established from CHO cells expressing hERG. The cells were grown in a standard culture medium, and the cell lines were kept for up to 2 weeks without any detectable changes in yield or ability to patch.

ELECTROPHYSIOLOGY

Ion channel drug screenings were performed on QPatch-16 using QPatch™ technology which contains the 16 patch-clamp tips, each containing a complete patch-clamp in and out solutions, flow channels, electrodes, and waste reservoirs (Mortensen et al., 2015). The QPatch™ is a standard microtitre plate (MTP) format. The patch-clamp tips (micro etched in the chip) is approximately 1 μm in diameter and has a resistance of ~2 MΩ.

Initial patch clamp protocol: The resistance was measured after applying the holding potential of -40 mV for 20-30 min, before stepping to -90 mV. Obtained IC50 data were recorded at -90 mV.

SOLUTIONS AND DRUGS

The physiological Ringer solutions consisted of 145 mM NaCl, 4 mM KCl, 2 mM CaCl2, 1 mM MgCl2, 10 mM HEPES (pH 7.4), 10 glucose. Intracellular ‘Ringer’ was 120 mM KCl, 5 mM MgCl2, 1.8 mM NaCl, 10 mM HEPES, 100 μM BaCl2, 0.04 M EGTA, 2.4 mM HEPES. Unknown test compounds for the blind study were provided by Aventis Pharmaceutical (Bridgewater, NJ, USA). Reference compounds were kindly supplied by Merck (Darmstadt, Germany) and another major pharmaceutical company. Verapamil was from Sigma, Switzerland. rBeKm-1 was from Alomone Labs, Israel.

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