APPLICATION OF QPATCH 16 FOR DRUG SCREENING OF LIGAND-GATED ION CHANNELS

The QPatch 16 screening station is a second generation automated patch-clamp system based on planar silicon chip technology. QPatch 16 has previously been employed for a series of screening studies on a number of voltage-gated ion channels (e.g. NMDA, KCNQ4, Nav1.1, 2, 4 and Nav1.5).

Recently, ligand-gated ion channels (LGIC) including GABA<sub>A</sub>, nACHR and ASIC have been targeted with QPatch 16. We have reported a study in which the GABA<sub>A</sub> receptor (β3, γ2) was targeted with 4-5 concentrations of an agonist (GABA), an antagonist (bicuculline) and 4 modulators (agonists, antagonists or modulators).

Subsequently we report a study on acetyl choline nicotinic channels (AChR) in which the effect of pH, i.e. protons which serve as the ligand, was examined.

The QPatch SCREENING STATION

In QPatch 16 patch-clamping takes place on the disposable QPlate which contains 16 individual patch-clamp positions that are operated in parallel. Salines and compounds (agonists, antagonists or modulators) are applied through four pipette heads that connect to bottom site for interfacing to QPatch amplifier. Glass-coated flow channels. Liquid flow is laminar with exchange time constants in the range 50-100 ms. The current rise-time at maximal GABA concentration (50 µM) was 60 msec.

GABA<sub>A</sub> - AGONIST STUDY

Recordings of whole-cell GABA<sub>A</sub> currents elicited in response to 10 µM GABA added for 5 seconds. The current rise-time at maximal GABA concentration was 60 msec in the presence of either pure Ringer’s solution or Ringer’s solution added 20 µM chlordiazepoxide (Concentrations of the antagonist chlordiazepoxide.

Ringer’s solution added 4 increasing concentrations (pH 7, 6, 5, 4).

The analyses presented here comprise I-t and concentration-response relationships, and rise-time determinations. The EC<sub>50</sub> and IC<sub>50</sub> values determined for the concentration-response relations in the present study are comparable to values listed in the literature (cf. e.g. Boileau et al., Neuropharmacol., 2002). The present study is comparable to values listed in the literature (cf. e.g. Boileau et al., Neuropharmacol., 2002).

CONCLUSION

Compound screening on ligand-gated ion channels (GABA<sub>A</sub> and ASIC) can be performed efficiently with the QPatch 16 automated patch-clamp system in order to characterize the effects of agonist, antagonist and modulators. In comparison to other systems on the market, the QPatch’s four pipette heads afford more efficient assays and higher throughput for gigaseal quality patch clamping.

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