Ligand-gated ion channel applications

Qube: 384-channel patch clamp screening system

Introduction

The Qube is the new giga-seal-based 384-channel planar patch clamp system (Figure 1). Sophion Bioscience A/S has designed, manufactured and built the Qube, a 384-channel patch clamp screening system designed as a high throughput screening tool for ligand-gated ion channels (LGICs). The Qube system has been designed to accelerate pharmacological compound screening by providing high reproducibility and high throughput screening of multiple compound solutions. The Qube will be offered as single-hole units.

Methods

For the experiments the intracellular solution was (mM): KCl 120, CaCl₂, MgCl₂, HEPES 2, MgATP 10, GTP 0.5, EGTA 10, NaCl 1.75, pH 7.4 with NaOH. Currents were measured using cell lines stably expressing nAChRα1 and ASIC1a currents were measured in a HEK-293 cell line stably overexpressing ASIC1a (kindly provided by Neurosearch A/S), nAChRα1-ASIC1a currents were measured in a HEK-293 cell line stably overexpressing nAChRα1. ASIC belongs to the ENaC/Deg family and ASIC1a is expressed in rhabdomyosarcoma cells natively expressing nAChR.

Figure 1 The Qube consumable

A) Photograph of the 384-well consumable for the Qube.

B) Schematic drawing of an individual recording cell line. Each cell line is separated from all others with disposable individual compartments. The consumable for the Qube, “QChip384” is built on Sophion’s tried-and-tested silicon technology for optimal giga-seal performance enabling high throughput screening.

C) The rise time for the liquid exchange process was 50 µs (10, 30, 100 and 300 µM). Currents were measured in a HEK-293 cell line stably overexpressing nAChRα1-ASIC1a currents were measured in a HEK-293 cell line stably overexpressing nAChRα1. ASIC belongs to the ENaC/Deg family and ASIC1a is expressed in rhabdomyosarcoma cells natively expressing nAChR.

Figure 2 Activation and steady-state inactivation of ASIC1a

A) Current traces from three consecutive activations of ASIC1a by pH 6.2 in the presence of increasing concentrations of amiloride (0, 1, 10 and 300 µM). Currents were measured in a HEK-293 cell line stably overexpressing ASIC1a. The Qube is real patch clamping, real fast. You get the highest data quality which accelerates your lead finding programs.

B) Dose-response relationships for ASIC1a.

References


Conclusion

In this work we have measured the liquid exchange properties of the QChip384 consumable developed for the new Qube system: the very first giga-seal-based 384-channel planar patch clamp system.

We have shown that the QChip384 supports multiple liquid additions with high reproducibility. The liquid exchange properties of the recording unit enable fast repetitive activation and blocking compound wash-out being used to screen pharmacological compounds such as ASIC 1a and nAChR. Further, we have shown that the Qube QChip384 is superior to existing systems in terms of wash-out rates in exponential transition ranges (3, 5) and that it is an efficient wash-out-of pharmacological compounds

The Qube system is the next-generation patch clamp platform aimed at the high-throughput screening of ion channels. SOPHION (Qube) you get the highest data quality which accelerates your lead finding programs.

The Qube is real patch clamping, real fast.