Characterization of hiPSC-derived neurological disease models using automated patch clamp (Qube and QPatch)

Kadia Raskva Rostholm1, Melanie Schupp1, Daniel Sauter1, Rasmus B Jönsson1

Introduction
Human induced pluripotent stem cells (hiPSCs) can be differentiated into motor neurons, enabling the generation of in vitro motor neuron models. These models can serve as replacement systems for diseased patient cells. Furthermore, the use of hiPSCs for disease modeling allows for the generation of disease-carrying cell lines that are genetically identical to the patient but are easily manipulated in culture. This enables the study of disease mechanisms and the testing of potential therapies. However, the high-throughput measurement of hiPSC-derived motor neurons faces several challenges, including the high variability in ion channel expression and functionality between individual cells.

Materials and methods
Cells: Spinal motor neurons were generated from the following healthy human iPSC lines: Sma9 (allele C96Y), Sma10 (allele C96Y), Sma26 (allele C96Y), Sna1 (allele Q338X), and Sna3 (allele Q338X) and from the following isogenic controls: Sma9_(TALEN) (allele C96Y), Sma10_(TALEN) (allele C96Y), Sma26_(TALEN) (allele C96Y), Sna1_(TALEN) (allele Q338X), and Sna3_(TALEN) (allele Q338X). The cells were differentiated into motor neurons using the BrainXell protocol. After 14 days, the cells were harvested using 2 mL Accumax and subjected to automated patch clamp (Qube platform) for further analysis.

Methods: The patch clamp protocol consisted of a voltage step protocol (VSP) with a voltage step from -90 mV to +60 mV. The current amplitude at +10 mV is significantly lower compared to the control. The Na V channel current versus step voltage is shown in Fig. 4. The average K channel current versus step voltage is shown in Fig. 5. The IV relationship of the SMA hiPSCs displayed, as previously shown in the literature, is shown in Fig. 6. The figure shows that the Na V channel current is significantly lower compared to the control. The K channel current is significantly higher compared to the control.

Acknowledgements
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References

Summary
Our results demonstrate the feasibility of conducting electrophysiological characterization and screening of hiPSC-derived motor neurons on platforms such as Qube and QPatch, thus paving the way for high-throughput screening of drugs for neurological disorders.

Section 1: Screening hiPSC-derived motor neurons using automated patch clamp (APC)
The major challenge when investigating neurons using APC platforms is the requirement to dissociate the cells from their neuronal network while maintaining cell viability and membrane integrity. By optimizing the harvest and whole-cell protocols, we have overcome this obstacle resulting in success rates of up to 60% using our 384-well APC system (Qube). On our medium-throughput system (QPatch), we achieved up to 50% success rates. Quantification of Na V and K channel current-voltage relationship yielded very similar results on the two systems (Fig. 2). The protocol consisted of a voltage step protocol (VSP) with a voltage step from -90 mV to +60 mV. The current amplitude at +10 mV is significantly lower compared to the control. The Na V channel current versus step voltage is shown in Fig. 4. The average K channel current versus step voltage is shown in Fig. 5. The IV relationship of the SMA hiPSCs displayed, as previously shown in the literature, is shown in Fig. 6. The figure shows that the Na V channel current is significantly lower compared to the control. The K channel current is significantly higher compared to the control.

Section 2: Electrophysiological characterization of hiPSC-derived motor neurons
Characterization of hiPSC-derived motor neurons was conducted using automated patch clamp (Qube and QPatch). The cells were differentiated into motor neurons using the BrainXell protocol. After 14 days, the cells were harvested using 2 mL Accumax and subjected to automated patch clamp (Qube platform) for further analysis.

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