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An "All Inclusive "Package for Cardiac Safety: The Six Big on One Automated Patch Clamp Chip

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Drug discovery is challenged by poor predictability of proarrhythmic effects of present cardiac safety screening approaches. The Comprehensive in Vitro Proarrhythmia Assay (CiPA), an FDA directed initiative, is specifically focused on improved preclinical assessment of torsade de pointes (TdP) risk. Striving to optimize the drug discovery process, either the usage of iPSC-derived cardiomyocytes or an enlarged cardiac ion channel panel for voltage clamp studies is discussed.

Patch Clamp assays, the gold standard of ion channel research, are distinguished by high complexity concerning the quality of cell tools, HTS instruments and a time-consuming analysis. The focus of this study was the establishment of standardized automated patch clamp assays on the cardiac ion channel panel, ready-to use. In this study, we used cell lines expressing the six most important cardiac ion channels (hERG, KVLQT, CaV1.2, KV4.3, KV2.1, NaV1.5) on two different automated patch clamp platforms (medium throughput – Patchliner and high throughput – SyncroPatch 384/768PE).

The Patchliner and the SyncroPatch 384/768PE both contain temperature control to enable recordings at physiological temperature – an important feature since drug efficacies may vary with temperature. We present pharmacological data on voltage-dependent channels of the CiPA panel at different temperatures. Furthermore, patch clamp data on hERG recordings using the Milnes protocol (Milnes et al., 2010; a voltage protocol allowing the observation of the timedependent development of block) and thus providing support for the development of an in silico AP ventricular model, are shown.