Current status and future perspectives in cardiovascular and neural toxicity testing using human iPSC technology

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Unexpected toxicities, such as cardiotoxicity and neurotoxicity, is one of the key issues for failure of novel drug candidates in development. Human iPSC technology hold great promise as in vitro models to study the pharmacological effects of drug candidates. Based on international efforts by CiPA (Comprehensive In Vitro Proarrhythmia Assay) and JiCSA (Japan iPS cardiac safety assessment), in vitro safety studies using iPSC-cardiomyocytes have demonstrated their ability to inform on drug-induced delayed repolarization and proarrhythmic risk. Notably, the new assay methodologies, such as iPSC-cardiomyocytes and in silico, has been discussed at ICH S7B/E14 from last autumn. CNS toxicity testing forms a part of the "core battery" of safety pharmacology. Drug-induced seizure is a major reason for drug attrition. Currently, human iPSC-neurons are expected to evaluate seizure liability by multi-electrode assay system by the non-profit worldwide organization HESI (NeuTox subteam). In addition to drug safety issue, developmental neurotoxicity (DNT) testing, which has been discussed at OECD, is focusing on iPSC technology by providing mechanistic data at the cellular and molecular levels.
Thus, iPSC technology is becoming a promising tool for various safety/toxicology fields. In the symposium, I would like to provide an overview of current status of the use of iPSC-derived cardiomyocytes and neural cells in toxicity testing and discuss future perspectives.