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Title: Human induced pluripotent stem cell models of cardiovascular diseases for drug screening

Theme: Stem Cells and Cardiovascular Disease

Key words: Human induced pluripotent stem cells; disease modelling; cardiomyocytes; electrophysiology; drug and gene therapy

Fee band: High cost laboratory-based research

Brief description: The recent finding that just four genetic factors can convert human somatic cells into induced pluripotent stem cells (hiPSCs) has triggered a global revolution in the development of in vitro disease modelling and drug screening strategies. We were one of the first groups to show that skin cells harvested from patients with the inherited and potentially fatal heart disorder, Long QT Syndrome 2, could be converted to hiPSC and then subsequently differentiated into cardiomyocytes (i.e. a disease in a culture dish: skin cells à hiPSC à heart cells; see Matsa et al., European Heart Journal 32:952-62, 2011). The diseased cardiomyocytes beat spontaneously in culture but these cells mirrored the activity of the patient's heart in that they developed arrhythmias, which could be prevented by the patient's own medication (nadolol, a beta-blocker). This novel in vitro disease model was then used to evaluate a small number of experimental drugs, including potassium channel enhancers, which also had a beneficial effect and blocked arrhythmias. We are now extending the repertoire of diseases to include electrical, structural and survival defects in the heart. The PhD project will be involved in developing and analysing hiPSC models for these conditions, as well as evaluating the potential of drug and gene therapy to correct them.