Intracardiac Electrophysiology: Cellular Modelling of Abnormal Repolarisation

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Abnormalities in cardiac repolarization have been implicated in cardiac arrhythmogenesis caused by disease, mutations and drugs. Of particular concern for regulatory agencies, pharmaceutical industry and society is the fact that certain drugs, in particular those not designed to affect the heart, can exhibit cardio-toxicity (i.e. unwanted side effects), which can put patients with otherwise healthy hearts at risk of developing lethal arrhythmias. Drug cardiotoxicity is often related to abnormalities in repolarization caused by drug-induced alterations at the ionic level. Given the limitations of in vitro and in vivo testing in preclinical prediction of drug cardiotoxicity, there is increasing interest in computational methods to complement experimental findings. This presentation will describe the state-of-the-art in computational cardiac electrophysiology and how this technology can be used to investigate the mechanisms of cardiac electrophysiological function and the implications of abnormalities in repolarization, from the ionic to the ECG level. Our main aim is to unravel the mechanisms of drug-induced arrhythmic risk in the context of high inter-subject electrophysiological variability, and to propose novel arrhythmic risk biomarkers based on this research.