Transgenic Rabbits with Long QT Syndrome: A Multi-Scale Approach to Sudden Cardiac Death

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The overall goal of my laboratory is to investigate new mechanisms that underlie SCD through the application of innovative technology, computer modeling and the use of new genetic models of long QT syndrome type 1and type 2 (LQT1 and LQT2). In this presentation I will describe our studies on mechanisms of arrhythmias in LQT1 and LQT2 rabbits at the organ and cellular scale. In addition I will describe a new model where we ablated the AV node (LQT1-AVB) causing sudden cardiac death. I will also debate the issue of how sympathetic tone and heart rate play a critical role in arrhythmogenesis. I will also present studies at the cellular levels with myocytes derived from LQT1 and LQT2 rabbits to illustrate the role of sex hormones in modulation of the function of key proteins that regulate calcium dynamics in cardiomyocytes. Finally, I will demonstrate how cardiac myocytes adapt to prolongation of action potential duration, and how this remodeling leads to triggered activity and cardiac arrhythmias.