expression and response to a hERG blocker E4031. MEA recordings showed a significantly higher response to Sotalol in iPSC-CMs from high-S compared with low-S subjects. Transcriptional profiling identified upregulation or down-regulation of genes (DLG2, KCNE4, PTFR, HTR2C, CAMK IV) involved in downstream regulation of cardiac repolarization and calcium handling machinery as underlying high sensitivity to Sotalol. In silico parameter sensitivity analysis corroborated transcriptomic profiling of select genes; upregulated KCNE4 and downregulated CAMK IV were predicted to positively and negatively correlate with iPSC-CM action potential duration when exposed to Sotalol, respectively. DISCUSSION/SIGNIFICANCE OF IMPACT: Our findings suggest subject-specific iPSCs can be used to model functional abnormalities observed in diLQTS and offer novel insights into iPSC-based screening assays for toxic drug reactions. Success of this study may help identify key components underlying diLQT susceptibility to ultimately develop novel therapeutic agents.

**Discovery and evaluation of FOXP3 dimerization inhibitors**

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OBJECTIVES/SPECIFIC AIMS: Immuno-oncology (IO) strategies are promising new approaches for the treatment of a variety of malignancies, including multiple myeloma (MM). Regulatory T cells (Tregs), which suppress effector T cell function, are a limitation to durable IO responses. The transcription factor FOXP3 is critical for the mature Treg phenotype. FOXP3 homodimerization is required for DNA binding and transcriptional activity, and mutations mapping to the dimerization region are associated with IPEX syndrome, resulting in dysfunctional Tregs in humans. We therefore hypothesize that inhibitors of FOXP3 dimerization will repress Treg suppression and enhance the anti-MM activity of IO. METHODS/STUDY POPULATION: To discover FOXP3 dimerization inhibitors, we are modeling FOXP3 homodimerization in vitro. Currentl...