

## Supplemental Information Inventory

### 1. Supplemental Figures and Legends

- a. Figure S1. Related to Figure 1: TALEN isogenic iPS model of PRKAG2 cardiomyopathy.
- b. Figure S2. Related to Figure 2: Single iPS-CM contractility, gene expression and viability.
- c. Figure S3. Related to Figure 4: Mitochondrial content and metabolic assays of iPS-CMs.
- d. Figure S4. Related to Figure 6: Growth factor production from iPS-CMs.
- e. Figure S5. Related to Figure 7: Gene expression analysis of control mice with A769662 treatment.

### 2. Supplemental Tables and Legends

- a. Table S1. Related to Figure 1: DNA sequences for (A) TALEN experiment and (B) sequencing primers.
- b. Table S2. Related to Figure 1: IPS genotypes for TALEN isogenic series.
- c. Table S3. Related to Figures 3, 4 and 6: Differentially regulated transcripts identified from RNA sequencing of TALEN isogenic IPS-CMs.
- d. Table S4. Related to Figures 3, 4 and 6: Differentially regulated transcripts identified from RNA sequencing of P-S iPS-CMs.
- e. Table S5. Related to Figure 3: Principle components gene list.
- f. Table S6. Related to Figure 5: Liquid chromatography – tandem mass spectroscopy (LC-MS/MS) of steady state metabolites in conditioned media from TALEN isogenic iPS-CMs correlated to AMPK activity.
- g. Table S7. Related to Figure 7: Differentially regulated transcripts identified from RNA sequencing of mouse HCM treated with A769662 or DMSO control.

### 3. Supplemental Movies and Legends

- a. Movie S1. Related to Figure 2: P<sub>AT</sub><sup>WT/WT</sup> CMT paced at 1 Hz.
- b. Movie S2. Related to Figure 2: P<sub>AT</sub><sup>N488I/WT</sup> CMT paced at 1 Hz.

### 4. Supplemental Experimental Procedures

- a. LC-MS/MS metabolomics
- b. Cardiac microtissue (CMT) platform
- c. Mouse protocols, cardiac imaging, and fibrosis quantification
- d. Traction force microscopy
- e. BRDU assay

### 5. Supplemental References