Supplementary Figure legends

Supplementary Figure 1. Validation of iPSC lines derived from patient blood mononuclear cells for DCM Patient 1. A) Immunofluorescence with pluripotency markers (left to right: Nanog, OCT4, SSEA-4 and TRA-1-60). B) Trilineage differentiation potential demonstrated with immunofluorescence for mesoderm, ectoderm and endoderm (left to right: Brachyury, Otx2 and Sox17). C) Quantified gene expression of pluripotency markers using RT-PCR in iPSCs vs. cardiomyocytes derived from iPSCs. D) Karyotyping showing normal chromosome number.

Supplementary Figure 2. Validation of iPSC lines derived from patient blood mononuclear cells for Control Subject 2. A) Immunofluorescence with pluripotency markers (left to right: Nanog, OCT4, SSEA-4 and TRA-1-60). B) Trilineage differentiation potential demonstrated with immunofluorescence for mesoderm, ectoderm and endoderm (left to right: Brachyury, Otx2 and Sox17). C) Quantified gene expression of pluripotency markers using RT-PCR in iPSCs vs. cardiomyocytes derived from iPSCs. D) Karyotyping showing normal chromosome number.

Supplementary Figure 3. Validation of iPSC lines derived from patient blood mononuclear cells for DCM Patient 2. A) Immunofluorescence with pluripotency markers (left to right: Nanog, OCT4, SSEA-4 and TRA-1-60). B) Trilineage differentiation potential demonstrated with immunofluorescence for mesoderm, ectoderm and endoderm (left to right: Brachyury, Otx2 and Sox17). C) Quantified gene expression of pluripotency markers using RT-PCR in iPSCs vs. cardiomyocytes derived from iPSCs. D) Karyotyping showing normal chromosome number.

Supplementary Figure 4. Clustering single cells into sub populations based on response levels of nuclear PKA. Pharmacological agents: Ang II: angiotensin II (1 μM); SI (10 μM); SII (10 μM); iso: isoproterenol (10 μM); nor: norepinephrine (10 μM); epi: epinephrine (10 μM); phen: phenylephrine (10 μM); carv: carvedilol (1 μM), ET-1: endothelin-1 (100 nM); fors: Forskolin (5 μM); PMA (1 μM); in healthy controls and dilated cardiomyopathy patients. Left panels: Response clusters generated per subject; right panels: percent of cells within each cluster. Water, acetic acid and ascorbic acid were vehicles for Ang II ligands, ET-1 and adrenergic receptor ligands.

Supplementary Figure 5. Clustering single cells into sub populations based on response levels of cytoplasmic ERK. Pharmacological agents: Ang II: angiotensin II (1 μM); SI (10 μM); SII (10 μM); iso: isoproterenol (10 μM); nor: norepinephrine (10 μM); epi: epinephrine (10 μM); phen: phenylephrine (10 μM); carv: carvedilol (1 μM), ET-1: endothelin-1 (100 nM); fors: Forskolin (5 μM); PMA (1 μM); in healthy controls and dilated cardiomyopathy patients. Left panels: Response clusters generated per subject; right panels: percent of cells within each cluster. Water, acetic acid and ascorbic acid were vehicles for Ang II ligands, ET-1 and adrenergic receptor ligands.

Supplementary Figure 6. Clustering single cells into sub populations based on response levels of nuclear ERK. Pharmacological agents: Ang II: angiotensin II (1 μM); SI (10 μM); SII (10 μM); iso: isoproterenol (10 μM); nor: norepinephrine (10 μM); epi: epinephrine (10 μM); phen: phenylephrine (10 μM); carv: carvedilol (1 μM), ET-1: endothelin-1 (100 nM); fors: Forskolin (5

μM); PMA (1 μM); in healthy controls and dilated cardiomyopathy patients. Left panels: Response clusters generated per subject; right panels: percent of cells within each cluster. Water, acetic acid and ascorbic acid were vehicles for Ang II ligands, ET-1 and adrenergic receptor ligands.

Supplementary Figure 7. Tracking differences in calcium handling in hiPSC-CMs between healthy control subjects and patients with dilated cardiomyopathy. Calcium handling features with and without treatment with 10 μM isoproterenol. Features shown: Time to 50% peak (s), Time to 90% peak (s), Inter event interval (s), Decay tau (s). Values are expressed as mean ± SEM (*p≤0.05, paired t-test, n=3 per subject).