Supplementary Data

Figure S1. Global gene expression analyses of re-programmed 3T3/D3 cells. (A) Heat map of z-scored values for 3286 genes showing significant differences (p<0.001 and absolute log fold change of >1) between 3T3 and 3T3/D3 cells and the expression level of same genes in D3 cells. (B) Heat map of z-scored 99 genes down-regulated in 3T3 cells and up-regulated in D3 and 3T3/D3 cells. A partial list of up regulated or down regulated genes common to 3T3/D3 and D3 cells is shown in table 1 of the main text. (C) 3,286 genes found to be differentially expressed between 3T3 and 3T3/D3 cell types were categorized with respect to functional groups as per the software EASE (<u>http://david.niaid.nih.gov/david/ease.htm</u>). These functional groups include the modulation in the expression of genes involved in chromatin remodeling and methyltransferase activities.

Figure S2: 3T3/D3 cells acquire Cardiomyocyte and endothelial cell morphology. Phase contrast images showing cardiomyocyte and endothelial cell-like morphology of 3T3/D3 cells when cultured under conditions conducive to CMC or EC differentiation, in vitro.

Figure S3: Neuronal and adipogenic differentiation of 3T3/D3 cells.

Cells were cultured under neuronal and adipogenic differentiation conditions (*see methods in main text*) and the expression of neuronal markers (**A**) and adipocyte marker (**B**) were assessed by immunocytochemical staining. Representative images are shown.

Figure S4: Endothelial and smooth muscle differentiation of 3T3/D3 cells transplanted in the ischemic hind limb. Tissue sections from ischemic hind limbs transplanted with 3T3/D3 or 3T3/3T3 cells were analyzed for EC and skeletal muscle differentiation of transplanted cells. Fluorescent microscopy was conducted to visualize co-localization of CD31+ (green) and DiI+ (red) cells and alpha-SMA+ (green) and DiI+ (red) cells to determine EC and muscle differentiation, respectively and images in the same visual field were merged to generate composite images. As shown in **Fig. S4A** many CD31+DiI double positive cells (indicated by yellow fluorescence) were observed in the ischemic tissue of mice treated with 3T3/D3 cells compared to those treated with 3T3/3T3 cells. Similarly, a large number of 3T3/D3 cells coexpressed muscle marker, α -SMA, in the ischemic hind limbs while very few α -SMA +DiI double positive cells in 3T3/3T3 treated mice were observed (**Fig. S4B**). Similar patterns were observed when tissue sections were stained with additional EC and muscle cell markers (Isolectin B4 and desmin; data not shown).

Figure S5. Transplanted 3T3/D3 cells proliferate in the ischemic myocardium. We determined the number of proliferating GFP+ transplanted cells in the infracted myocardium 28 days following AMI and cell transplantation. A higher number of proliferating cells, (nuclei stained positive for Ki67 (red) were also observed in the myocardial sections from 3T3/D3 (yellow fluorescence) treated mice as compared to 3T3/3T3 cell treated mice (p<0.05).







1=Apoptosis (1%) 2=Catalytic activity (2.5%) 3=Cell cycle (3%) 4=Cell differentiation (2.5%) 5=Cell growth (9%) 6=Cell proliferation (5.5%) **7=Chromatin (1.2%)** 8=Cytoskeleton (0.8%) 9=Development (4.3%) 10=Intracellular (6.7%) 11=Kinase activity (2.5%) **12=Metabolism (11.8%)** 13=Methyltransferase (0.9%) 14=Transcription (7.1%) 15=Physiol. process (9.6%) **16=Signal transduction (7%) 17=Protein modification (2%)** 18=Other/unknown (22.6%)

Figure S1C



3T3/D3



Cardiomyocyte Differentiation

Endothelial Cell Differentiation



3T3/D3



Neuronal

Adipocyte



DiI+CD31

DiI+aSMA

