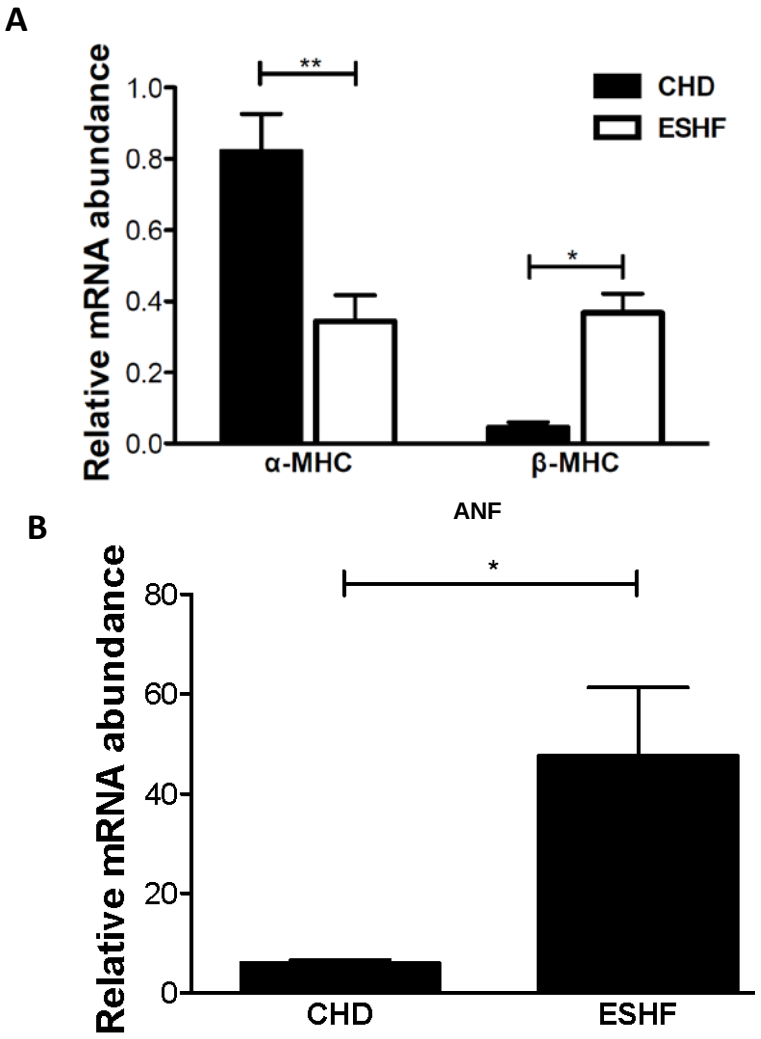

Fig. S1. ESHF myocardium switches back to a fetal gene program. Quantitative RT-PCR from ESHF myocardium demonstrated decrease expression of **(A)** α-MHC as compared to CHD myocardium (α-MHC: CHD, n=5, 0.82±0.1%, vs ESFH, n=5, 0.34±0.7%, *P*<0.001) and increased expression of β-MHC as compared to CHD myocardium (β-MHC: CHD n=5, 0.05±0.01 vs. ESHF, n=4, 0.37±0.05, *P*<0.05) as analyzed by 2 Way ANOVA. **(B)** Expression of ANF in ESHF as compared to CHD myocardium (CHD, n=5, 6.0±0.63%, vs ESHF n=4, 47.7±13.7%, *P*= 0.0159). Data analyzed by t-test (non-parametric) and presented as mean±SEM.

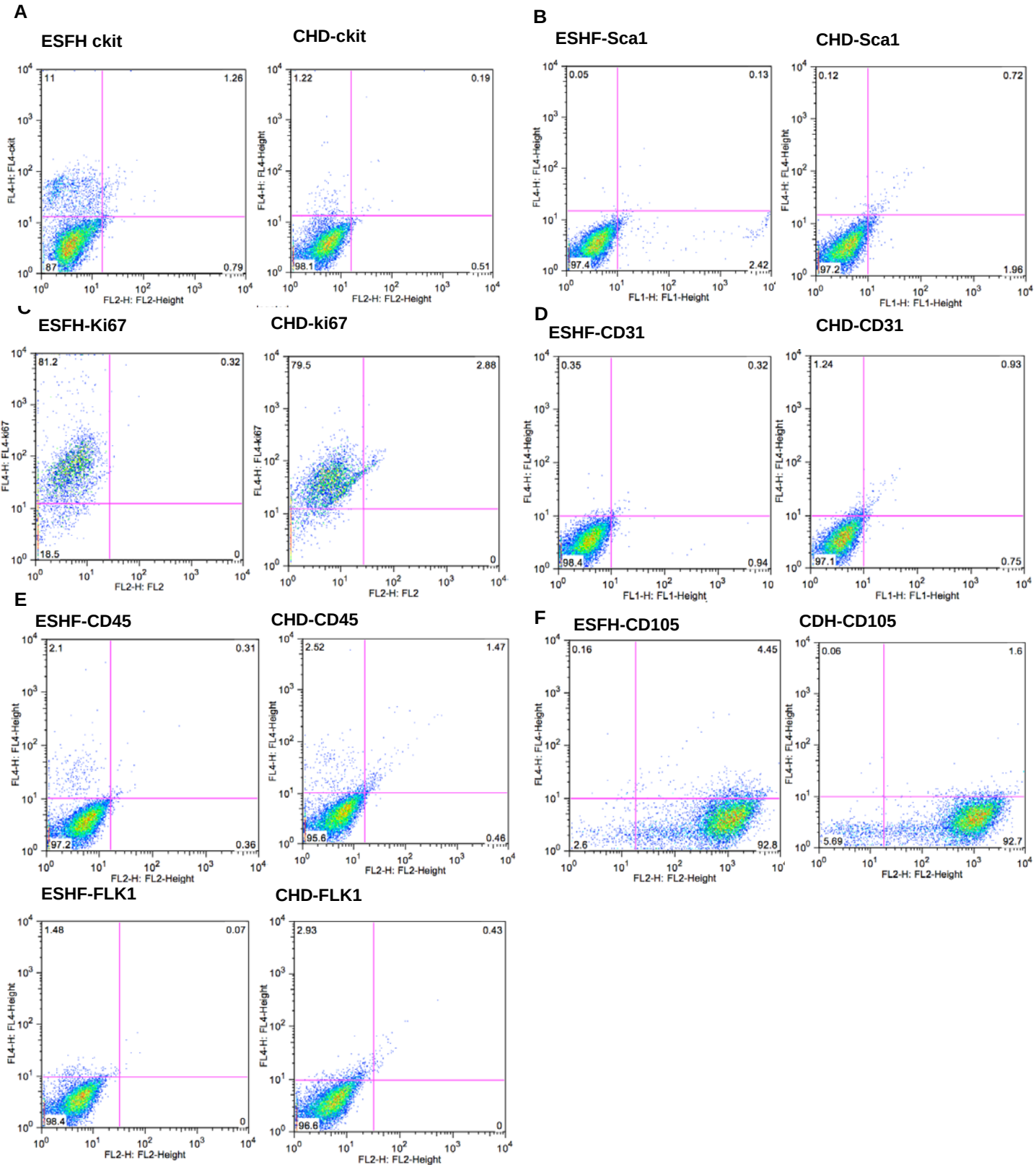

Fig. S2. Representative dot plot of FACS analysis of antigenic phenotype of ESHF and CHD derived CDCs. Stem cell related markers, c-kit+ and Sca-1, expression was significantly higher in ESHF derived CDCs in comparison to CHD derived CDCs. Both types of CDCs had similar growth potential as determined by expression of Ki67. No significant differences was determined for expression of CD105, CD31, FLK and CD45.

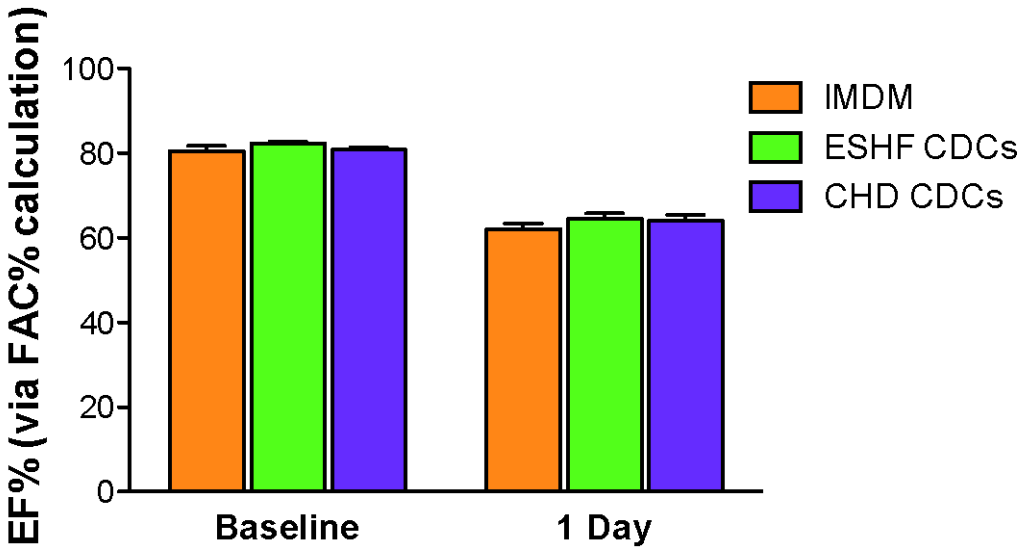

Fig. S3. Validation of MI model. To ensure the consistency of the acute MI model, echocardiography was randomly performed 1 day after LAD ligation in all three groups and demonstrated similar EFs in all three groups.

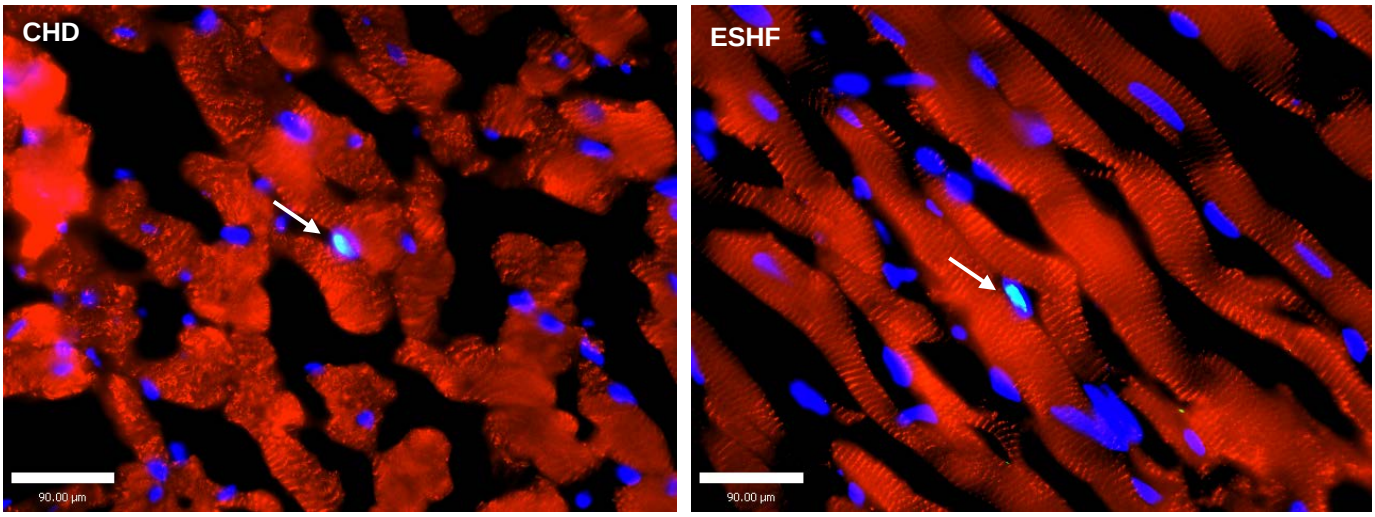

Fig. S4. Differentiation and retention of injected CDCs. ESHF (left) or CHD (right) derived CDCs have the potential to differentiate into cardiomyocytes at 4 weeks after transplantation in infarcted myocardium of rodents. After 28 post-operative days, very few (<0.05%) ESHF-derived or CHD derived CDCs were tracked in the rodent myocardium.

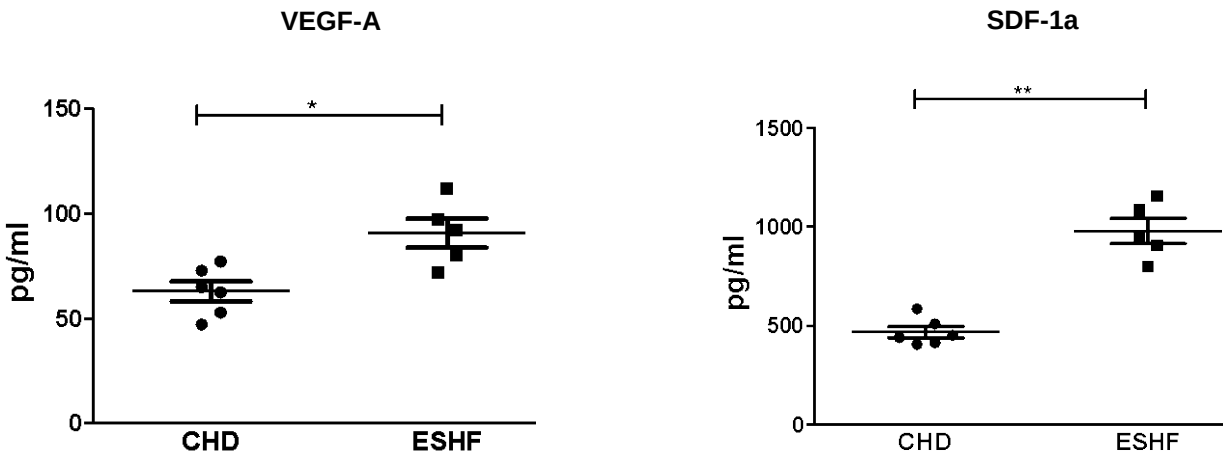

Fig. S5. Secretome profile of CHD and ESHF derived CDCs. The secretion of paracrine factors VEGF-A (*P*= 0.0173) and SDF-1α (*P*= 0.0043) was significantly higher from ESHF derived CDCs as compared to CHD derived CDCs (*P*= 0.0173, *P*= 0.0043; respectively). Data was analyzed using non-parametric test followed by Mann-Whitney post hoc test

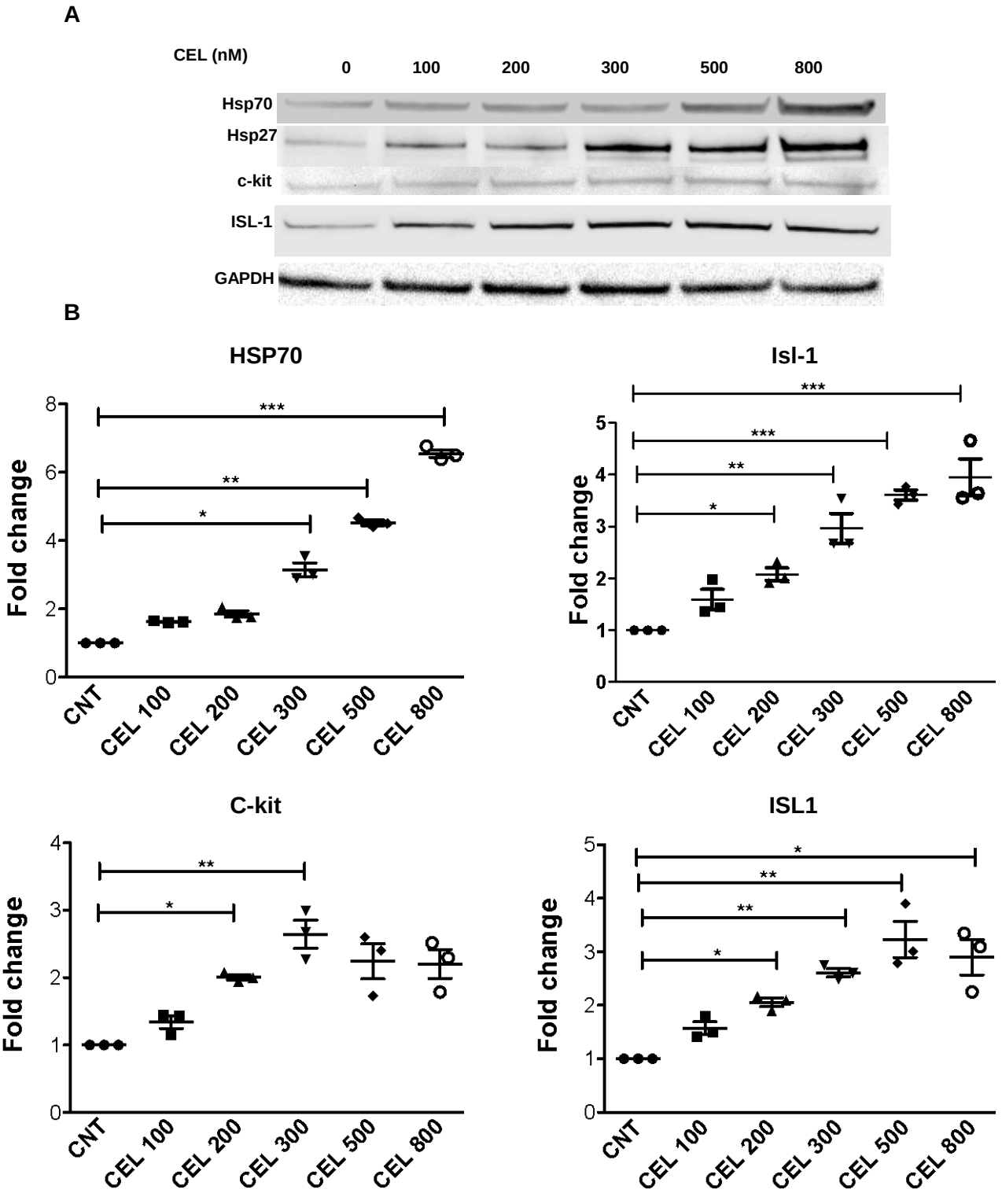

Fig. S6. Effect of CEL on CDH derived CDCs. (**A).** Immunoblot analysis showed that the HSR increased Hsp70 and Hsp27. (**B).** Bands were quantified on Odyssey Systems®. Quantification with respect to GAPDH normalization. ANOVA (Tukey test) and represented as Mean± S.E.M. *P < 0.05, **P < 0.01,***P < 0.001.

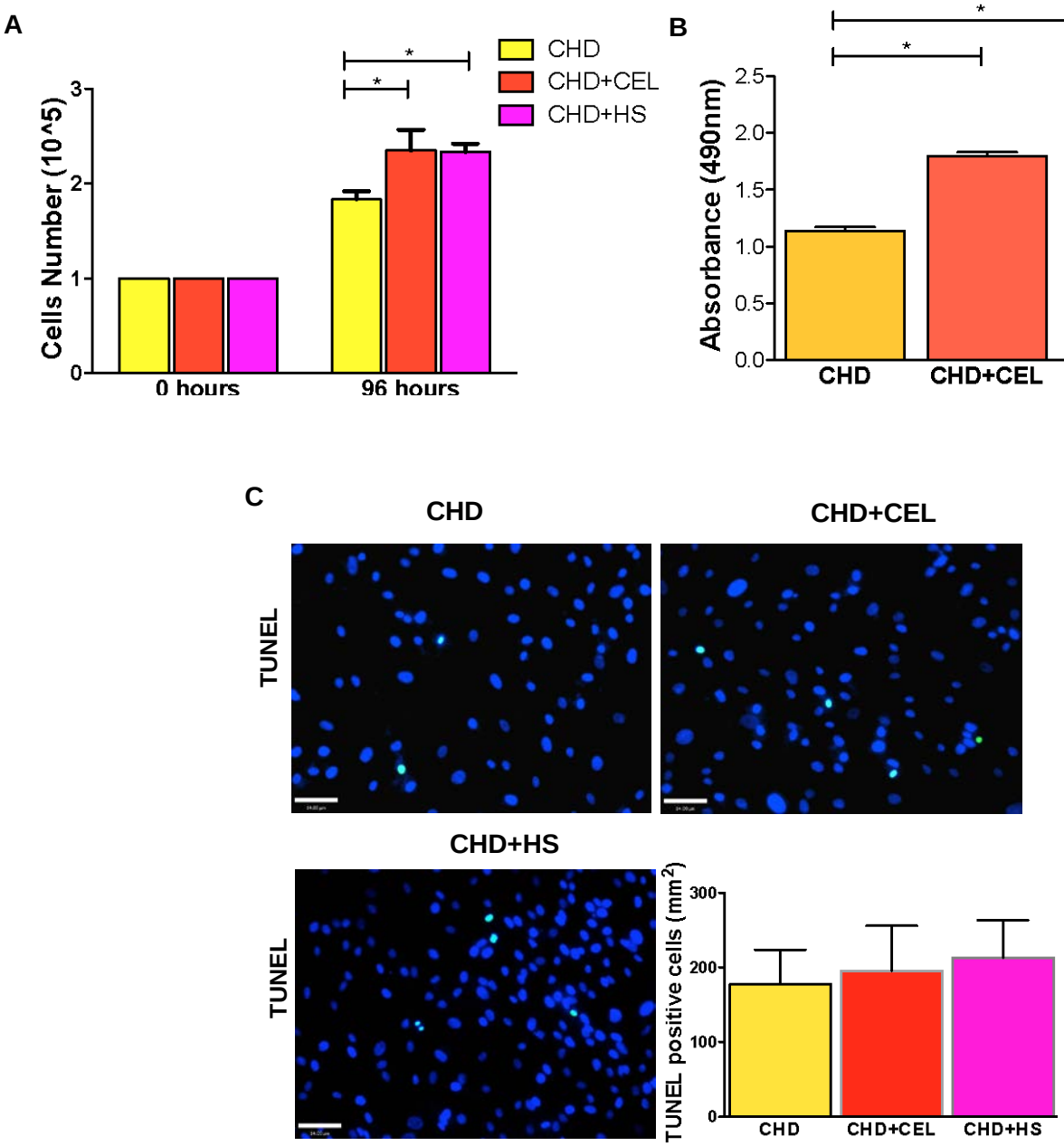

Fig. S7. Effect of HSR or CEL treatment on cell proliferation, viability, and apoptosis of CHD derived hCDCs. **(A)** CHD derived CDCs resulted in a significant increase in cell numbers (**P* <0.05). **(B).** HS or CEL treatment significantly increased cell viability of CHD derived CDCs as determined by MTS assay (*P<0.5). **(C).** HS or CEL treatment of CHD derived CDCs resulted in no significant cell death as assessed by TUNEL assay. Data are analyzed by one way ANOVA, followed by Kruskal-Wallis post hoc test, **P*<0.05 was considered significant.

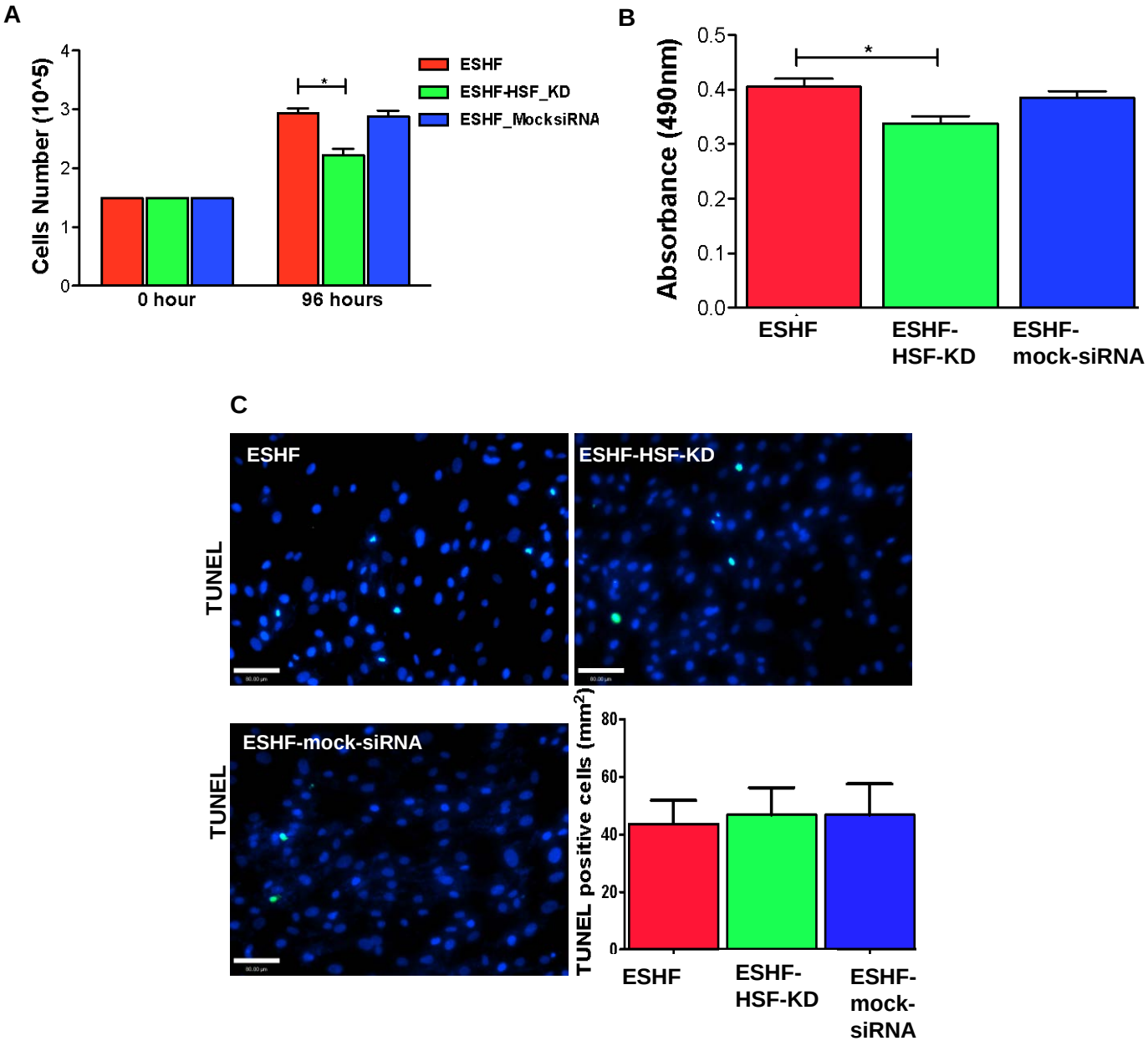

Fig. S8. Effect HSF-KD on ESHF derived CDCs. **(A)** HSF-1 knock down in ESHF derived CDCs resulted in a decrease in cell numbers after 96 hours as compared to control or mock siRNA (P <0.05).
(B). Knock down of HSF-1 showed a reduction in cell viability (P=0.0218) as determined by MTS assay.
(C) HSF-1 knockdown in ESHF derived CDCs resulted in no significant cell death as assessed by TUNEL assay. Data are analyzed by one way ANOVA, followed by Kruskal-Wallis post hoc test, *P<0.05 was considered significant.

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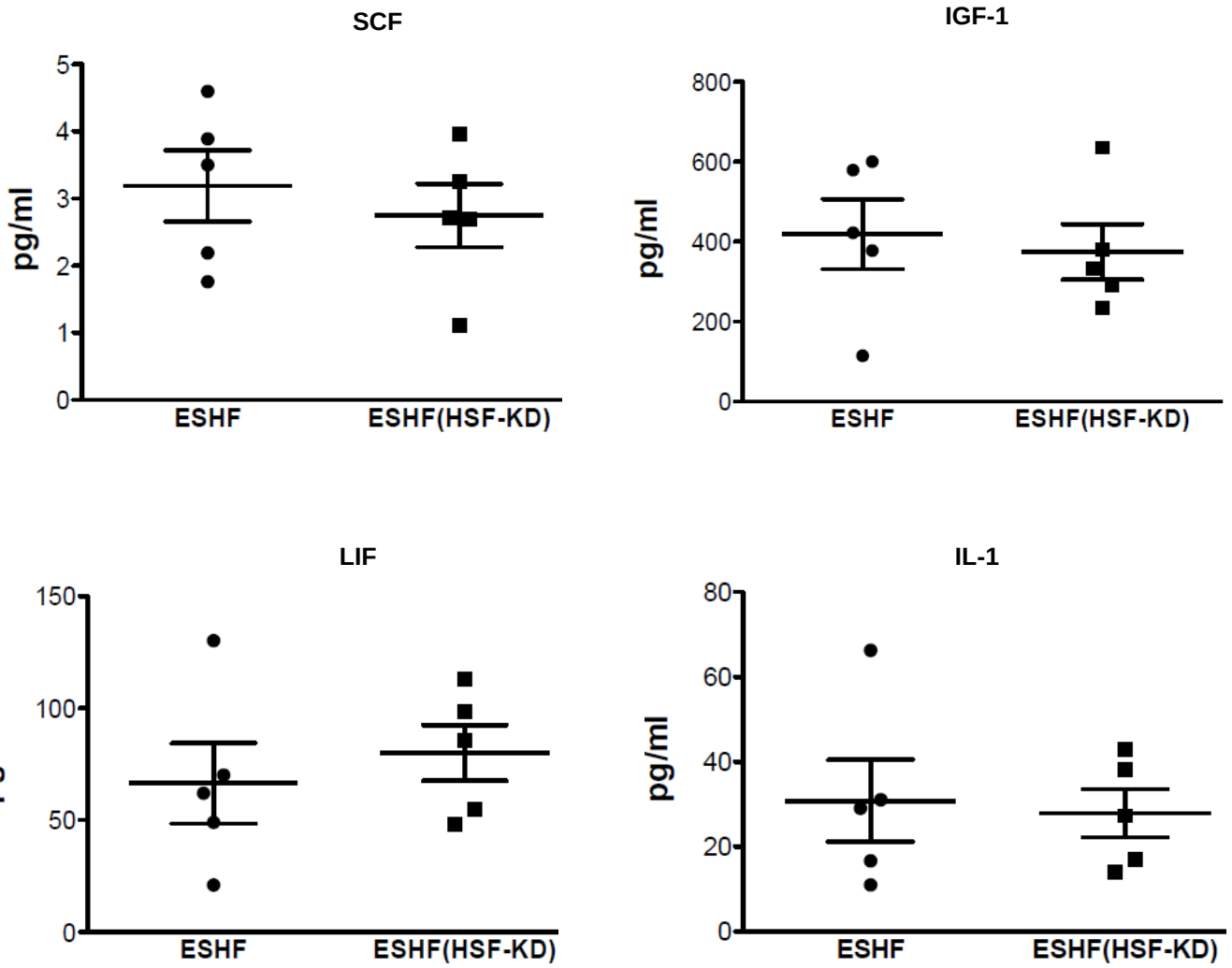

Fig. S9. Effect of HSR on the release of paracrine factors by CDH-derived CDCs. HSF-1 expression was inhibited in ESHF-derived CDCs using siRNA. Inhibition of HSR resulted in no significant difference in SCF, IGF1, LIF and IL-1. Data are analyzed by non-paramatric t-test followed by Mann-Whitney's post hoc test and represented as mean± S.E.M.

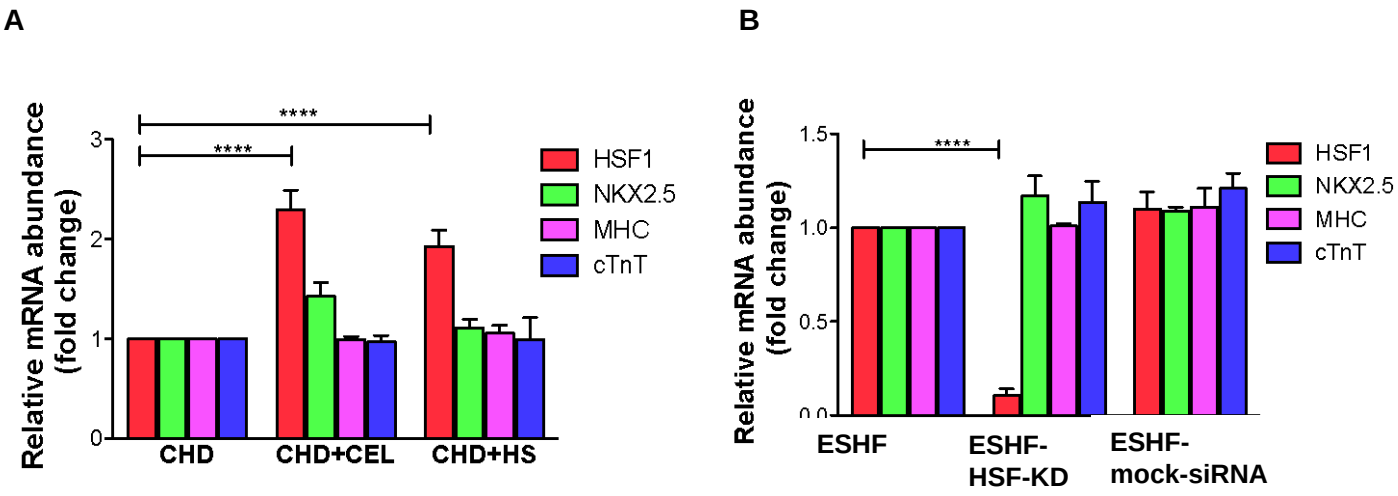

Fig. S10. Effect of HSR on expression of cardiovascular commitment/differentiation genes. CHD derived CDCs were treated with CEL or HS or ESHF derived CDCs were knocked down for HSF1. Then, the expression levels of HSF1, Nkx2.5, MHC and cTnT were assayed. **(A).** HSF-1 expression was significantly higher after CEL or HS treatment but the expression levels of Nkx2.5, MHC or cTnT remained unaffected. **(B).** HSF-1 expression was knocked down in ESHF derived CDCs using siRNA. Inhibition of HSF-1 resulted in no significant change in expression levels of Nkx2.5, MHC or cTnT . Data are analyzed by non-parametric t-test followed by Mann-Whitney's post hoc test and represented as mean± S.E.M.

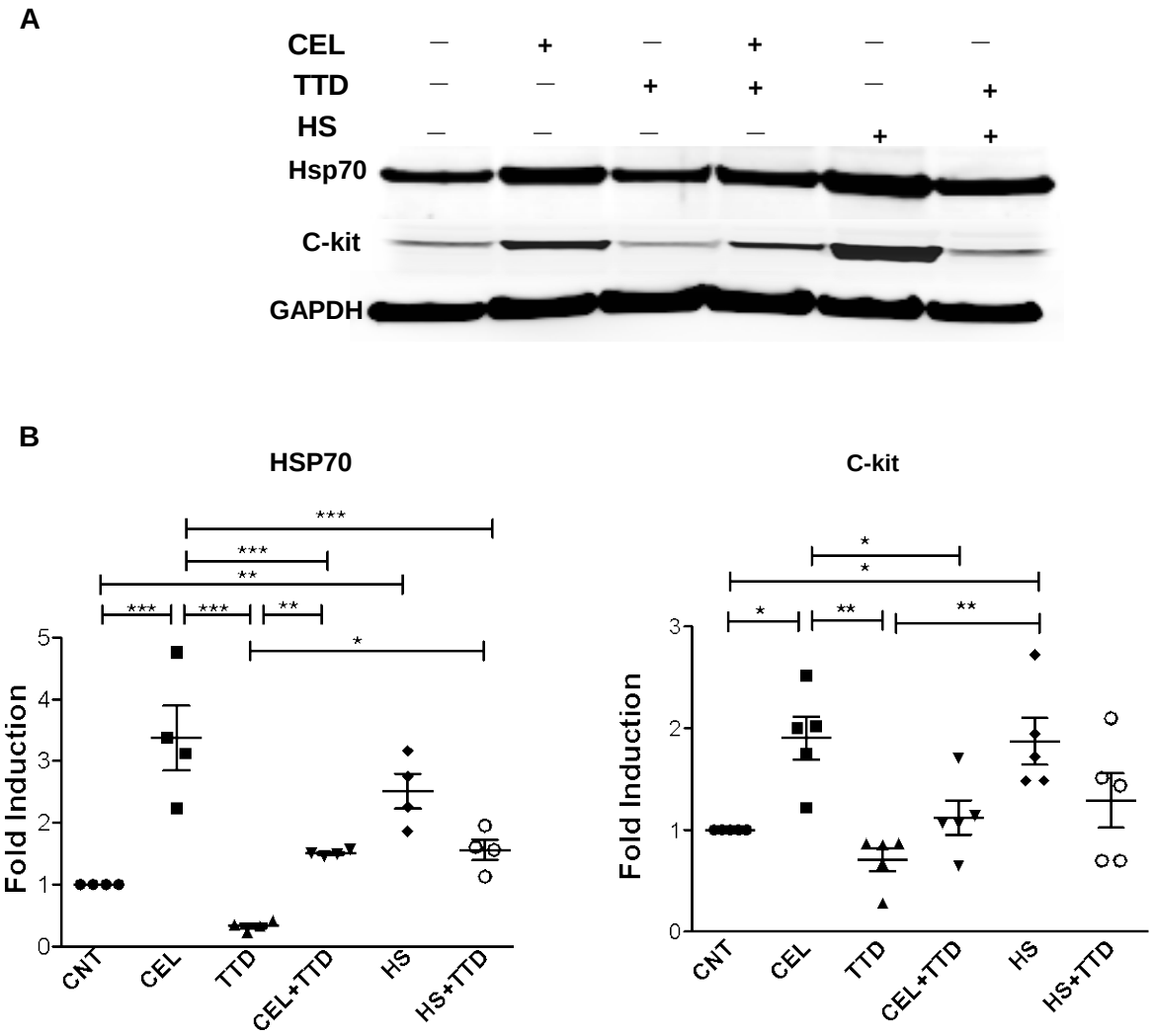

Fig. S11. Effect of CEL on CHD derived CDCs. **(A)** CDH derived CDCs were pre-treated with CEL or HS in the presence or absence of TTD and after 24 hours immunoblot analysis showed a 2 fold increase of c-kit expression and 3 fold increase of HSP70 expression after CEL or HS treatment which was diminished by TTD. (**B)** Quantification of Hsp70 (CEL, n=4, 3.4±0.5, HS, n=4, 2.5 ±0.3, TTD, n=4, 0.3±0.1 CEL+TTD, n=4, 1.5±0.02 and HS+TTD, n=4, 1.5±0.2) and c-kit protein (CEL, n=5, 1.9±0.2, HS, n=5, 1.88 ±0.23, TTD, n=5, 0.7±0.,1 CEL+TTD, n=5, 1.1±0.17 and HS+TTD, n=5,1.2±0.3) with respect to GAPDH after normalization with control per lane. Bands were quantified on Odyssey Systems®.Data using repeated measures. ANOVA (Tukey test) and represented as Mean± S.E.M. *P < 0.05, **P < 0.01, ***P < 0.001.

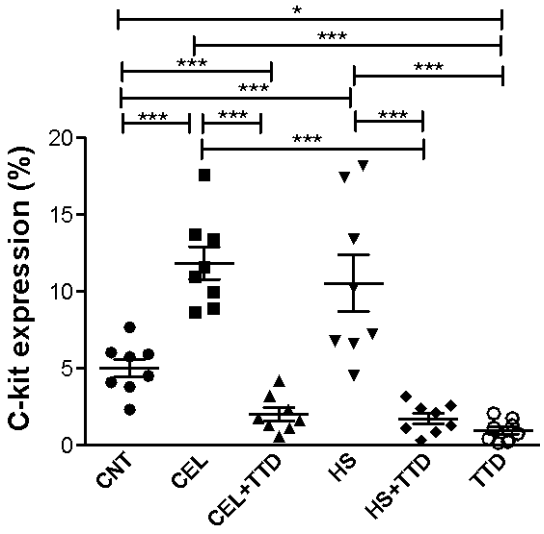

Fig. S12. FACS analysis showed HSR by CEL significantly increase c-kit^{+} cells in CHD-derived CDCs (CNT, n=8, 5.0±0.6%: vs CEL, n=8, 11.82±1.1%; vs CEL+TTD, n=8, 2.0±0.5%, TTD, n=8, 0.9±0.3%, HS, n=8, 10.5±1.8% and HS+TTD, n=8, 1.7±0.4%). Data are analyzed by repeated measures ANOVA, followed by Tukey post hoc test *P<0.05, **P<0.001, ***P<0.0001.