Supplementary Procedure:

1. *Masson's Trichrome (MT) Staining*- After sacrifice (on day 15th after surgery) Left ventricular tissue was fixed overnight in Karnovsky's fixative at 4^{0}C, followed by dehydration and paraffin embedding.[22] Processed tissues were sectioned (5µm thick) and stained with Accustain® Trichrome Stains (Masson) kit (Sigma-Aldrich, MO, Cat# HT15) to detect collagen deposition in the heart tissue following manufacturer's protocol. The components of the cardiac tissue were identified for collagen fibers (blue), myocytes (red) and interstitial space (white). Interstitial collagen volume fraction (CVF) was determined for the entire section of the heart stained with MT using an automated image analyzer (Image-Pro Plus version 6.1). The digitalized profiles were used to calculate CVF (the sum of all connective tissue areas divided by the sum of all connective tissue and myocyte areas).

2. *Immunofluorescence Study*- Cells grown on cover slips were treated with IL-6 (for 20min) and stained with primary phospho-antibodies of STAT1(Tyr701), STAT3(Tyr705), p38MAPK and ERK1/2, followed by incubation with labelled secondary antibodies [Alexa fluor®488, Alexa fluor®594, Alexa fluor®633 (Molecular Probes, OR) as described earlier.[22] After mounting with Vectashield [with DAPI] (Vector Laboratories, CA), slides were examined under fluorescent microscope (OlympusBX51, Progres®C5).

3. *Cell viability assay*- Viability of the cells in culture upon treatment with different inhibitors was determined by CellTiter96® AQ_{ueous} One Solution Cell Proliferation Assay (Promega, WI) kit following manufacturer's protocol. In brief, 75-80% confluent cells were treated with different inhibitors for different time period in mammalian cell culture environment followed by 4h incubation with CellTiter reagent. The colour formation was quantified spectrophotometrically at 490nm. The absorbance is directly proportional to the number of living cells in culture and the percent viability of cells was calculated considering 100% viability of untreated cells.

Supplementary Table 1-2:

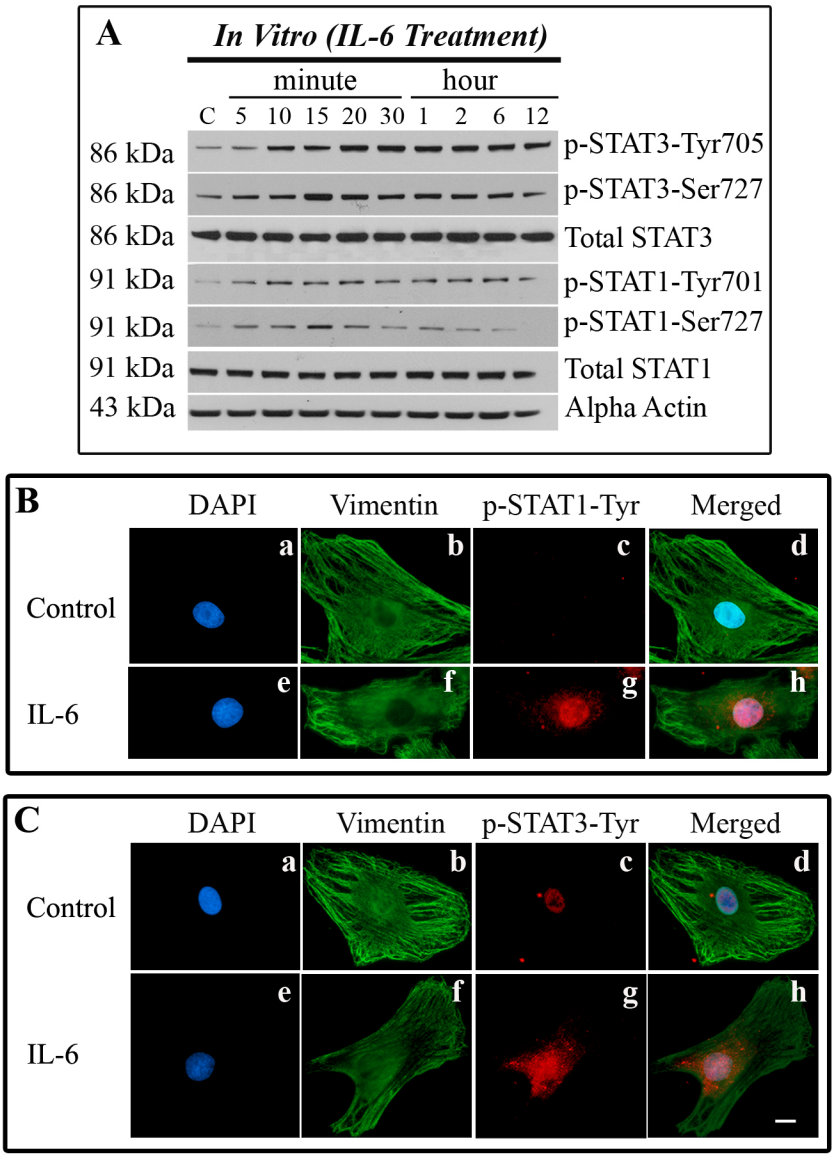
Table-1: Table showing RT-PCR Primer sequences, Annealing Temperature and Amplified Product size:

Gene Name	Primer Sequence (5'-3')	Annealing Temperature (°C)	Product Size (bp)
ANF	F- CACCAAGGGCTTCTTCCTC R- CGAGAGCACCTCCATCTCTC	57.5	272
β-MHC	F- CCATACAGAGGACGGAGGAG R- GCCTCCTTCTGGGAAGACTC	57.5	286
c-myc	F- CCACTGGTCCTCAAGAGGTG R- CTGTTCTCGCCGTTTCCTC	58.5	399
c-jun	F- ACAGTGAGCCTCCGGTCTAC R- GCTCCTGAGACTCCATGTCG	58.0	273
c-fos	F- GGAGGAGGGAGCTGACAGA R- GGTGAAGGCCTCCTCAGACT	58.5	251
collagen 1	F- CTGCTGGAGAACCTGGAAAG R- GAAACCTCTCTCGCCTCTTG	58.0	282
collagen 3	F- GCCTTCTACACCTGCTCCTG R- GATCCAGGATGTCCAGAGG	55.5	303
MMP-2	F- ACACTGGGACCTGTCACTCC R- AGTGGCTTGGGGTATCCTCT	55.0	290
MMP-9	F- CACTGTAACTGGGGGCAACT R- AGGGGAGTCCTCGTGGTAGT	59.0	286
TIMP-1	F- TCCCCAGAAATCATCGAGAC R- GAGCAGGGCTCAGATTATGC	55.0	259
TIMP-2	F- GCATCACCCAGAAGAAGAGC R- GGGTCCTCGATGTCAAGAAA	56.0	250
LOX	F- CCAACATTACCACAGCATGG R- CCAGGTAGCTGGGGTTTACA	55	281
GAPDH	F- GGGGTGATGCTGGTGCTGAG R- GATGCAGGGATGATGTTCTG	58.0	370

Table-2: Table showing Real time RT-PCR Primer sequences, Annealing Temperature and Amplified Product size:

Gene Name	Primer Sequence (5'-3')	Annealing Temperature (°C)	Product Size (bp)
collagen 1	F- AGCAAAGGCAATGCTGAATCGTCC R- TGCCAGATGGTTAGGCTCCTTCAA	59.0	125
collagen 3	F- ATGTCCTTGATGTACAGCTGGCCT R- CATTGCCATTGGCCTGATCCATGT	59.0	114
MMP-2	F- TGTGCTGAAGGACACCCTCAAGAA R- TCTGATTCTTGTCCCACTTGGGCT	59.0	167
MMP-9	F- TTCTCGAATCACGGAGGAAGCCAA R- AAGGCTGAGTTCAACTTTGCAGGC	59.0	89
TIMP-1	F- TCCCTTGCAAACTGGAGAGTGACA R- CCAAGGTATTGCCAGGTGCACAAA	59.0	136
TIMP-2	F- AGTTTCTTGACATCGAGGACCCGT R- ACTAGCGTGAACCCACTTGGATGA	59.0	153
LOX	F- TGAATTCAGCCACTACGACCTGCT R- TGTGTGTGCAGTACAGGCAAATCG	59	136
GAPDH	F- TGACTCTACCCACGGCAAGTTCAA R- ACGACATACTCAGCACCAGCATCA	59.0	141

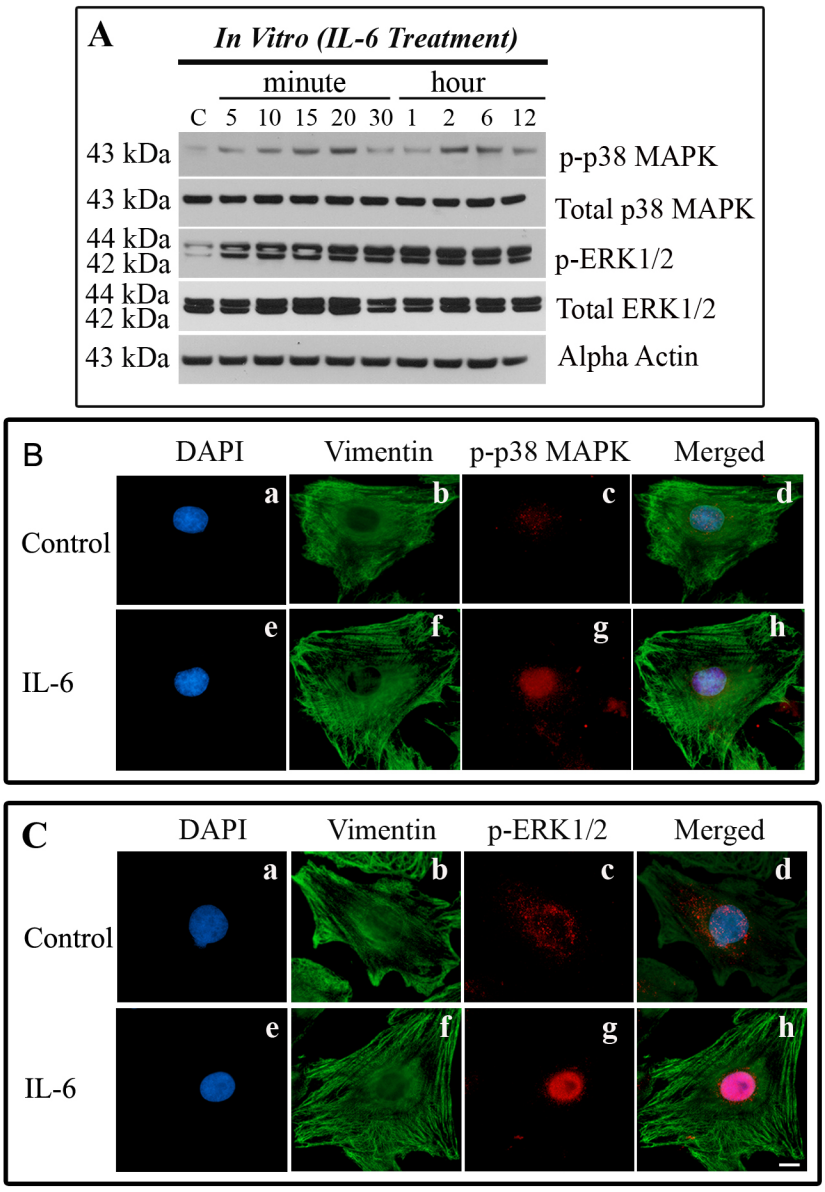
Supplementary Figure 1



Supplementary Figure-1:

Phosphorylation of STAT proteins during hypertrophy *in vitro*.
A. Western blot analysis showing time dependent phosphorylation of STAT3 at Tyr705 as well as Ser727 and STAT1 at Tyr701 as well as Ser727 position in cardiac fibroblasts treated with IL-6. Total STAT1 and STAT3 remained unchanged in both treatments (n=3).
B-C. Immunofluorescence micrographs (100X) of cultured cardiac fibroblasts grown on coverslips, treated with IL-6 for 20m and stained with p-STAT1-Tyr701 and p-STAT3-Tyr705 antibodies. Micrograph showing phosphorylation and nuclear translocation (red; c,d,g,h) of STAT1 (B) and STAT3 (C) upon induction with IL-6 (e-h) compared to untreated cells (a-d). Fibroblast specificity was confirmed by counterstaining the cells with anti-vimentin antibody (green; (b,d,f,h). Nuclei were stained with DAPI (blue). At least 200 cells per experiment (n=5) were examined during the experiment.
[Bar=50μM].

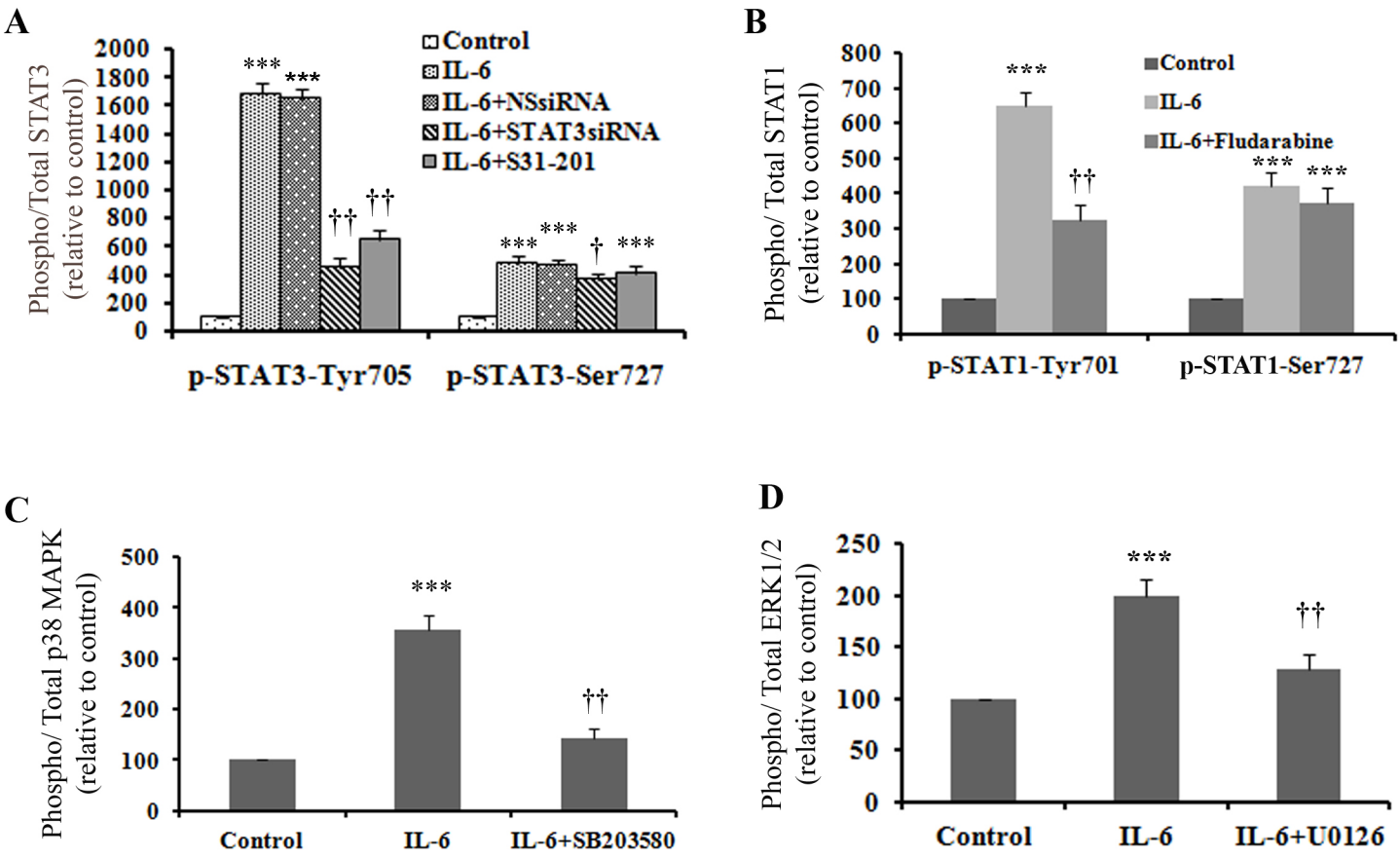
Supplementary Figure 2



Supplementary Figure-2:

Phosphorylation of MAPK and ERK1/2 proteins during hypertrophy *in vitro*.
A. Western blot analysis showing time dependent phosphorylation of p38MAPK and ERK1/2 *in vitro*, in IL-6 treated fibroblasts compared to untreated cells. Total p38MAPK and ERK1/2 expression was unchanged in both groups (n=3).
B-C. mmunofluorescence micrographs (100X) of cultured cardiac fibroblasts grown on cover slips, treated with IL-6 (20 min) and stained with p-p38MAPK and p-ERK1/2 antibody. Micrograph showing phosphorylation and nuclear translocation (red; c,d,g,h) of p38MAPK (B) and ERK1/2 (C) upon induction with IL-6 (e-h) compared to untreated cells (a-d). Fibroblast specificity was confirmed by counterstaining the cells with anti-vimentin antibody (green; b,d,f,h). Nuclei were stained with DAPI (blue). At least 200 cells per experiment (n=5) were examined during the experiment.
[Bar=50μM].

Supplementary Figure 3



Supplementary Figure-3:

A. Graphical representation of Western blotting results showing phosphorylation of STAT3 (Tyr705) and (Ser727) in cultured cardiac fibroblasts upon IL-6 treatment (20min). Phosphorylation of STAT3 at Tyr705 was significantly reduced by treatment with S31-201 and STAT3 siRNA. No significant change in p-STAT3-Ser727 and total STAT3 level was observed with S31-201 treatment. However, p-STAT3-Ser727 level showed significant reduction (1.3 ±0.14 fold; $p<0.05$) with STAT3 siRNA treatment. Results are expressed as ±SEM of 3 independent experiments. (***$p<0.001$ with respect to Control, †† $p<0.01$ and † $p<0.05$ with respect to IL-6+DMSO or IL-6+NSsiRNA treatment; NS siRNA= non specific siRNA treatment)

B. Graphical representation of western blotting results showing significant downregulation of p-STAT1-Tyr701 but no significant change in p-STAT1-Ser727 with fludarabine in IL-6 induced cultured cardiac fibroblasts. Results are expressed as ±SEM of 3 independent experiments. (***$p<0.001$ with respect to control; †† $p<0.01$ with respect to IL-6 treatment).

C. Graphical representation of western blotting results showing significant downregulation of p-p38 MAPK with SB203580 in IL-6 induced cultured cardiac fibroblasts. Results are expressed as ±SEM of 3 independent experiments. (***$p<0.001$ with respect to control; †† $p<0.01$ with respect to IL-6 treatment).

D. Graphical representation of western blotting results showing significant downregulation of p-ERK1/2 with U0126 in IL-6 induced cultured cardiac fibroblasts. Results are expressed as ±SEM of 3 independent experiments. (***$p<0.001$ with respect to control; †† $p<0.01$ with respect to IL-6 treatment).