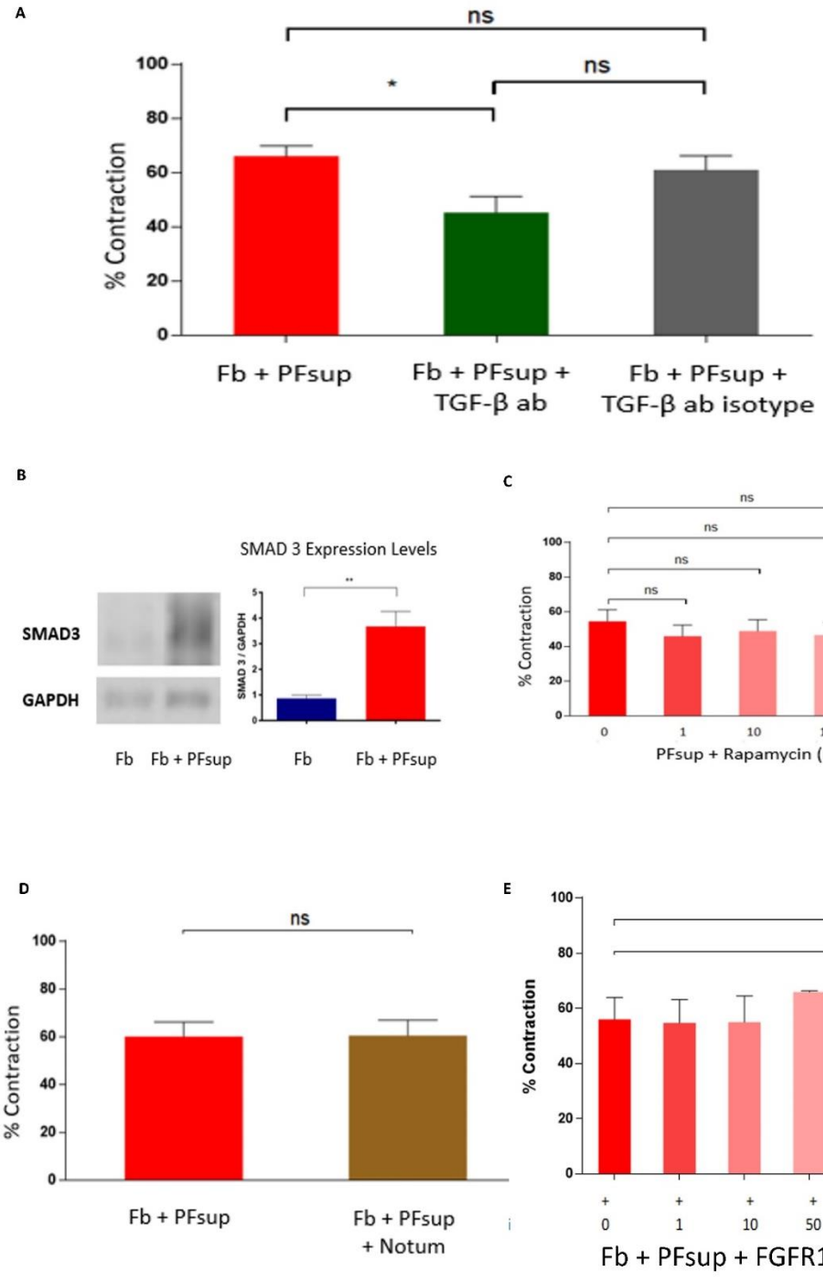
Supplemental Figure 1 Evaluation of potential upstream mediators of differentially expressed genes in the PFsup stimulated human cardiac derived fibroblasts. The ligands with the highest z-score are on the left (orange), whereas the ligands with the lowest z-score on the right (blue).

Supplemental Figure 2
(A) A pan TGF-β antibody and isotype was added to cardiac fibroblasts (n=10) exposed to PFsup, resulting in reduced fibrotic activity in vitro. (B) Lysates from human cardiac fibroblasts (n=3) exposed to PFsup were probed at the protein level using western blotting, confirming the expression of the SMAD proteins, where SAMD3 expression levels were significantly increased in fibroblasts treated with PFsup. (C) The addition of rapamycin to PFsup did not inhibit fibroblast activity in vitro (n=5). (D) The addition of Notum, an inhibitor of Wnt signaling, to the cardiac fibroblasts (n=5) that were exposed to PFsup did not significantly reduce fibrotic activity in vitro. (E) The addition of an FGF receptor inhibitor (FGFR1i) to cardiac fibroblasts (n=11) treated with PFsup did not result in a significant attenuation of fibrotic activity in vitro. For statistical purposes, a Student t-test was used and a $p<0.05$ was considered to be significant. Data are presented as mean +/- SD and $p<0.05$ is denoted with *, $p<0.01$ with **, and $p<0.001$ with ***.



Supplemental Figure 3

(A) Cardiac fibroblasts (n=5) treated with a concentration range of exogenous recombinant TGF-β1, where 10 nM was required to result in significant fibrotic activity in vitro. Student t-test was used for statistical purposes where p<0.05 was taken to be significant. (B) Upstream regulators were compared, identifying 8 plasma membrane proteins, including bone morphogenic protein receptor-1 (BMPR1). (C) Further in silico analysis revealed BMP4 to be a potential effector molecule for BMPR1. (D) Multiplex analysis confirmed the presence of BMP4 in PFsup of 8 patients undergoing CABG. (E) Dorsomorphin, a known inhibitor of BMP signaling was added to cardiac fibroblasts (n=9) exposed to PFsup, resulting in a notable reduction in fibrotic activity in vitro. A Student t-test was used and p<0.05 was taken to be significant. (F) Cardiac fibroblasts (n=5) treated with exogenous recombinant BMP4 had significant fibrotic activity in vitro at the same concentration range as was found in PFsup. A Student t-test was used where p<0.05 was considered to be significant. Data are presented as mean +/- SD and p<0.05 is denoted with *, p<0.01 with **, and p<0.001 with ***.