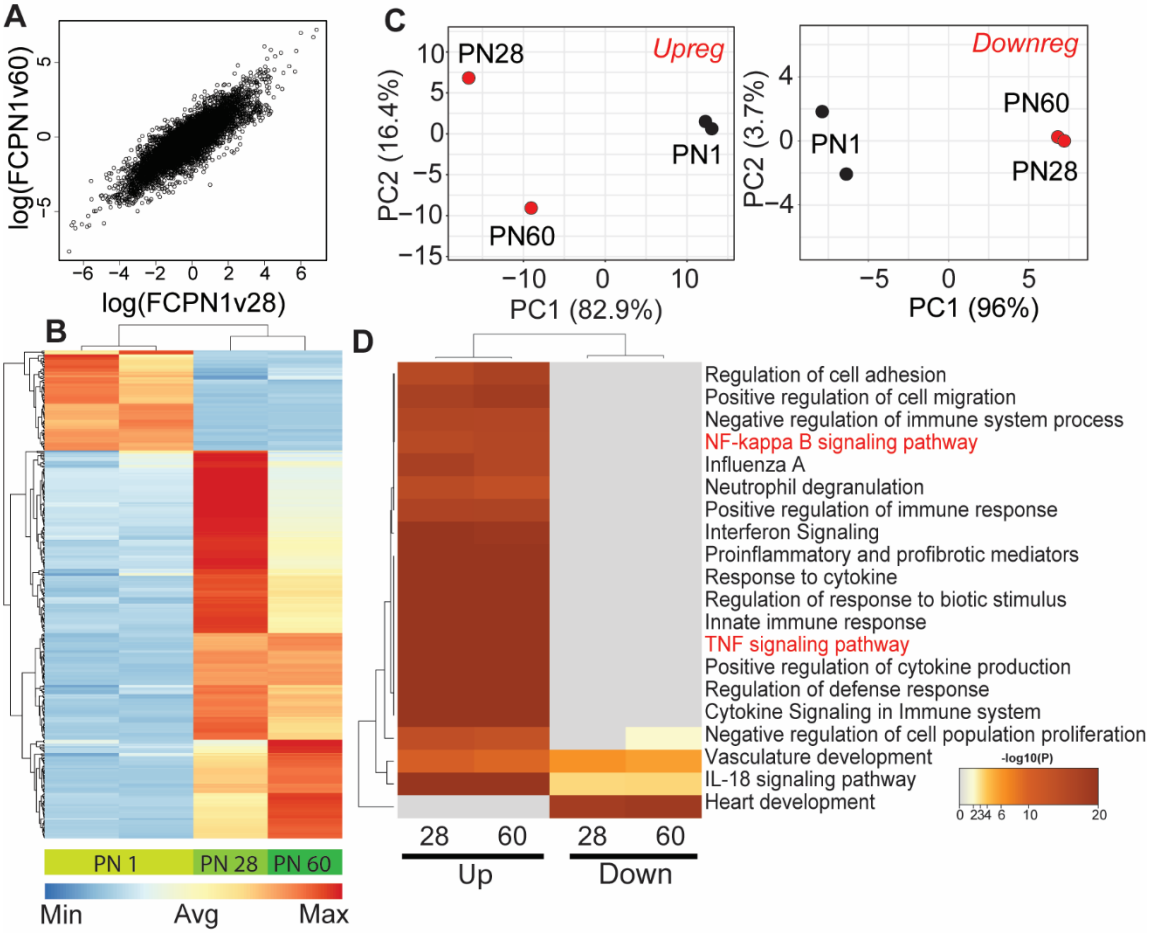

Fig. S1. Inflammatory signatures dampen regenerative capacity in adult hearts. (A) Scatter plot showing strong correlation between up/down-regulated genes after 28 and 60 days. **(B)** Heatmap of top 500 differentially expressed genes. **(C)** Principal component analysis (PCA) of differentially expressed genes. Age drives the majority of variance in the dataset. **(D)** Metascape gene ontologies of differentially expressed genes.

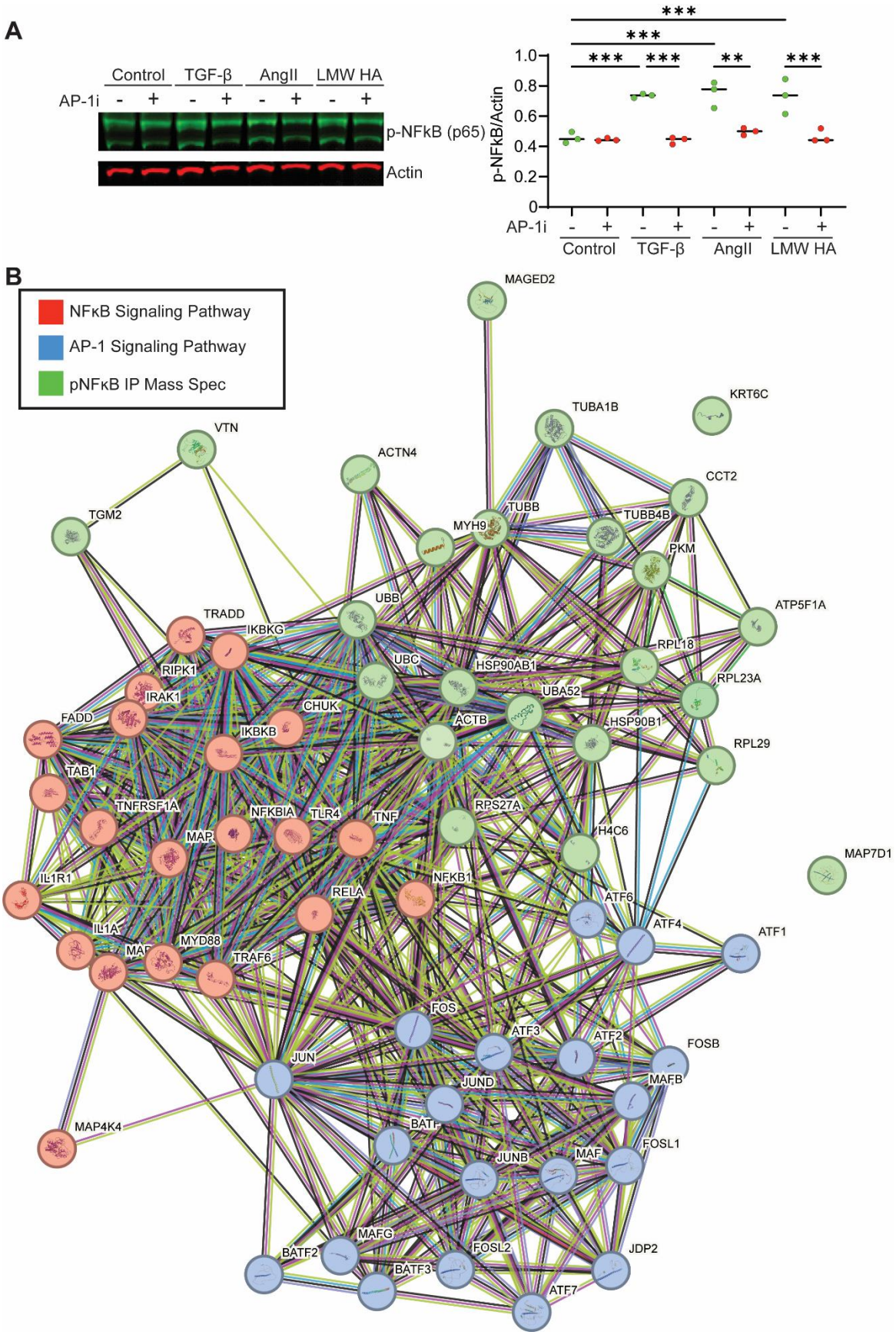
A
Control
TGF-β
AngII
LMW HA
AP-1i
p-NFkB (p65)
Actin
p-NFkB/Actin
***
**
B
NFκB Signaling Pathway
AP-1 Signaling Pathway
pNFκB IP Mass Spec
MAGED2
KRT6C
TUBA1B
VTN
ACTN4
CCT2
TGM2
TUBB
TUBB4B
MYH9
PKM
UBB
ATP5F1A
TRADD
IKBKG
RPL18
RIPK1
UBC
HSP90AB1
RPL23A
IRAK1
UBA52
CHUK
FADD
ACTB
HSP90B1
IKBKB
RPL29
TAB1
TNFRSF1A
NFKBIA
TLR4
TNF
RPS27A
H4C6
MAP7D1
MAP
IL1R1
NFKB1
RELA
ATF6
ATF4
ATF1
IL1A
MYD88
TRAF6
FOS
ATF3
ATF2
FOSB
JUN
JUND
MAFB
MAP4K4
BATF
FOSL1
JUNB
MAF
MAFG
FOSL2
JDP2
BATF2
BATF3
ATF7

Fig. S2. Interactions between AP-1 and NFκB pathways. (A) Representative Western blot (left) and quantification (right) of phosphorylated NFκB following 60 minutes of agonist treatment and with/without AP-1 inhibitor (T-5224). Error bars denote Mean ± SD, * $p < 0.05$ as determined by one-way ANOVA with Dunnet test comparison to control. Statistical significance was determined by one-way ANOVA with Dunnet test comparison to control, $p<0.05$, n=3. **(B)** Protein-protein association maps of known NFκB and AP-1 signaling pathways combined with proteins detected by mass spectrometry on p-NFκB IP samples. Plot generated by STRING.

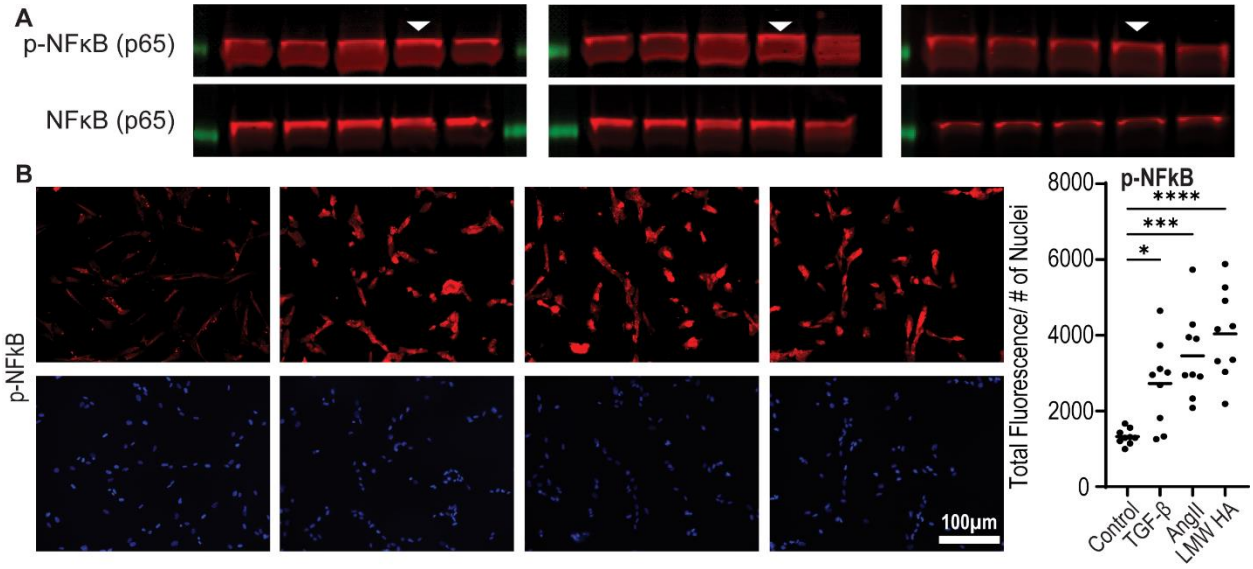

Fig. S3. Agonist treatment activates NFκB signaling: (A) Representative Western blots of phosphorylated and total NFκB following 0, 15, 30, 60, and 120 minutes of agonist treatment. (**B**) Representative immunofluorescence images (left) and quantification (right) of phospho-p65 (60 minutes post-agonist treatment). Error bars denote Mean ± SD, * $p < 0.05$ as determined by one-way ANOVA with Dunnet test comparison to control. Statistical significance was determined by one-way ANOVA with Dunnet test comparison to control, $p<0.05$, n=3.

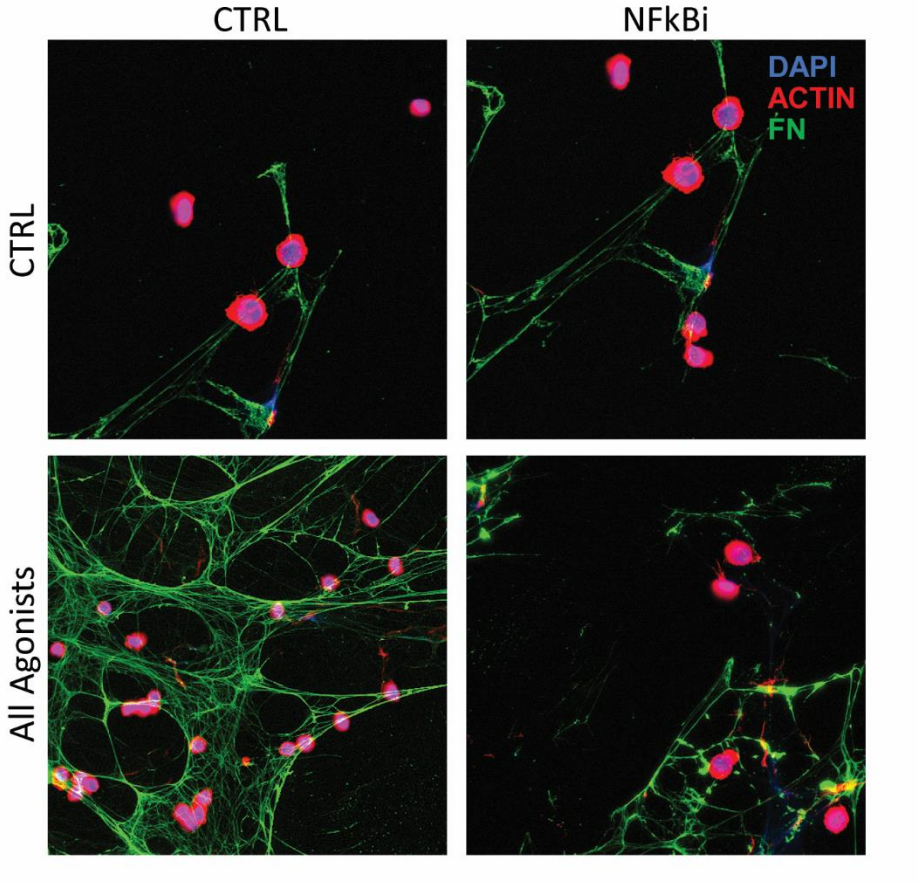

Fig. S4. Monocytes adhere to assembled FN matrix. U937 monocytes adhered primarily to decellularized fibronectin matrix created and assembled by control vs. NFκB iCFs treated with TGFβ, LMW HA, and ANGII for 72 hours.

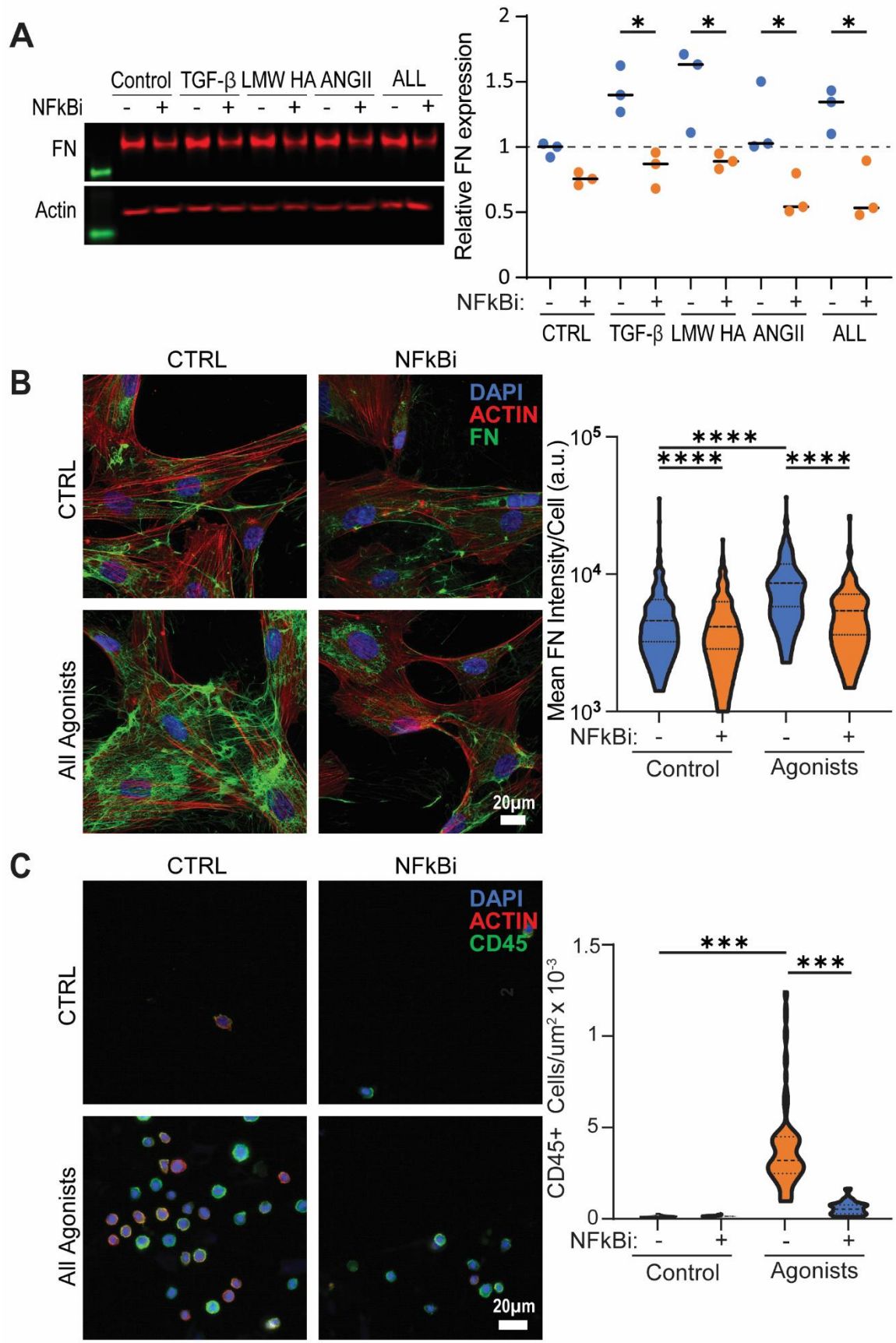

Fig. S5. NFκB mediates agonist matrix responses. (**A**) Representative Western blot (left) and quantification (right) of cellular fibronectin (FN) in control vs. NFκB inhibitor (BMS-345541) treated iCFs exposed to TGFβ, LMW HA, ANGII, or a combination of all agonists. Error bars denote Mean ± SD for three independent experiments, * $p < 0.05$ as determined by one-way ANOVA. (**B**) Representative immunofluorescent images of iCFs treated with TGFβ, LMW HA, and ANGII for 72 hours (left) and quantification of mean FN signal per cell (right), * $p < 0.05$ as determined by one-way ANOVA. (**C**) Representative immunofluorescent images of U937 monocytes adhered to decellularized matrices obtained from control vs. NFκB iCFs treated with TGFβ, LMW HA, and ANGII for 72 hours, * $p < 0.05$ as determined by a nonparametric Kruskal-Wallis test.

Table S1. Proteins identified by mass spectrometry following p-NFκB IP. Data shown indicate (left to right): the Protein.Group, Protein.ID, Accession, Area.Sample.1, Post-translational Modification (PTM), Average Mass, Description, MassNormPeak, and RelAbund.

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https://journals.biologists.com/jcs/article-lookup/doi/10.1242/jcs.261152#supplementary-data

Table S2. Summary of ATAQ-Seq on iCFs. Summary includes separate tabs for analysis of all peaks, differentially accessible regions (DARs), RR regions with AP-1 motifs, RKO regions with AP-1 motifs, RR regions with GATA motifs, and RKO regions with GATA motifs. Data shown indicate (left to right): ID, seqnames, start, end, width, Conc,Conc_RR, Conc_RKO, Fold, p.value, FDR, Chr, Start, End, Annotation, Detailed.Annotation, Distance.to.TSS, Nearest.PromoterID, Entrez.ID,Nearest.Unigene, Nearest.Refseq, Nearest.Ensembl, Gene.Name, Gene.Alias, Gene.Description, and Gene.Type.

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Table S3. Regions predicted to have both AP-1 and GATA binding sites. This table annotates regions containing predicted motifs for both AP-1 and GATA. Data shown indicate (left to right): Chr, Start, End,Annotation, Distance to TSS,Nearest PromoterID, Nearest Refseq, Gene Name, and Gene Type.

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https://journals.biologists.com/jcs/article-lookup/doi/10.1242/jcs.261152#supplementary-data

Table S4. Transcriptional expression of AP-1 factors in Risk and Risk KO iPSC-cardiac fibroblasts. TPM values for the indicated samples from RR and RRKO cell lines.

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