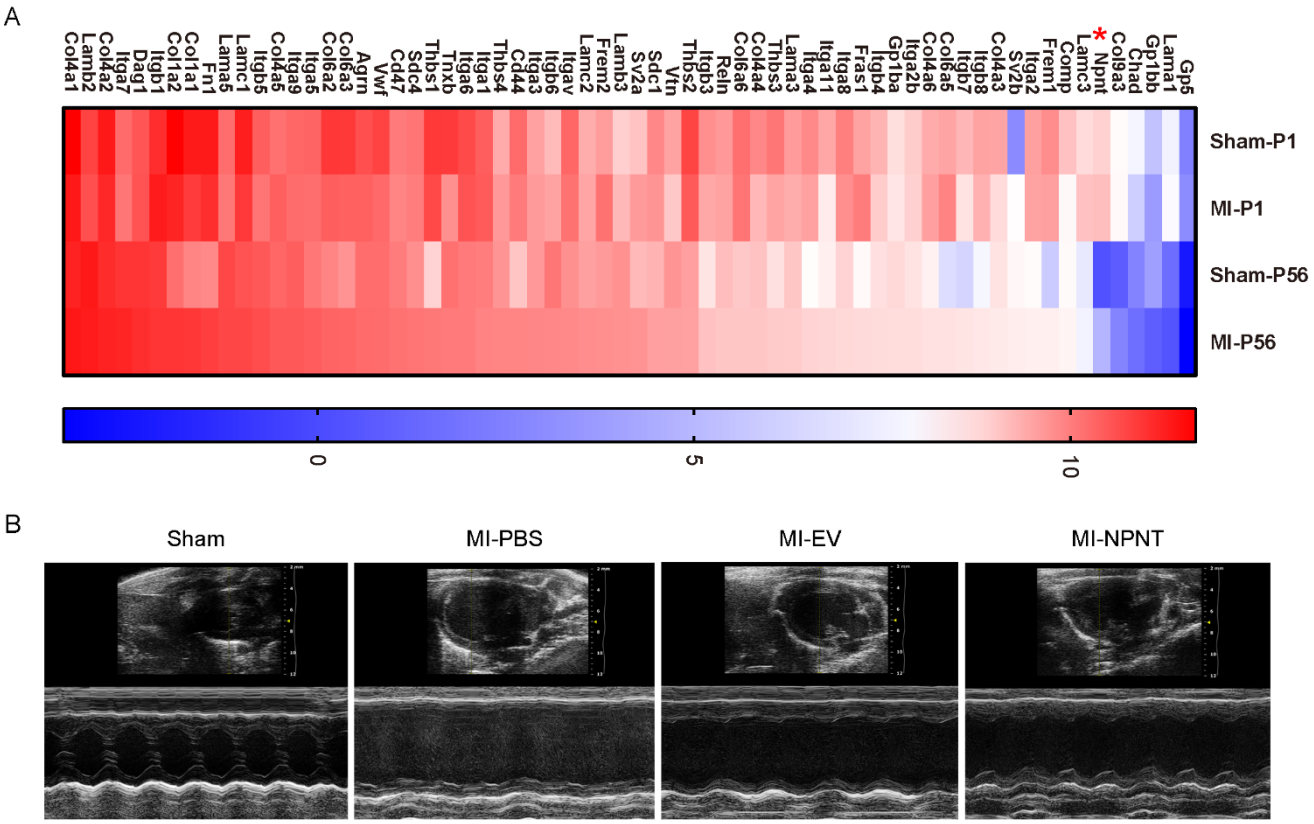
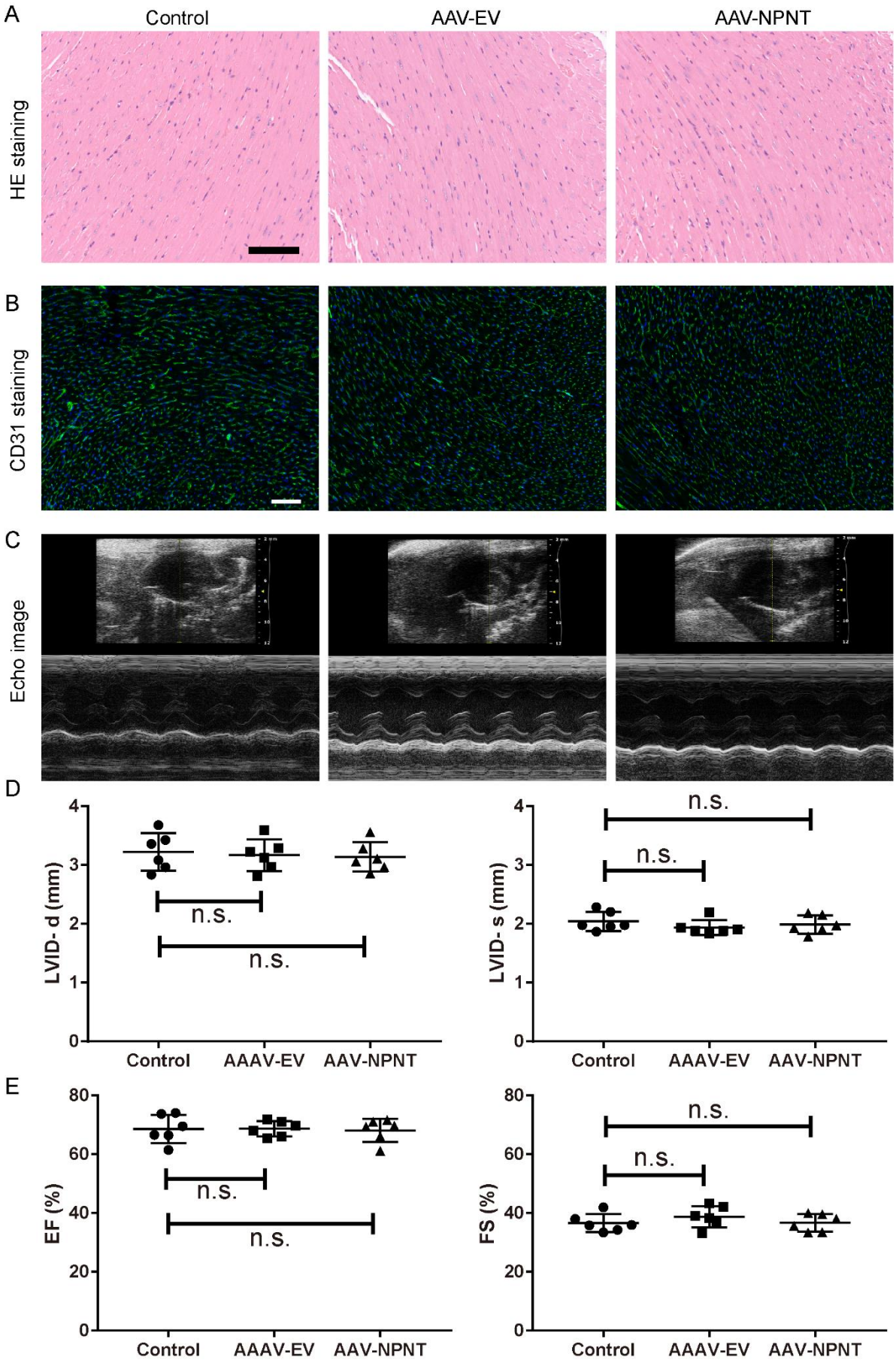
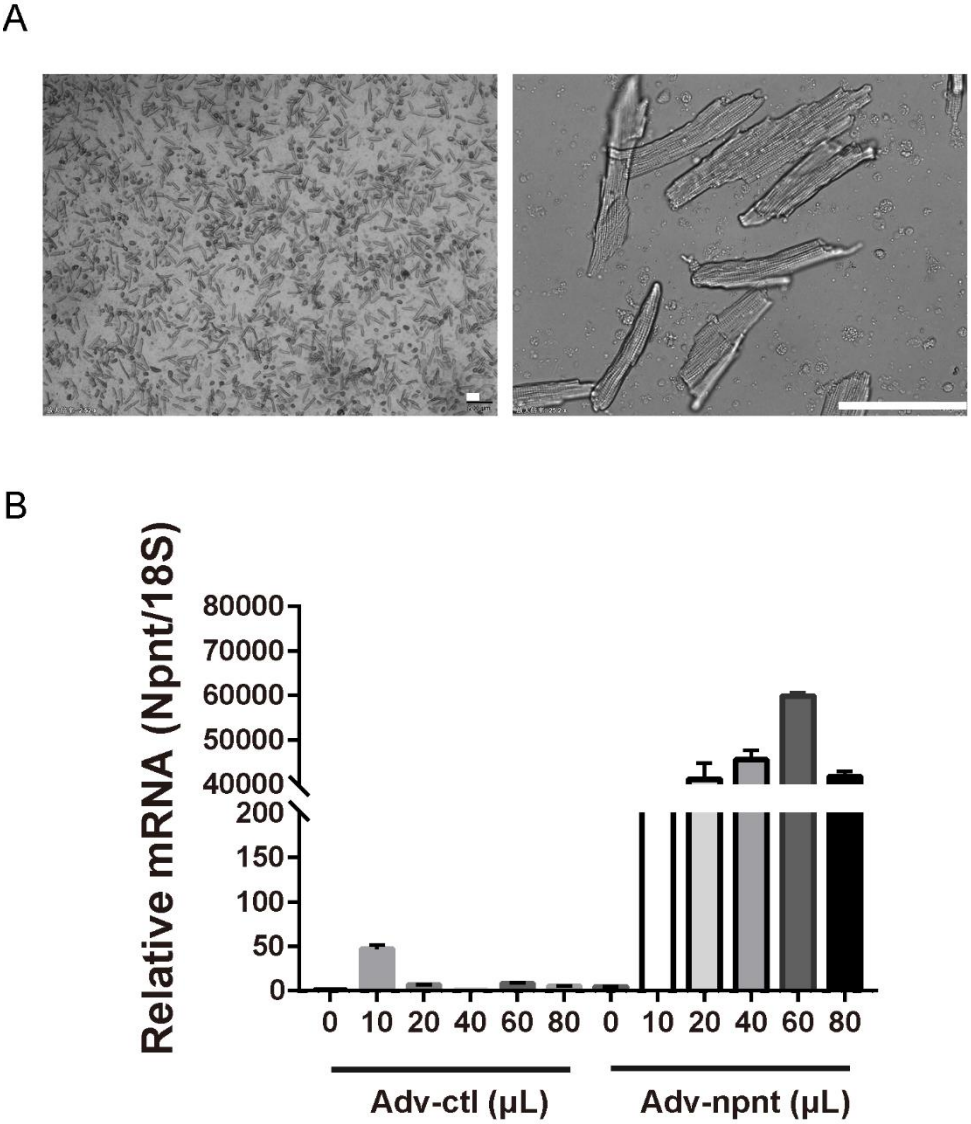
Supplementary Material



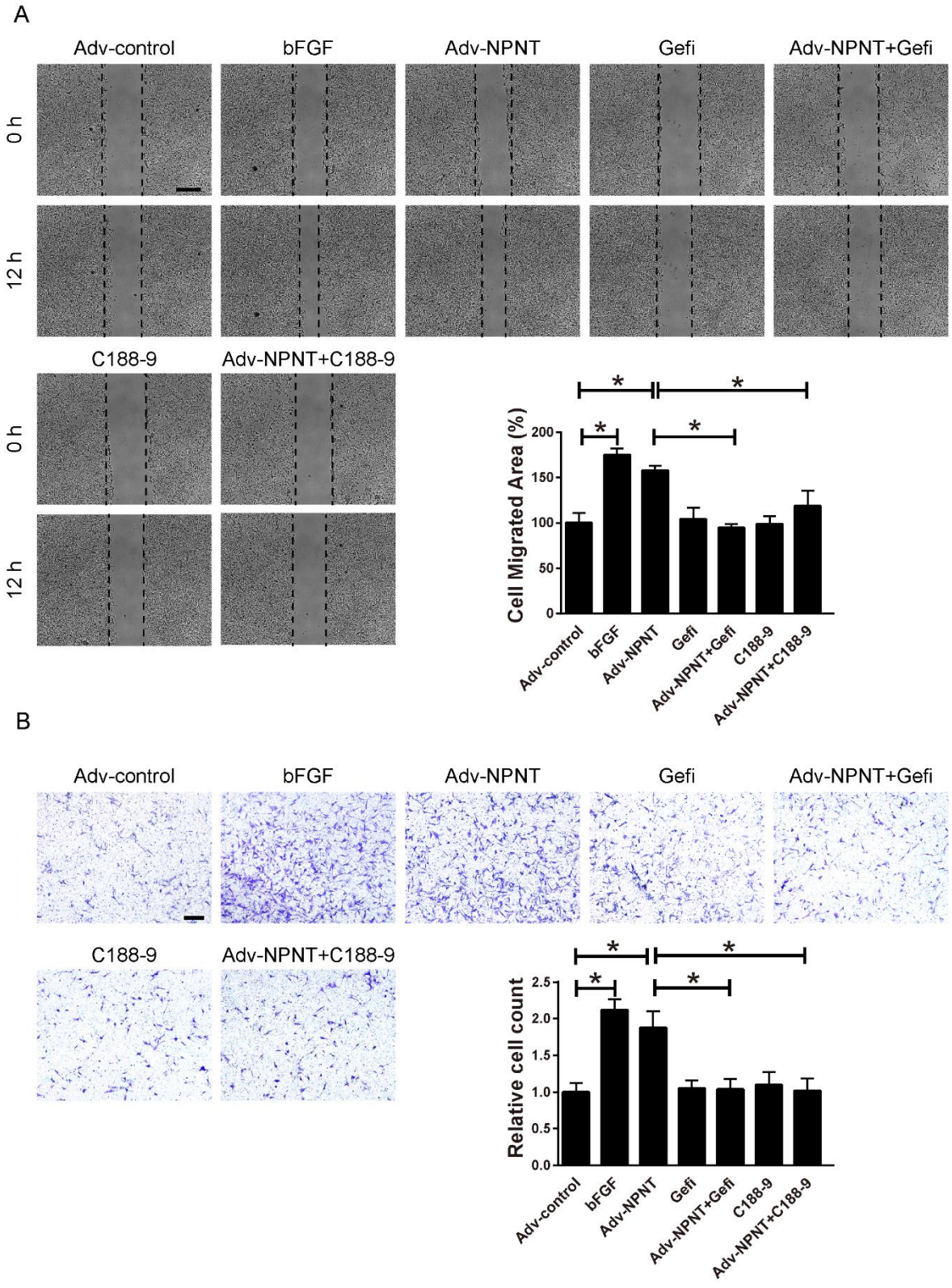
Supplementary Figure 1. NPNT plays a role in cardiac development and during MI insult. (A)Heatmap focused on ECM protein genes reassembled based on open access RNA-seq data from Gene Expression Omnibus under the accession number GSE95755. (B) Representative images of standard M-mode echocardiography performed on day 28 post MI in the Sham group, MI-PBS group, MI-EV group and MI-NPNT group.


A
Control
AAV-EV
AAV-NPNT
HE staining
B
CD31 staining
C
Echo image
D
LVID- d (mm)
n.s.
n.s.
Control
AAAV-EV
AAV-NPNT
LVID- s (mm)
n.s.
n.s.
Control
AAAV-EV
AAV-NPNT
E
EF (%)
n.s.
n.s.
Control
AAAV-EV
AAV-NPNT
FS (%)
n.s.
n.s.
Control
AAAV-EV
AAV-NPNT

Supplementary Figure 2. NPNT gene overexpression by adeno-associated virus (serotype 2/9) in mouse hearts did not affect myocardial morphology, capillary density, or cardiac function. Three weeks after the AAV injection, several mice from the MI-EV, MI-NPNT group and control group (n= 3-6 for each group) were sacrificed and subjected to (A) HE staining, scale bar, 200 μm; (B) CD31staining, Scale bar, 100 μm; (C-E) echocardiography to explore myocardial morphology, capillary density, and cardiac function under the premise of overexpression of NPNT in hearts.

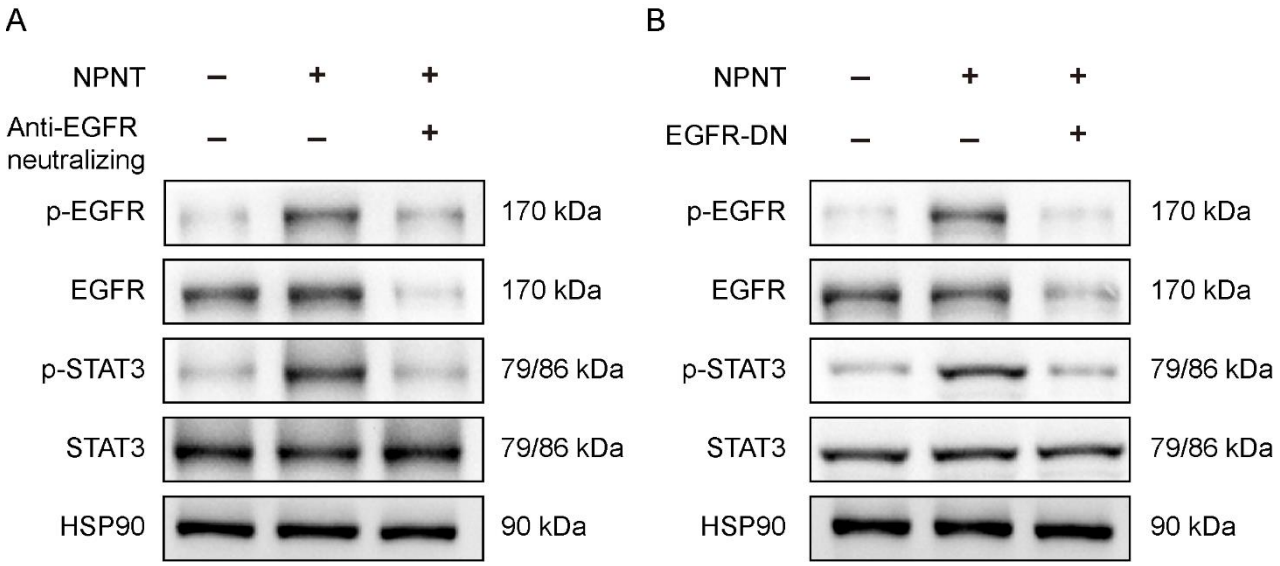


Supplementary Figure 3. Adult mouse cardiomyocytes (AMCM) expressing mouse NPNT via being infected by pAd/CMV/V5-DEST-NPNT. A. Adult mouse cardiomyocytes (AMCM) representative images with different magnifications in brightfield (these two images come from two experiments). Scale bar, 100 μm; B. qPCR results showed pAd/CMV/V5-DEST-NPNT infected AMCM in different virus titer. Sixty μl/mL virus titer was used in the later experiments.



Supplementary Figure 4. Gefitinib and C188-9 impaired Adv-NPNT-induced mouse endothelial cell migration in vitro. (A) Representative images and quantification of scratch wound healing assays, (B) Transwell assay indicating that Adv-NPNT-promoted endothelial cell migration and were

significantly inhibited by Gefitinib (10 μM) or C188-9 (10 μM). Quantitative analysis of NPNT-induced cell migration. * $P < 0.05$. Scale bar, 100 μm.



Supplementary Figure 5. Anti-EGFR neutralizing antibody and EGFR dominant negative plasmid abrogated EGFR/JAK/STAT3 activation by NPNT. A. Anti-EGFR neutralizing antibody was added to culture medium 1 hour before NPNT stimulation and then EGFR/JAK/STAT3 pathway was detected. B. EGFR dominant negative plasmid was transfected in HUVEC for 24 hours before NPNT stimulation and then EGFR/JAK/STAT3 pathway was detected.