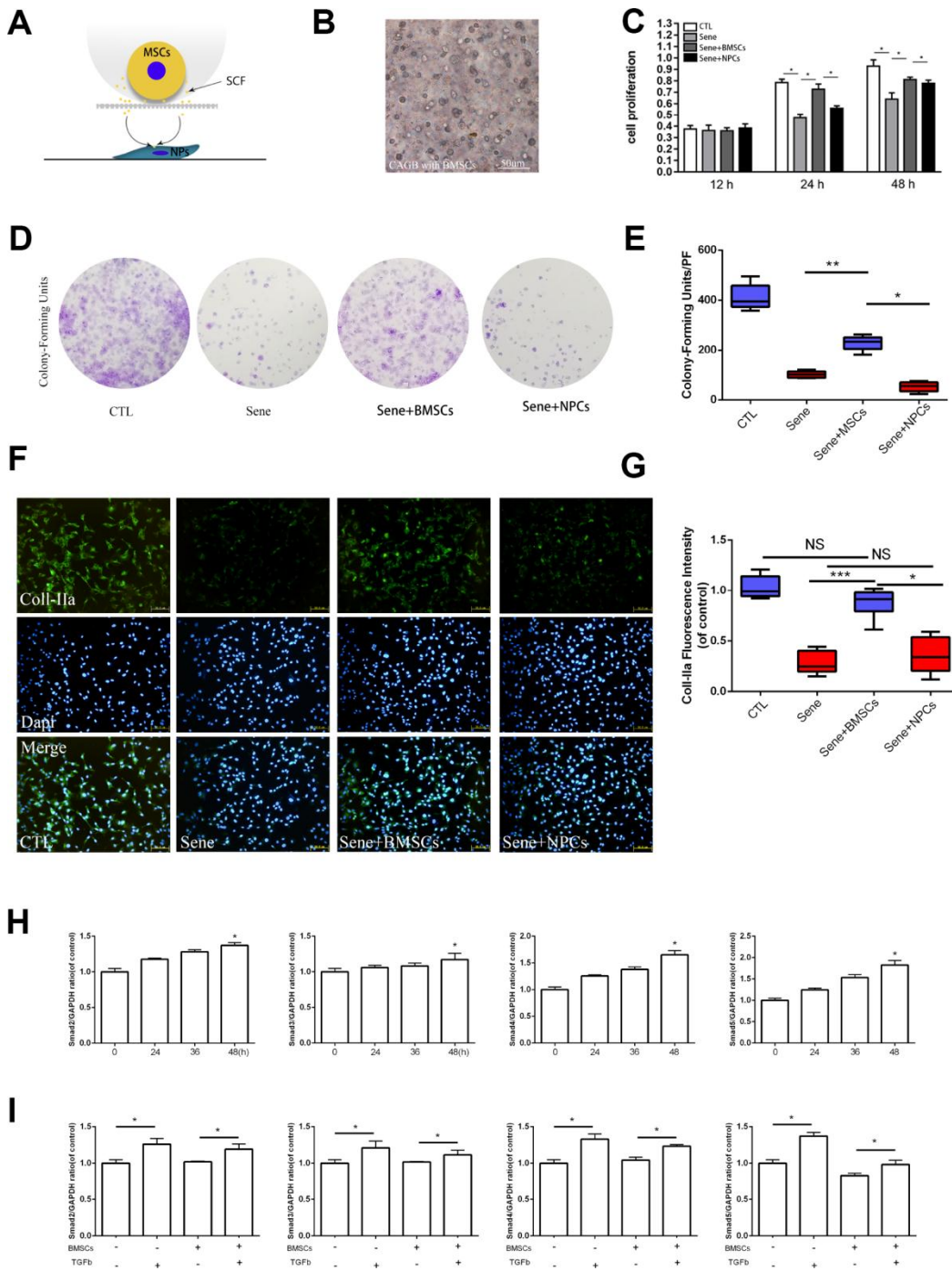
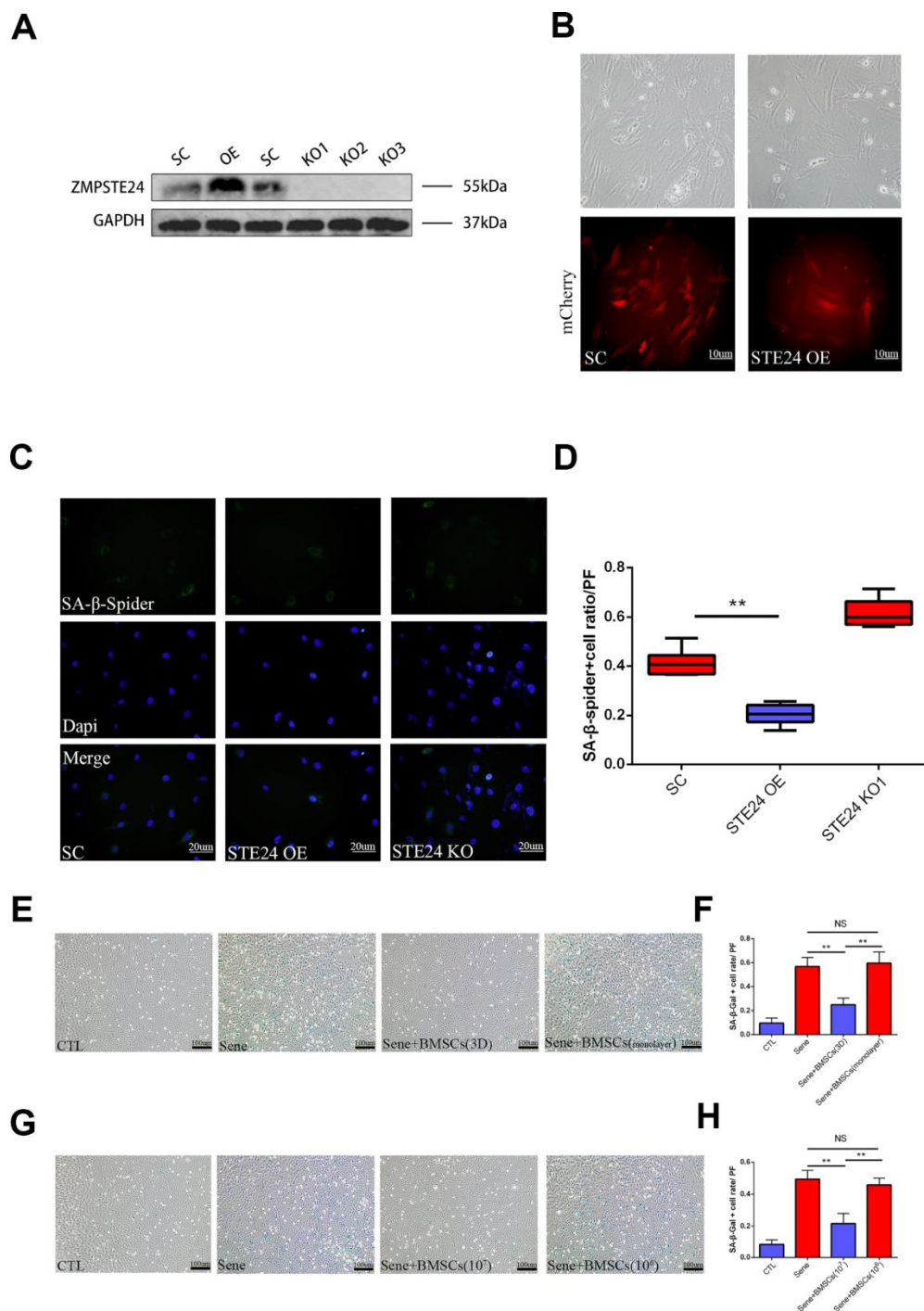


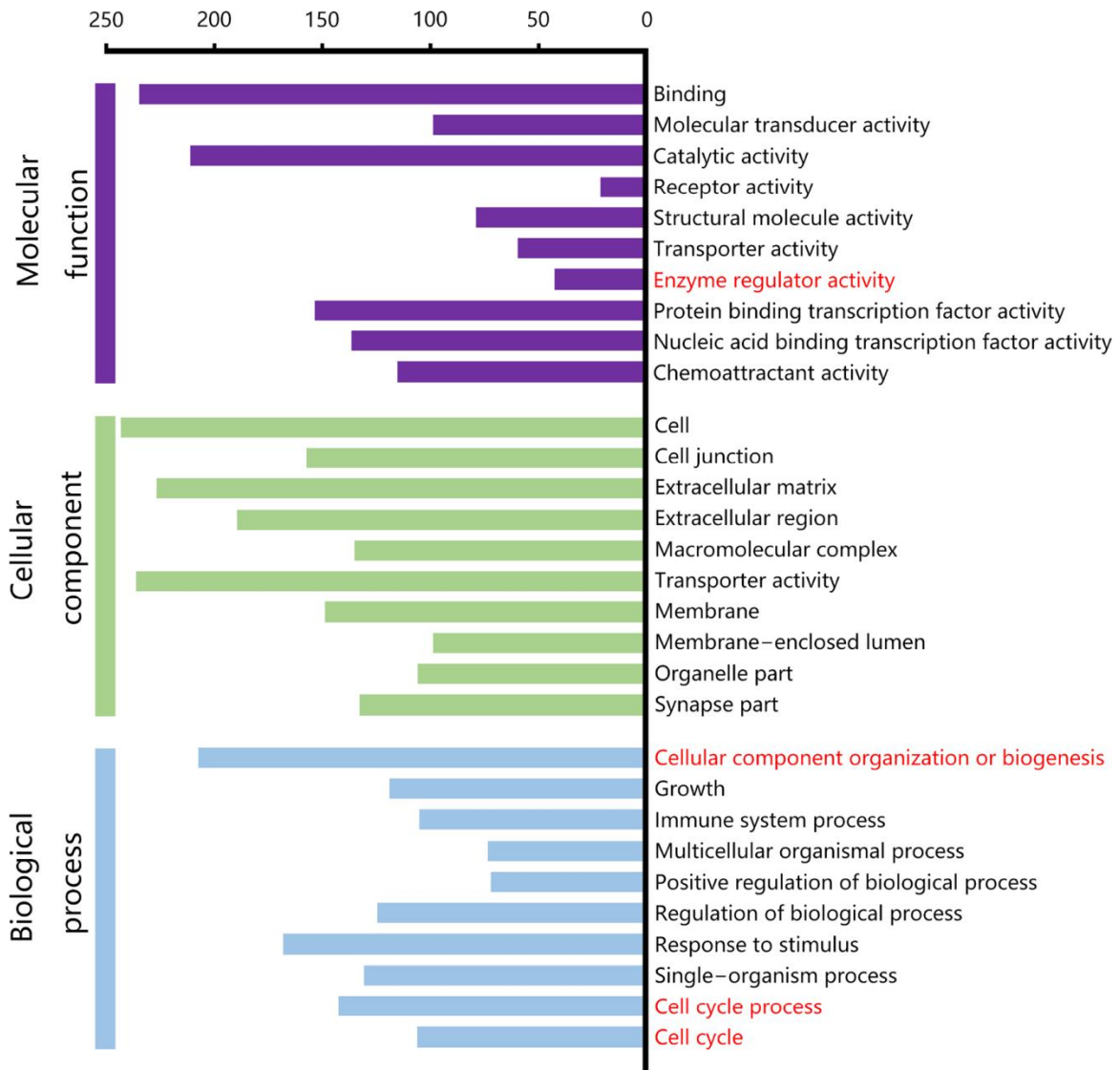
SUPPLEMENTARY FIGURES



Supplementary Figure 1. (A) Co-culture schematic diagram, the possible effect of stem cell paracrine on nucleus pulposus cells (B) Bone marrow mesenchymal stem cells encapsulated in sodium alginate pellets under light microscope, Scale bar, 50um (C) Proliferative rate of nucleus pulposus cells in different groups. (D–E) Nucleus pulposus cells cloning ability varies in different groups. (F–G) Immunofluorescence staining of Col-Ia combined with DAPI staining for nuclei. n=5, Scale bar, 50um. Col-Ia fluorescence intensities were determined by using Image J software. (H) Protein expressions of Smad2, Smad3, Smad4 and Smad5 under TNF-α inducing were quantified by Image J. n=3. (I) Protein expression of Smad2, Smad3, Smad4 and Smad5 were quantified by Image J. n=3. Values represent means±S.D. Significant differences between different groups are indicated as *P < 0.05, **P < 0.01, ***P < 0.001. PF: per field.



Supplementary Figure 2. (A) The ZMPSTE24 overexpressed and knocked out in nucleus pulposus cells were verified by western blots. (B) Red fluorescence(mCherry) excited by fluorescence microscopy of nucleus pulposus cells overexpressing ZMPSTE24 (C–D) Different positive rates of senescence staining (Spiderβgal) stimulated by TNF-α between overexpression and knockout of ZMPSTE24. Combined with DAPI staining for nuclei. n=5, Scale bar, 20µm. (E–F) SA-β-Gal staining of senescent NP cells after 2 days coculture of normal NP cells +blank calcium alginate gel balls(CTL), senescent NP cells+ blank calcium alginate gel balls(Sene), senescent NP cells +calcium alginate gel balls with BMSCs(Sene +BMSCs,3D), senescent NP cells +BMSCs in 2D coculture model(Sene +BMSCs,2D), n=3, Scale bar, 50µm. SA-β-Gal positive cell rate between CTL, Sene, Sene +BMSCs(3D) and Sene + BMSCs(2D) groups were determined by using Image J software. (G–H) SA-β-Gal staining of senescent NP cells after 2 days coculture of normal NP cells +blank calcium alginate gel balls(CTL), senescent NP cells+ blank calcium alginate gel balls(Sene), senescent NP cells +calcium alginate gel balls with BMSCs(10⁷/ml)(Sene +BMSCs,10⁷), senescent NP cells + calcium alginate gel balls with BMSCs(10⁶/ml)(Sene +BMSCs, 10⁶), n=3, Scale bar, 50µm. SA-β-Gal positive cell rate between CTL, Sene, Sene +BMSCs(10⁷) and Sene + BMSCs(10⁶) groups were determined by using Image J software. Values represent mean±S.D. Significant differences between different groups are indicated as **P < 0.01. PF: per field.



Supplementary Figure 3. Functional characterization of novel candidate identified by differential gene $\log_2\text{FoldChange} > 2$ between BMSCs and NPCs coculture groups. The top ten GO terms with the smallest P value in the indicated categories are shown (Fisher's exact test, one tailed). The number of proteins for each individual term is also shown. Related to mitosis are marked in red.