## **Description of Additional Supplementary Files**

Name: Supplementary Data 1

Description: Basic information for MSCs sample donors and scRNA-seq analysis.

Name: Supplementary Data 2

Description: Pseudobulk DEGs of each MSC cluster.

Name: Supplementary Data 3

Description: Lists of genes used in gene set analysis

Name: Supplementary Data 4

Description: Results for GSVA analysis

Name: Supplementary Data 5

Description: Regulon targets information for SCENIC analysis

Name: Supplementary Data 6

Description: Results of generalized linear model (GLM) analysis

Name: Supplementary Data 7

Description: Differentially expressed Proteins on MSC EVs Proteome level.

Name: Supplementary Data 8

Description: Pseudobulk DEGs of each young and aged BM-MSC cluster.

Name: Supplementary Data 9

Description: Results of generalized linear model (GLM) analysis in Fig. S5h

Name: Supplementary Data 10

Description: Differentially expressed Proteins or Genes on MSC Proteome level or

pseudobulk scRNA level.

Name: Supplementary Data 11

Description: Results of 2D enrichment analysis.

Name: Supplementary Data 12

Description: Supporting information for Fig. 6e.

Name: Supplementary Data 13

Description: Sequences of primers and shRNA.