

Figure S1

Schematic representation of the study design and workflow. **A)** Briefly, bone marrow stromal cells were cultured and isolated from a mouse model with doxycycline-inducible expression of $G\alpha_s^{R201C}$ in cells of the osteogenic lineage in the appendicular skeleton through passage enrichment and negative immunoselection against hematopoietic markers CD45 and CD11b. After that, cells from each mouse were cultured in two groups. At 80% confluency, cultures were transferred to FBS-depleted media and $G\alpha_s^{R201C}$ expression was induced in one of the groups by adding 5 mg/mL of doxycycline. **B)** Human BMSCs were cultured from surgical waste FD tissue and bone marrow specimens from healthy volunteers. At 80% confluency, cells were transferred to FBS depleted media. Plasma was obtained from FD patients. **C)** Media was collected from human and mouse cells 48h later, concentrated by filtration, and used to determine cAMP and secreted factor concentrations. Attached cells were lysed with TRIzol for RNAseq. FD patient plasma was used for detecting BMSC-secreted factors in circulation.

Figure S2

Pathways affecting several biological processes are enriched by genes found within the FD Signature. Using a statistical threshold of adjusted $p < 0.01$, genes within the signature were loaded into the STRING database to determine potential protein-protein interactions of differentially regulated genes in FD. The most highly enriched processes involved “Extracellular matrix organization” (Cluster 1, C1), “Cellular metabolism” (C2), “Mesenchymal cell proliferation” (C3), “ATPase activity” (C4), “cAMP signaling” (C5), and “Metallopeptidase activity” (C6).

Figure S3

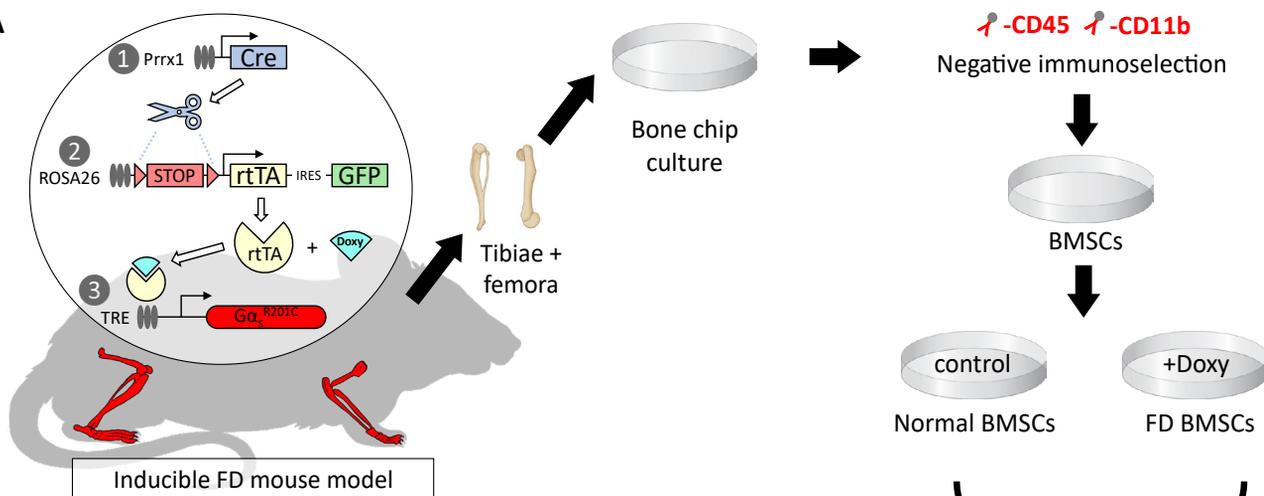
Cultured BMSCs derived from healthy volunteers (HVs) and patients with FD released pro-inflammatory cytokines, but differences were unable to be detected. Additionally, several factors were undetectable (IL-10, IL-12, IL-13, IL-17, G-CSF, and GM-CSF).

Figure S4

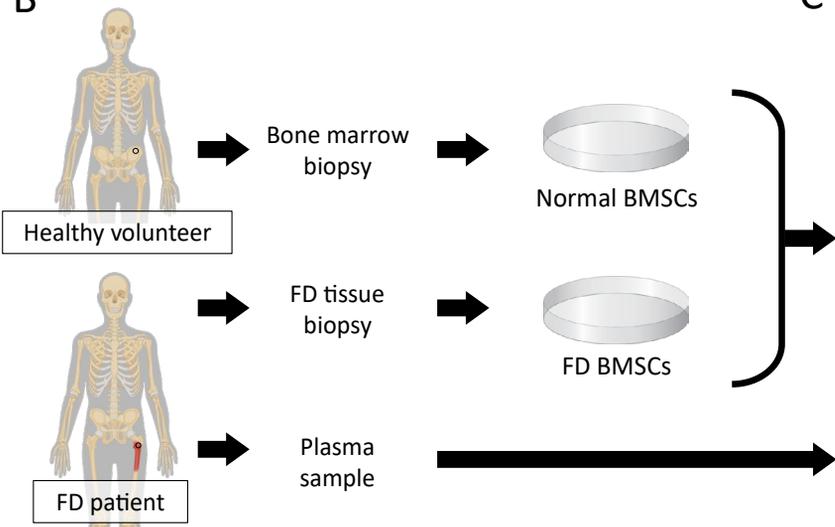
Additional cytokines expressed by cultured murine BMSCs. No differences were detected. IL-4, IL-9 were undetectable.

Fig S1

A



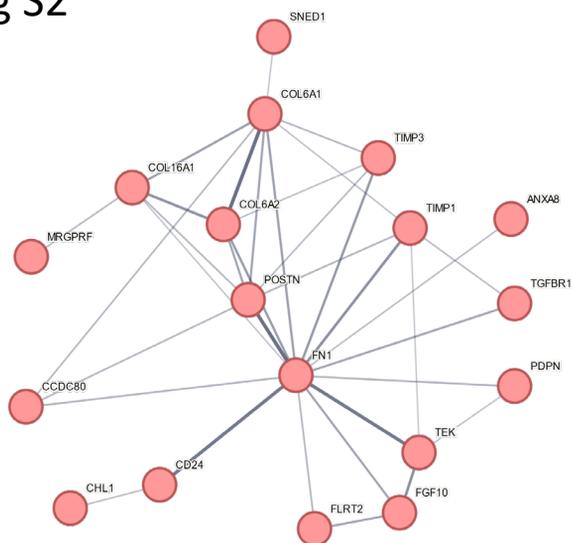
B



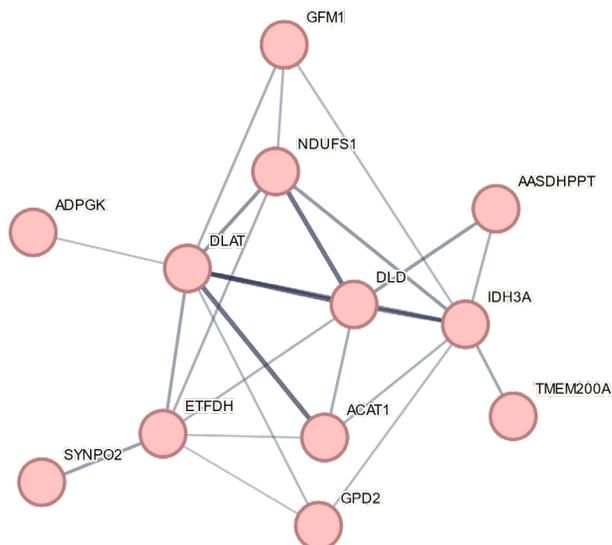
C

- Culture media:** Concentration through 30 kDa filtering
 - cAMP determination in eluent
 - Secreted factors (ELISA/Luminex) in concentrated media
- Cells:**
 - RNAseq
- Secreted factors (ELISA/Luminex)

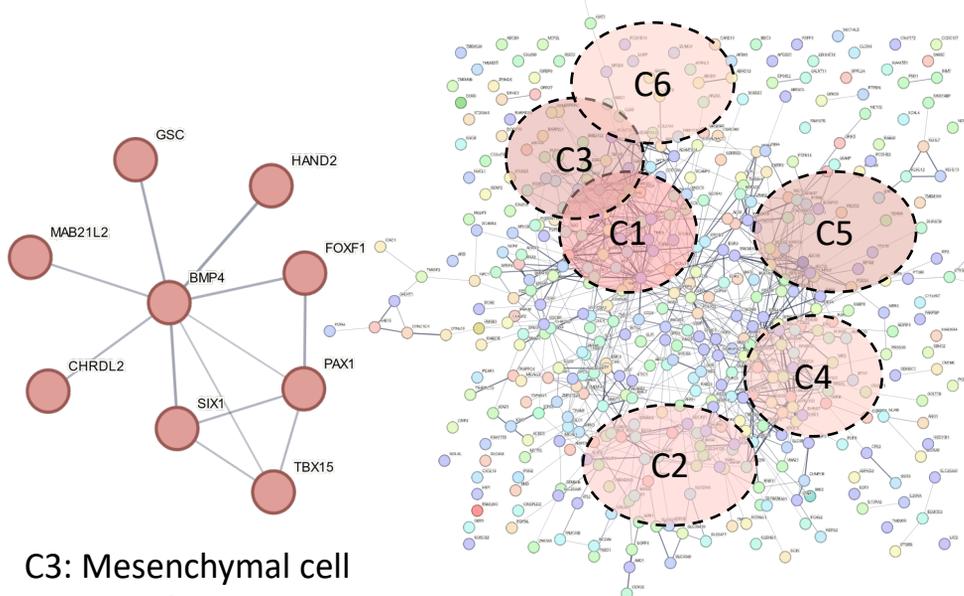
Fig S2



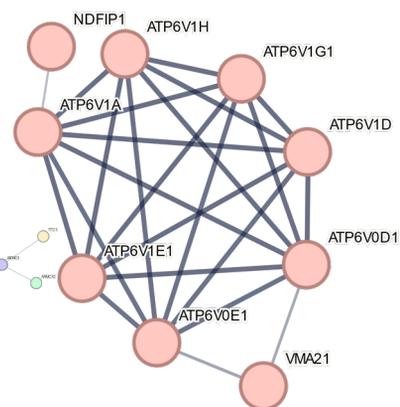
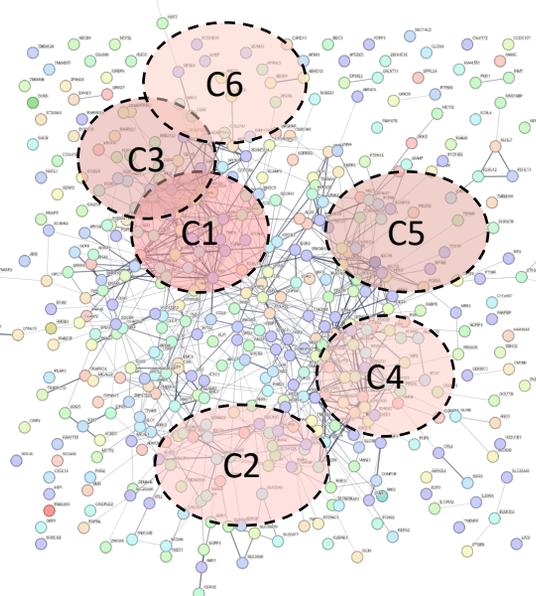
C1: Extracellular matrix organization



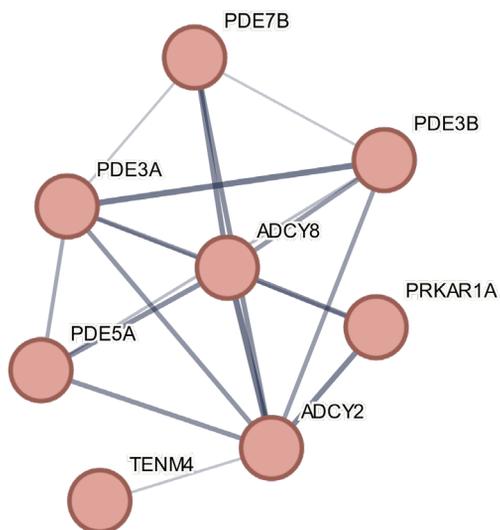
C2: Cellular metabolism



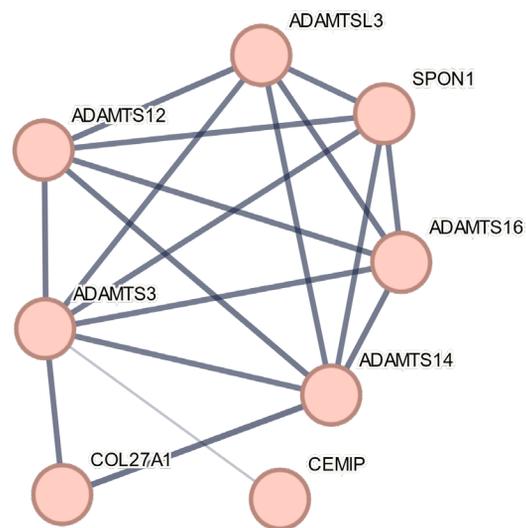
C3: Mesenchymal cell proliferation



C4: ATPase activity



C5: cAMP signaling



C6: Metallopeptidase activity

Fig S3

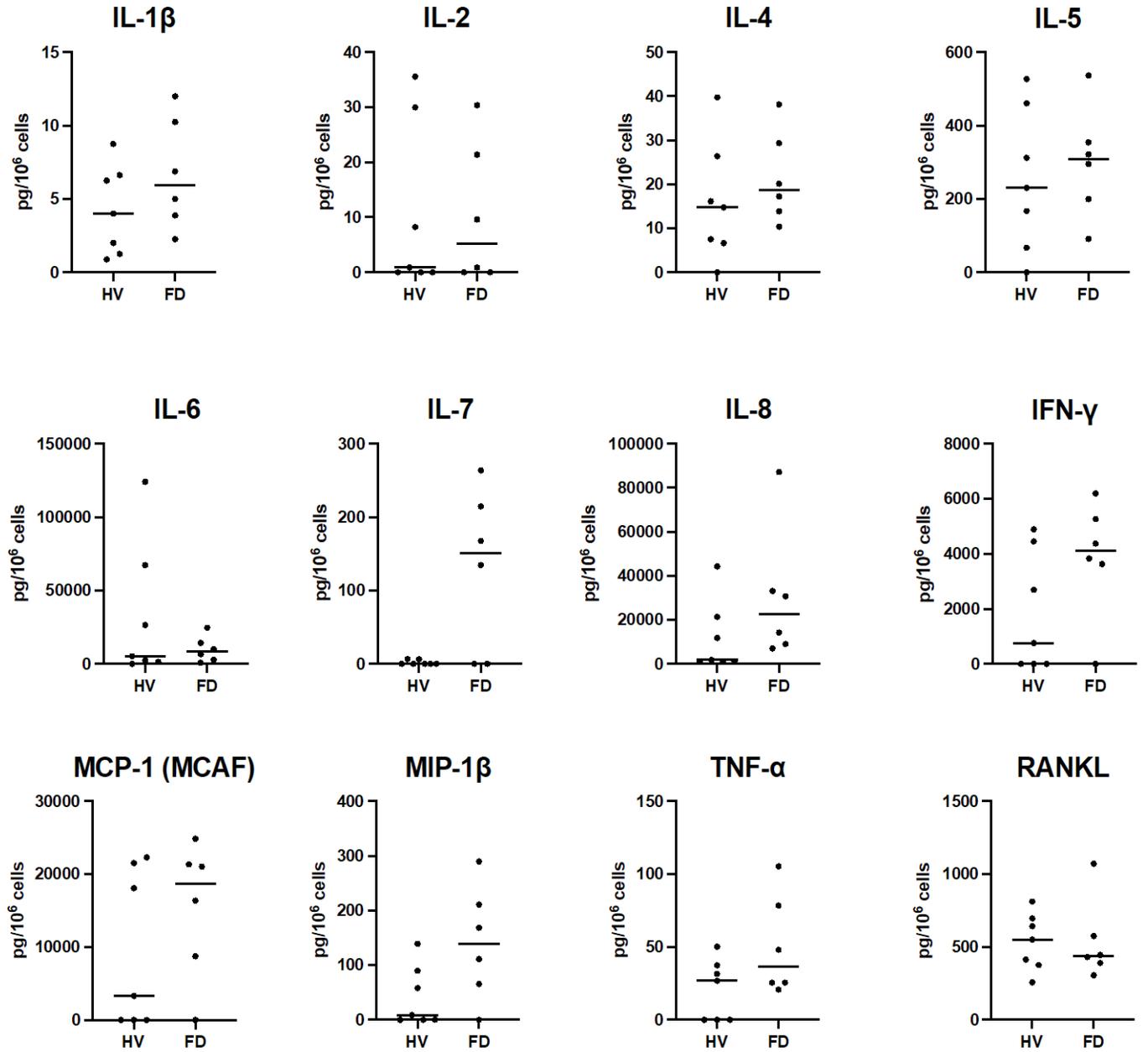


Fig S4

