

Altered mesenchymal and endothelial subsets in interstitial bone marrow and focal lesions in myeloma patients and SCID-hu mice


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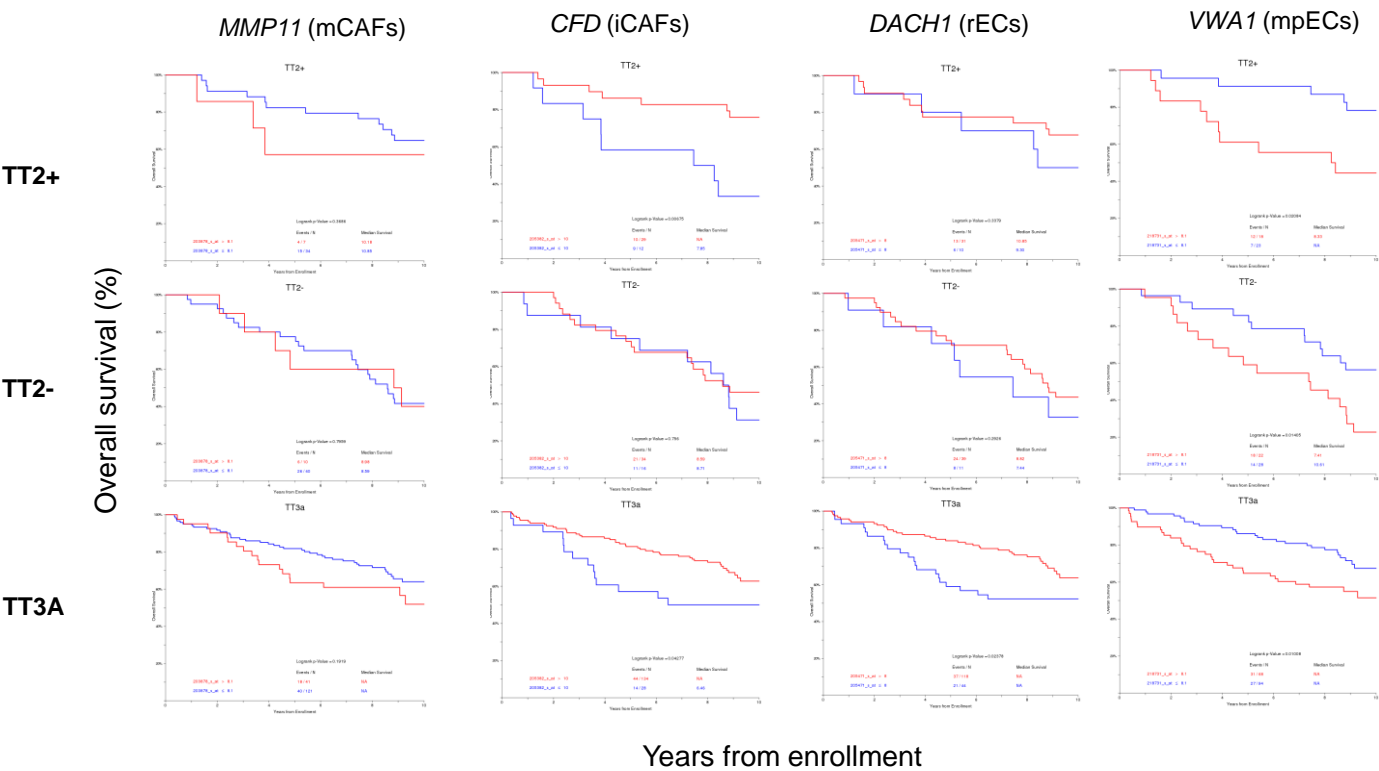
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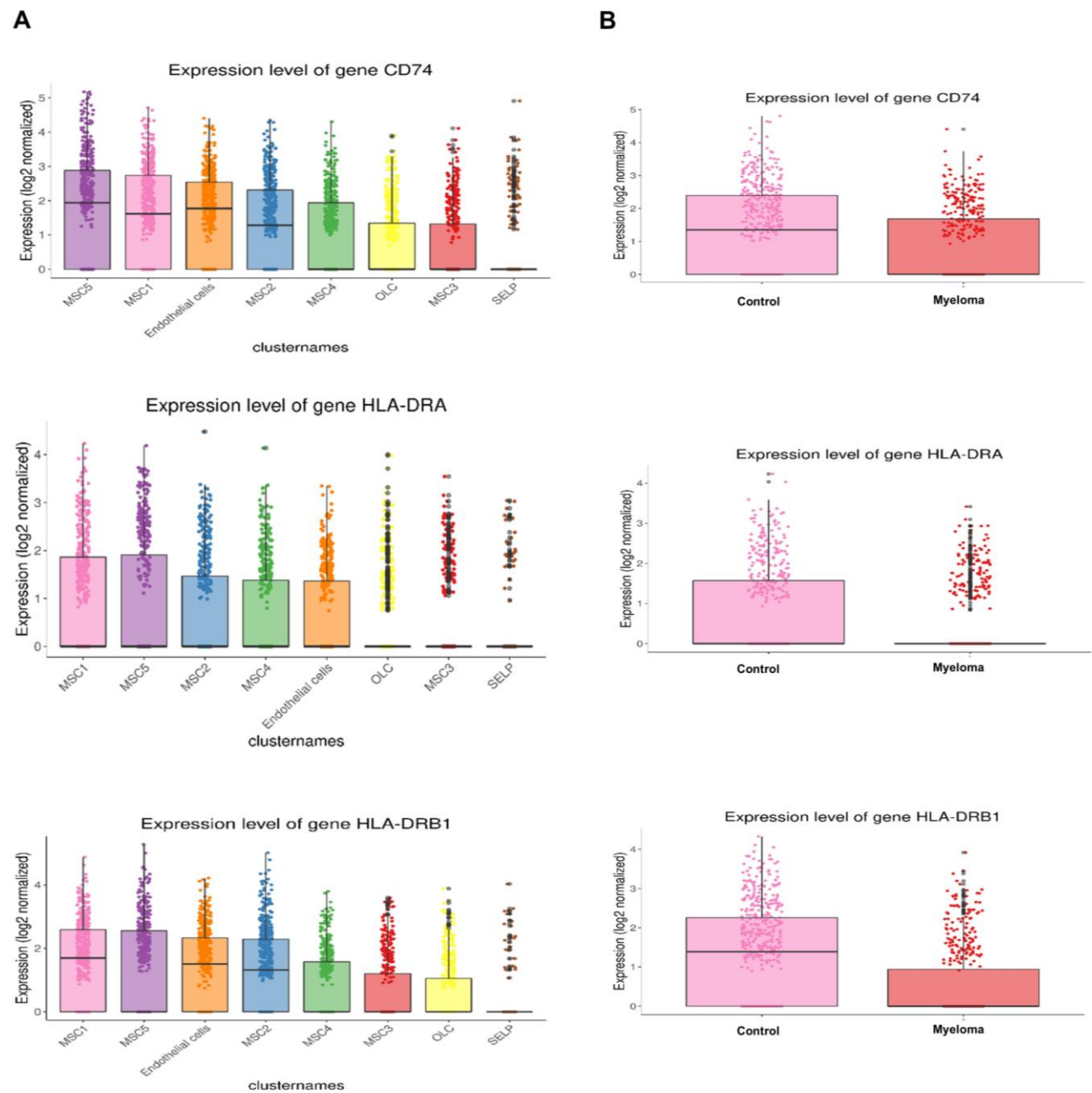
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Supplemental Figures

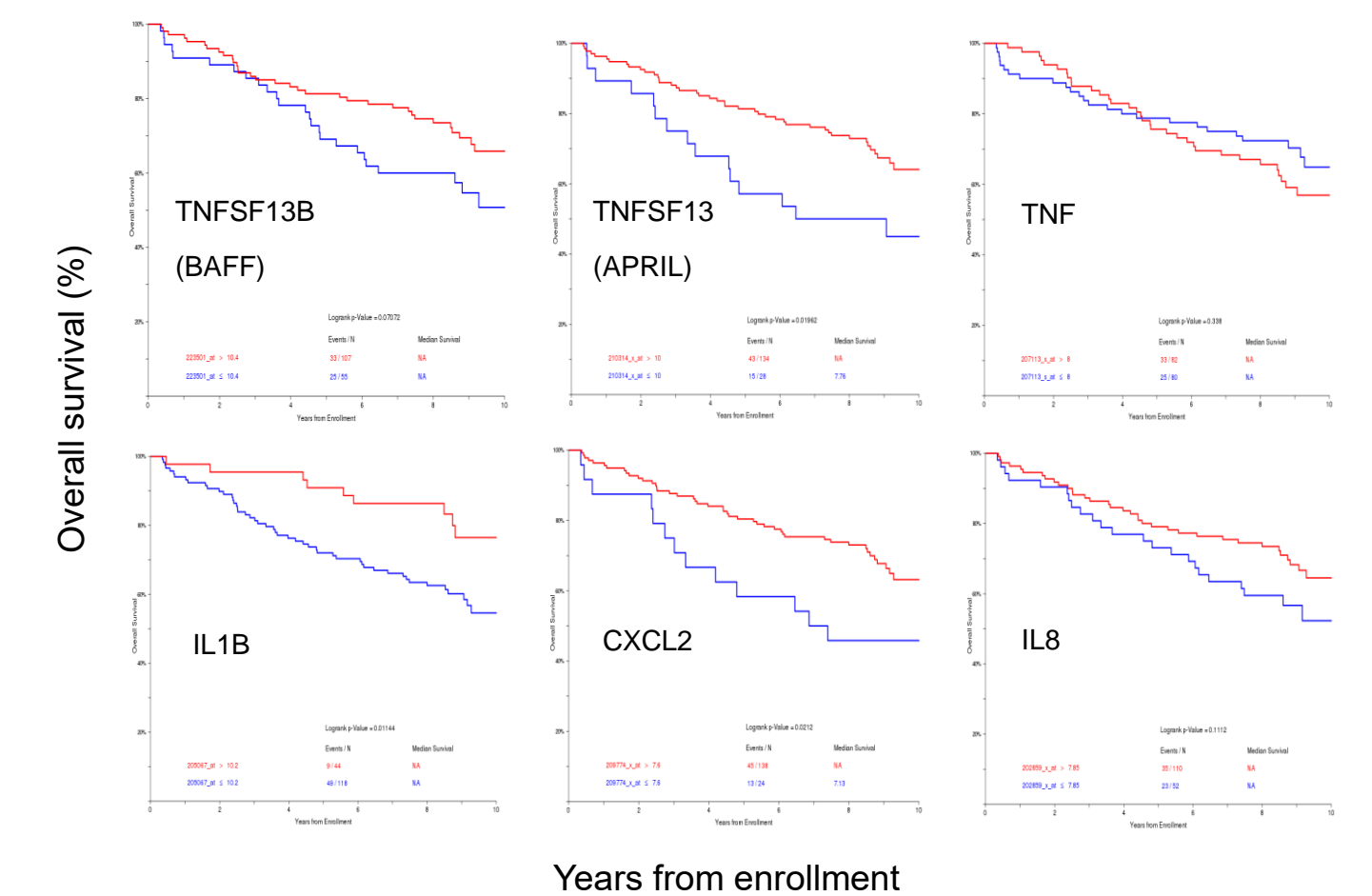
Supplemental Figure 1. Association between gene expression of *MMP11* (mCAFs), *CFD* (iCAFs), *DACH1* (rECs), and *VWA1* (mpECs) with overall survival in Total Therapy patients enrolled in TT2-, TT2+, and TT3a. Patients were treated without novel drugs (TT2-), with thalidomide (TT2+), or with thalidomide and bortezomib (TT3a).¹ Overall survival data is presented for the first 10 years of each trial. Red and blue lines represent cases with high and low expression of the indicated genes, respectively.



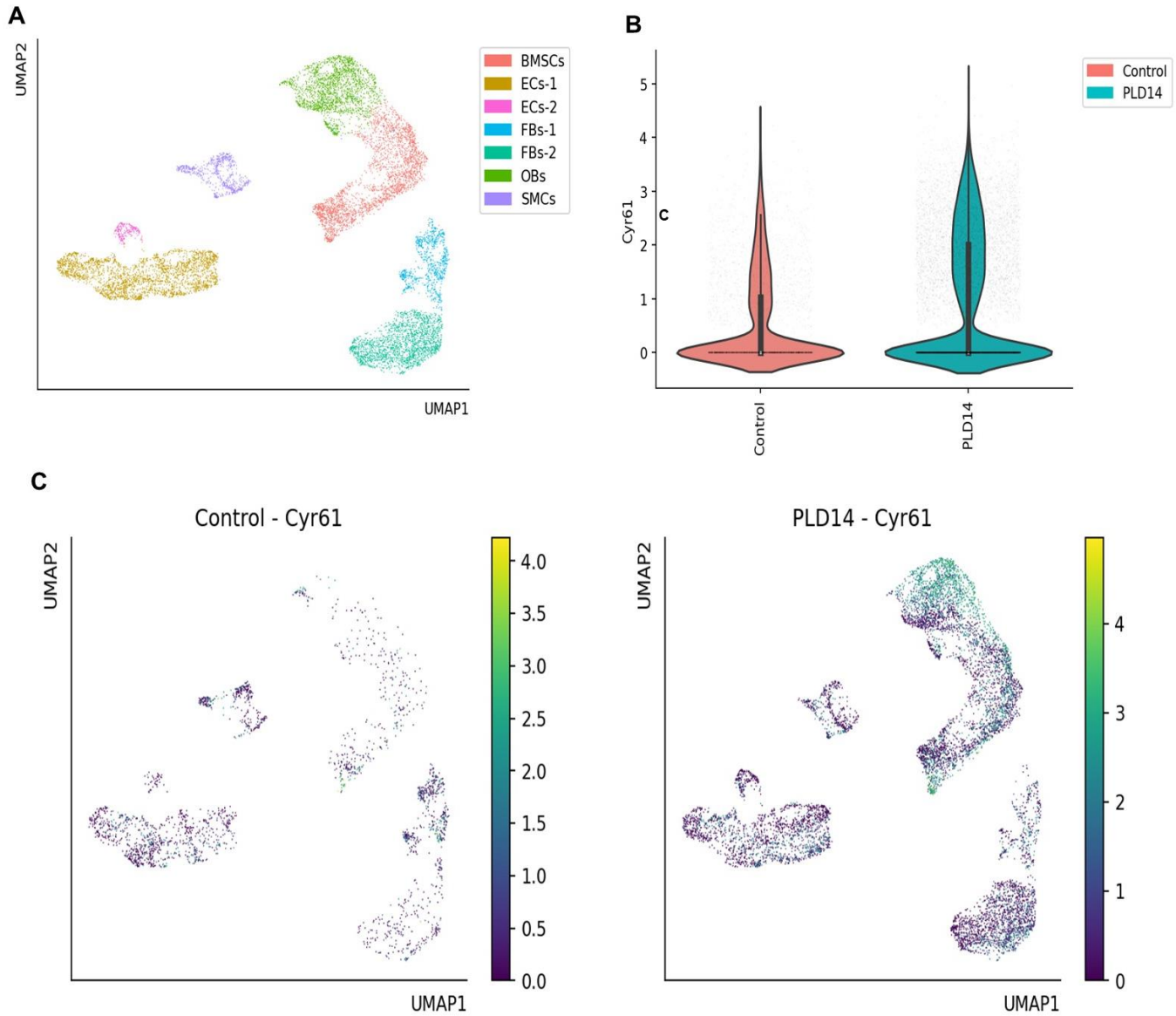
Supplemental Figure 2. Expression of genes associated with antigen-presenting cells in non-hematopoietic BM cells. The publicly available scRNA-seq-based atlas by de Jong et al., 2021² was used to demonstrate gene expression of *CD74*, *HLA-DRA*, and *HLA-DRB1* in the non-hematopoietic cells from BM of healthy donors and patients with MM. **A.** Expression of indicated genes in various subsets. **B.** Expression of indicated genes in the non-hematopoietic cells from healthy donors (Control) and newly diagnosed MM patients (Myeloma).



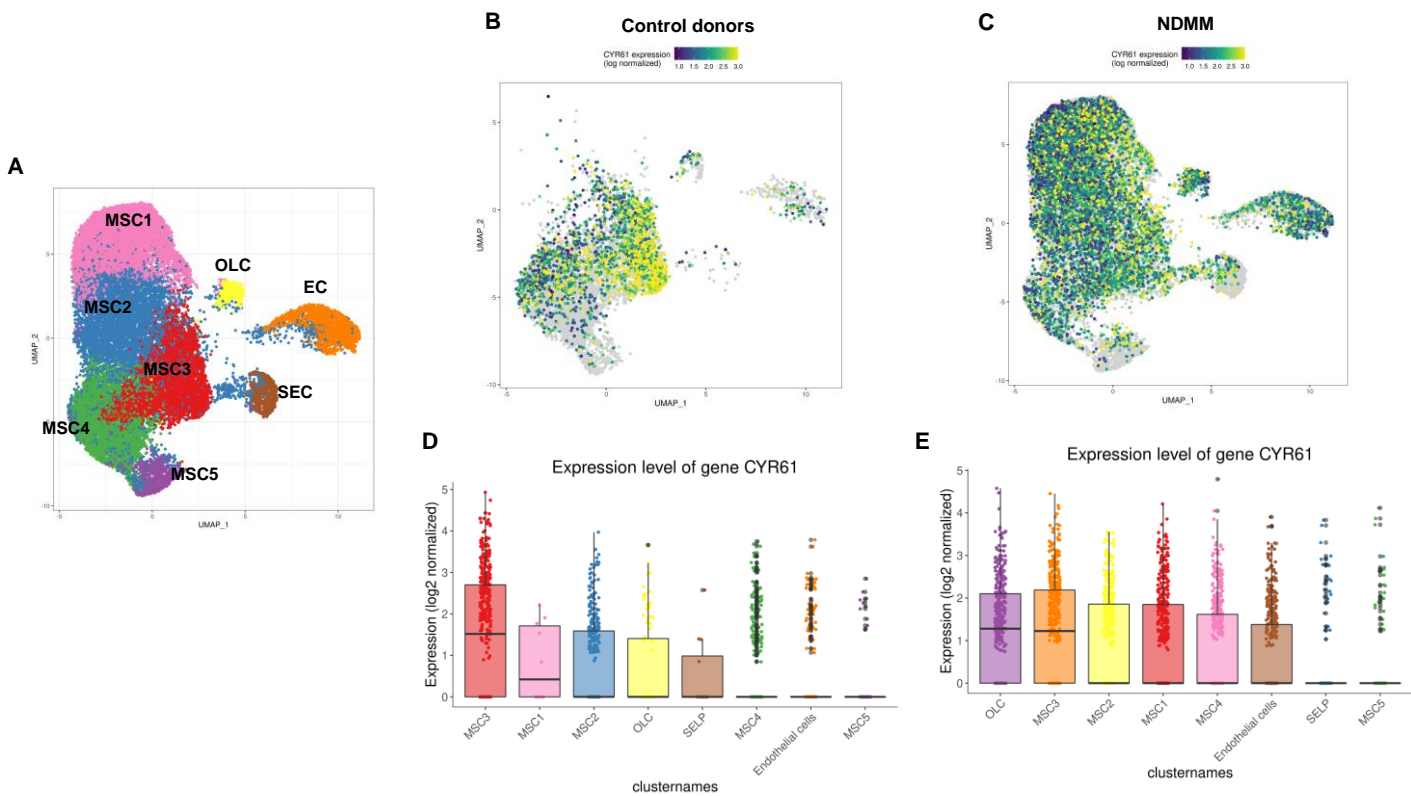
Supplemental Figure 3. Higher expression of genes associated with reciprocal interactions between inflammatory MSCs and neutrophils correlates with favorable overall survival in MM patients enrolled in the TT3A trial. These genes identified based on de Jong et al., 2021, 2024,^{2,3} exhibit elevated expression in iMSCs (e.g., CXCL8, IL8, IL1B) and inflammatory neutrophils (e.g., BAFF, APRIL, TNF, IL1B). Gene expression in whole bone biopsy samples was assessed using GEP, as detailed in the Methods section. Overall survival data is presented for the first 10 years of the trial.



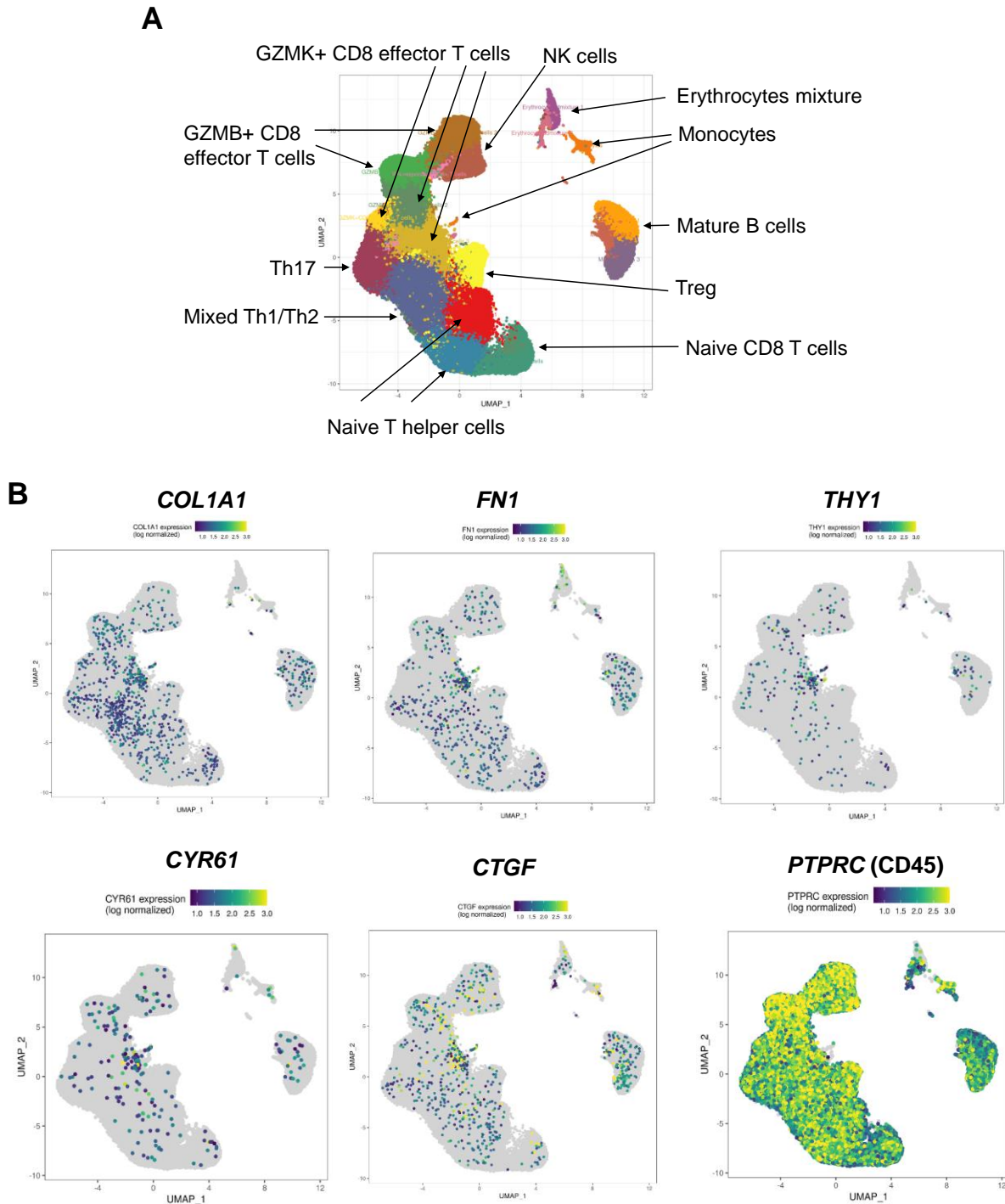
Supplemental Figure 4. Expression of *cyr61* in injured mouse calvaria. The publicly available scRNA-seq-based atlas by Bixel et al., 2024⁴ was used to demonstrate gene expression of *cyr61* in calvaria cells without injury (Control) and 14 days post-injury (PLD14). **A.** Cells' classifications based on the atlas. **B.** Violin diagram of *cyr61* expression in calvaria cells from Control and PLD14 groups. **C.** Expression of *cyr61* in cells from Control (left panel) and PLD14 (right panel) groups.



Supplemental Figure 5. Expression of *CYR61* in non-hematopoietic BM cells. The publicly available scRNA-seq-based atlas by de Jong et 2021² was used to demonstrate gene expression of *CYR61* in non-hematopoietic cells from BM aspirates of healthy donors and patients with MM. **A.** Cells' classifications based on the atlas. **B-E.** *CYR61* expression in control donors (**B, D**) and NDMM patients (**C, E**).



Supplemental Figure 6. Expression of mesenchymal markers in CD38- hematopoietic cells from patients with MM. The publicly available scRNA-seq-based atlas by de Jong et al 2021 was used to demonstrate the expression of indicated genes in the BM hematopoietic CD38- cells from BM of patients with MM. **A.** BM CD38- cells' classification based on the atlas. **B.** Expression of mesenchymal markers *COL1A1*, *FN1*, *THY1*, *CYR61* and *CTGF*. *PTPRC* (CD45) is shown as a reference marker for hematopoietic cells.



References

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2. de Jong MME, Kellermayer Z, Papazian N, et al. The multiple myeloma microenvironment is defined by an inflammatory stromal cell landscape. *Nat Immunol*. 2021;22(6):769-780.
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