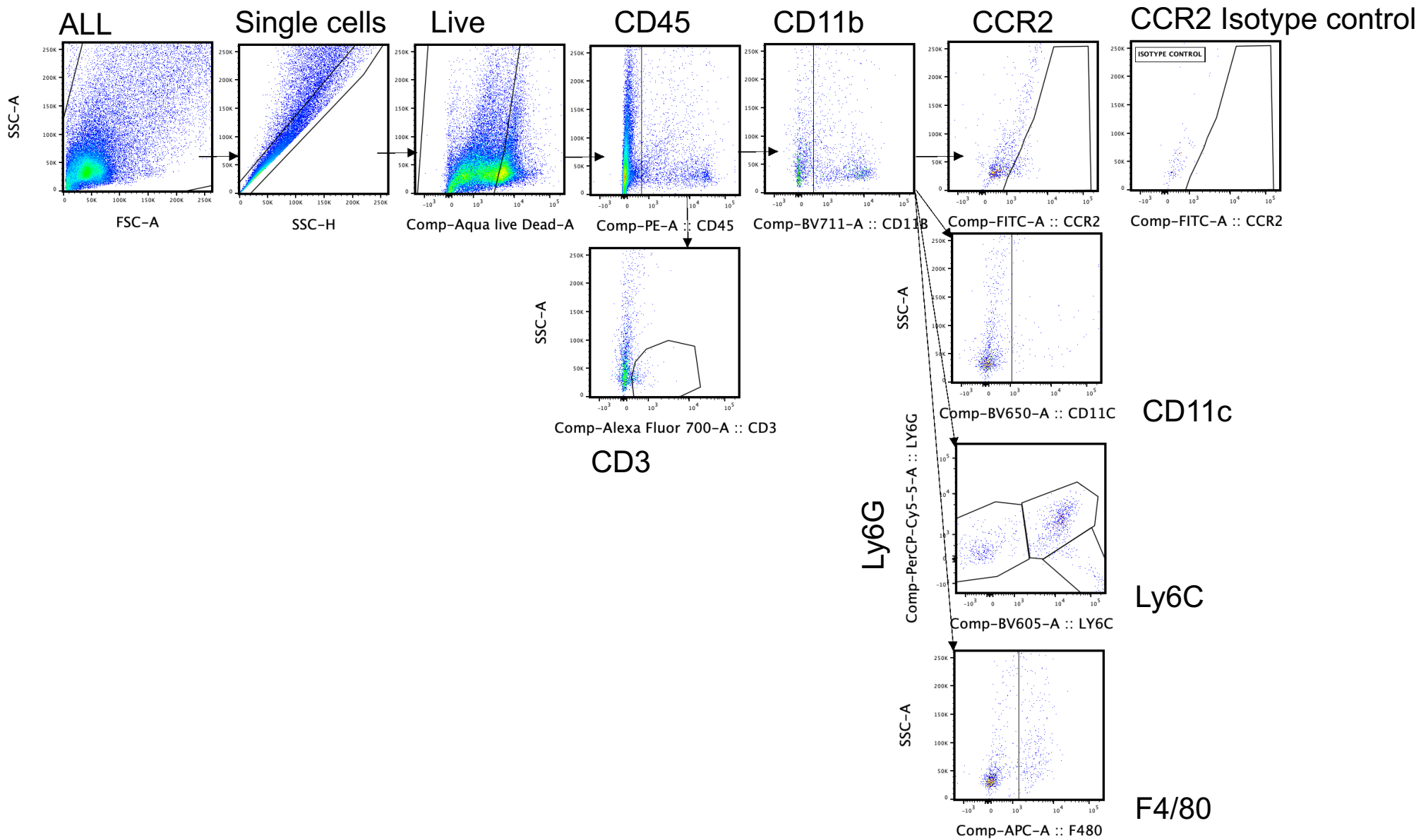
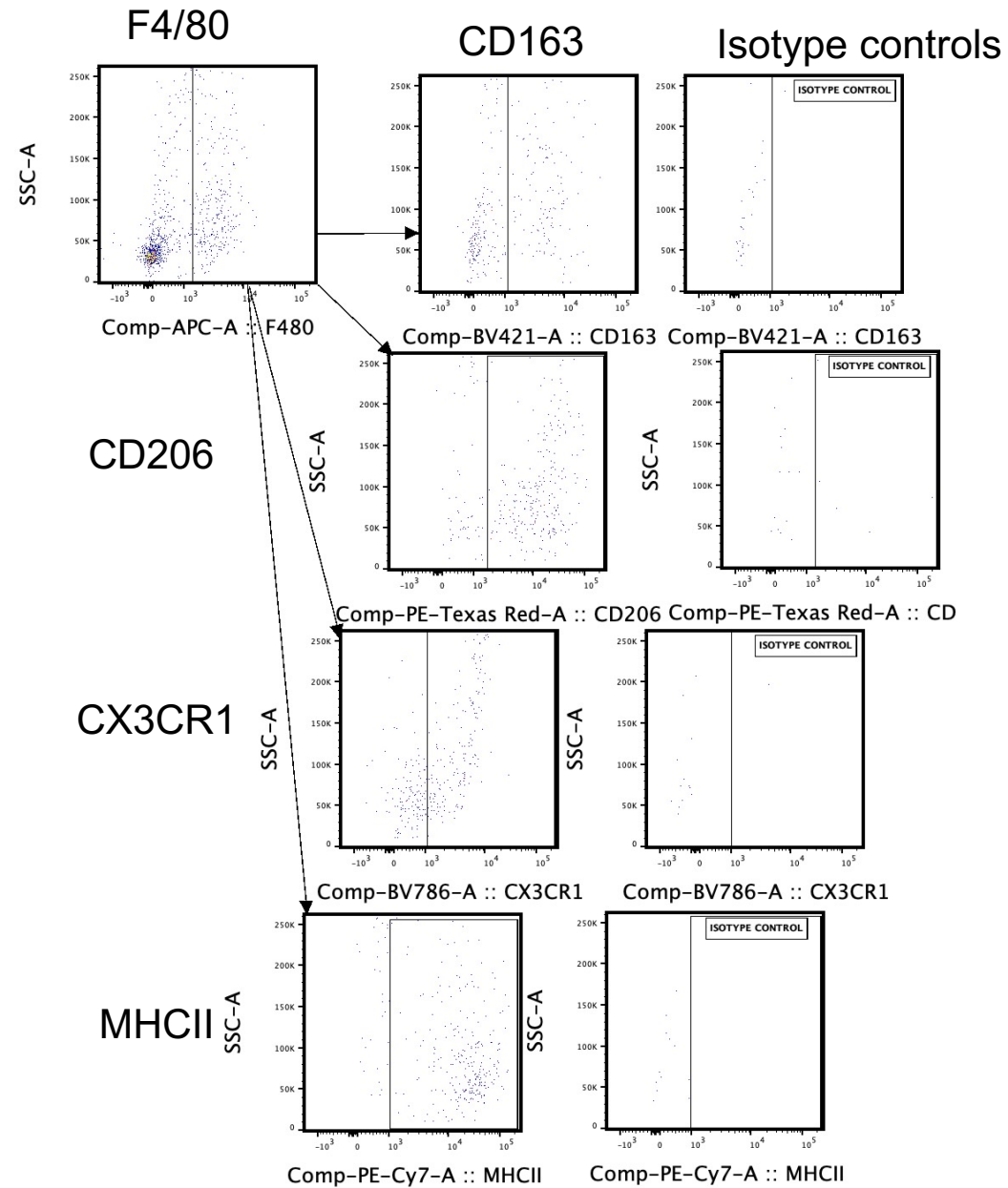


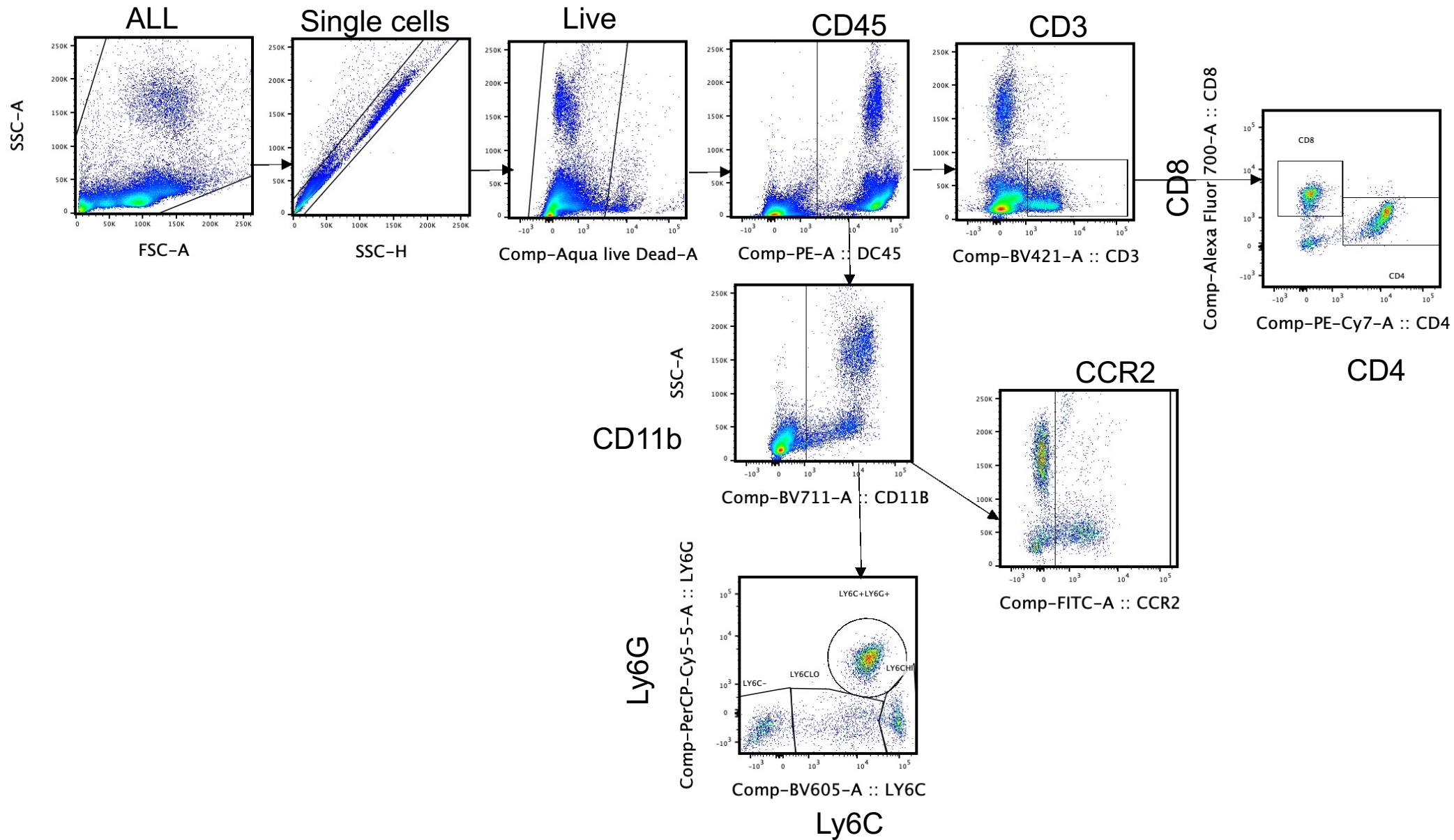
**Suppl. Fig. 1.** Schematic flow chart demonstrating the experimental design of mouse and human subjects used in this study.



**Suppl. Fig. 2.** DRG Gating strategy. Representative gating strategy used for all DRG flow cytometry samples in this study. First, cells were gated for single cells to exclude doublets and clumps. Next cells were gated on live cells (Aqua live/dead negative for dye stain). Single live cells were then gated for CD45+ cells, followed by CD11b+ or CD3+ cells. Under CD11b+ cells, remaining populations were gated for CCR2+ cells, F4/80+ macrophages, CD11c+ dendritic cells, Ly6C+ monocytes, and Ly6G+ granulocytes. Isotype controls were used to draw gates, exemplified here via Isotype control for CCR2.



**Suppl. Fig. 3.** Gating strategy of DRG Macrophage subpopulations. Representative gating strategy used for all DRG flow cytometry samples in this study. Under F4/80+ cell gate, macrophage populations were gated for CD163, CD206, CX3CR1, or, MHCII+ using Isotype controls to inform gating.

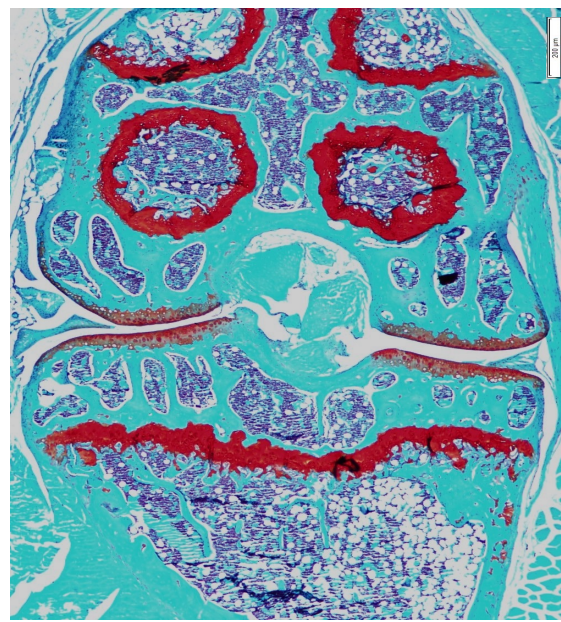


**Suppl. Fig. 4.** Representative gating strategy used for all peripheral blood flow cytometry samples in this study. First, cells were gated for single cells to exclude doublets and clumps. Next cells were gated on live cells (Aqua live/dead negative for dye stain). Single live cells were then gated for CD45+ cells, followed by CD11b+ or CD3+ cells. Under CD3, cells were gated for CD4 or CD8. Under CD11b+ cells, remaining populations were gated for CCR2+ cells, Ly6C+ monocytes, and Ly6G+ granulocytes.

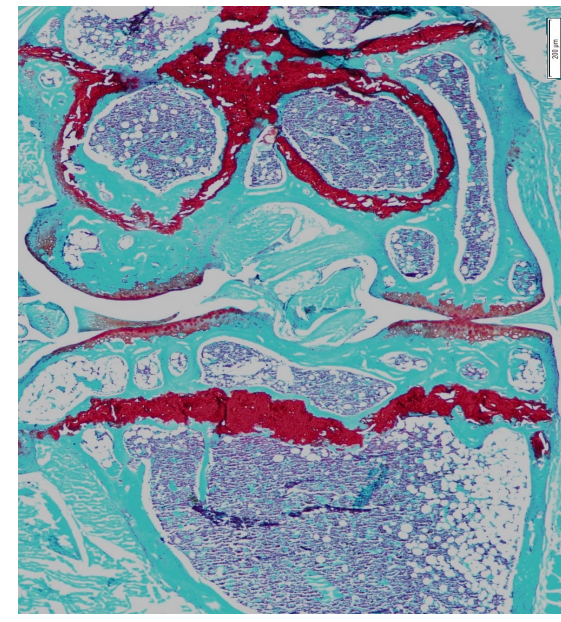
**Males**

**Females**

**6 months**

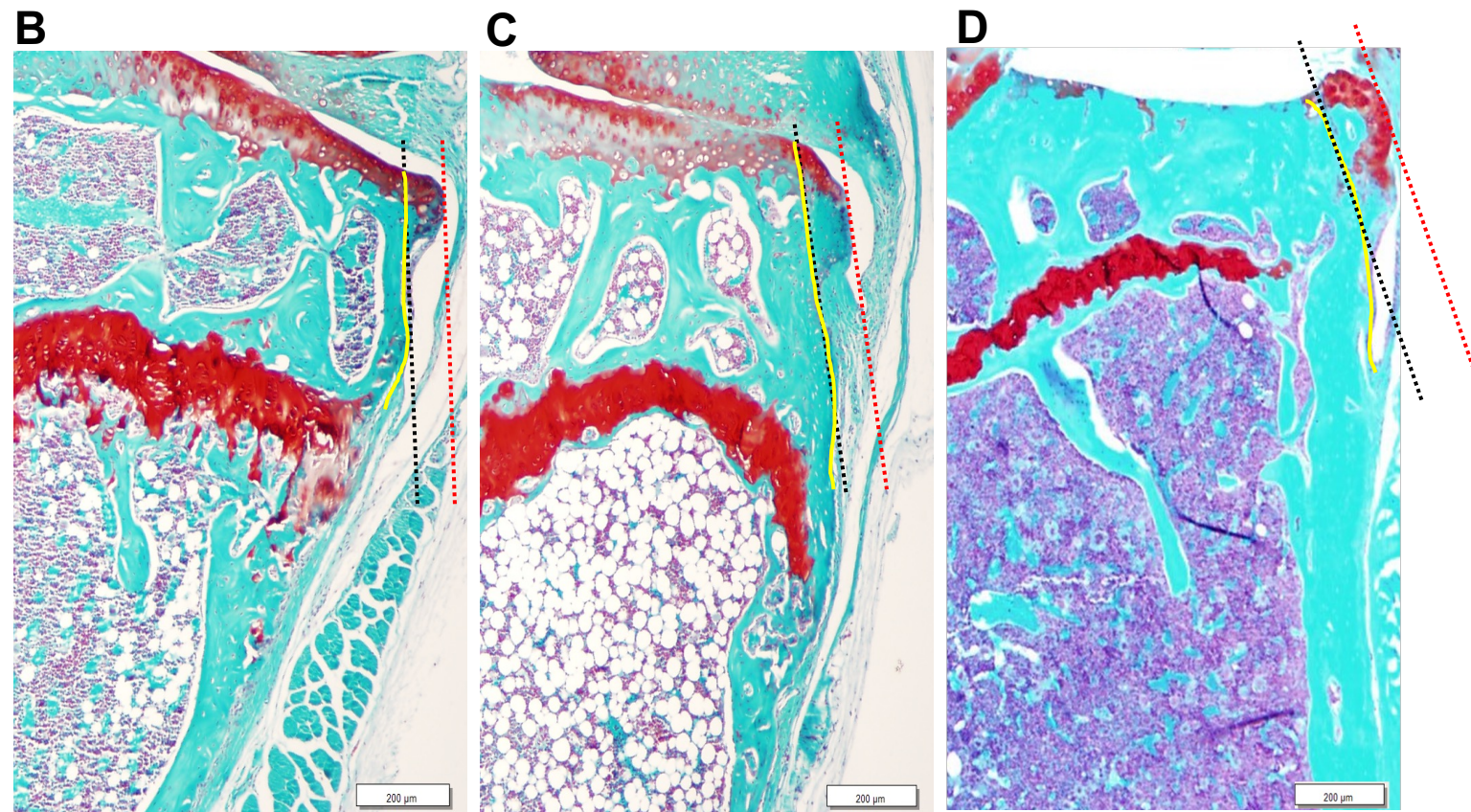
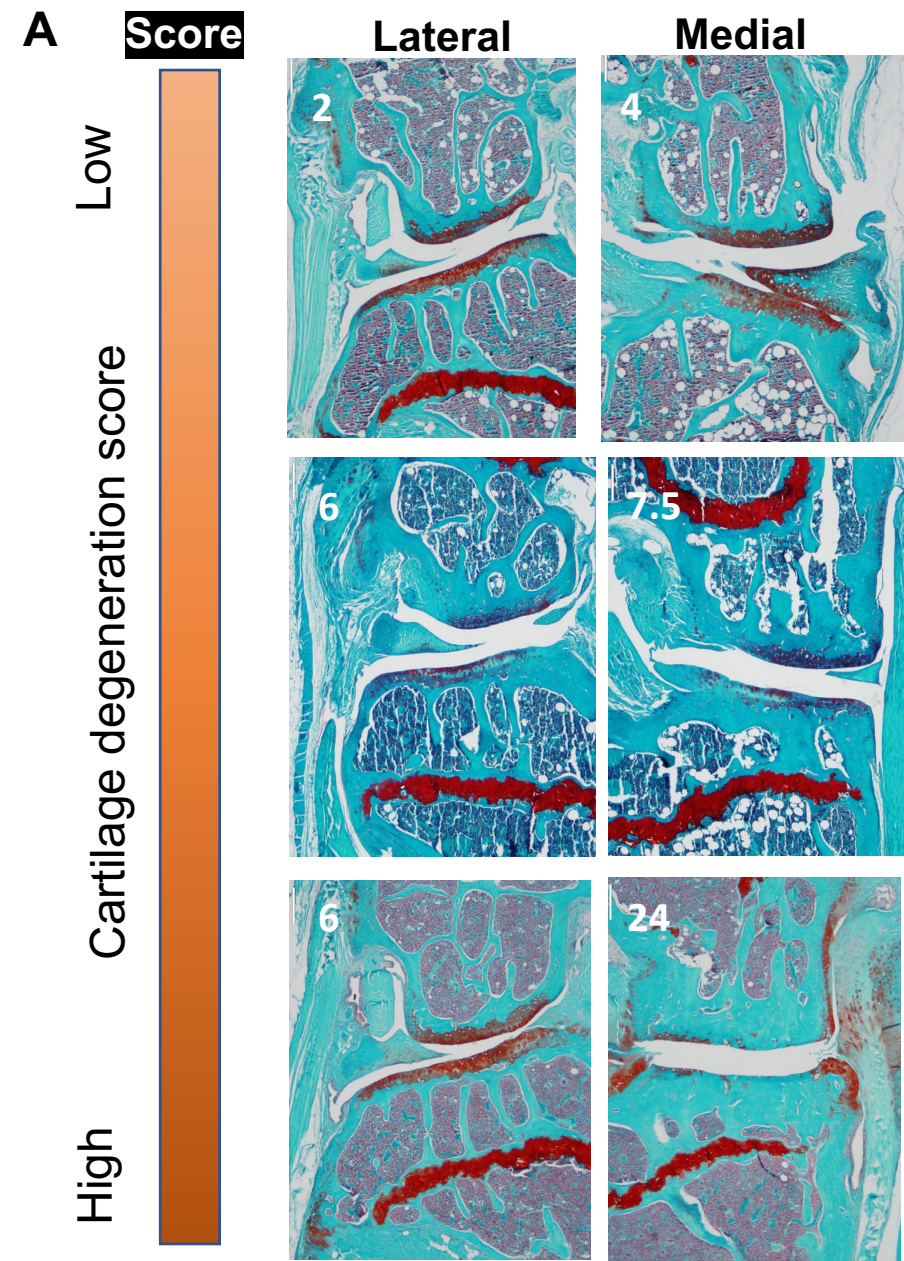


**20 months**

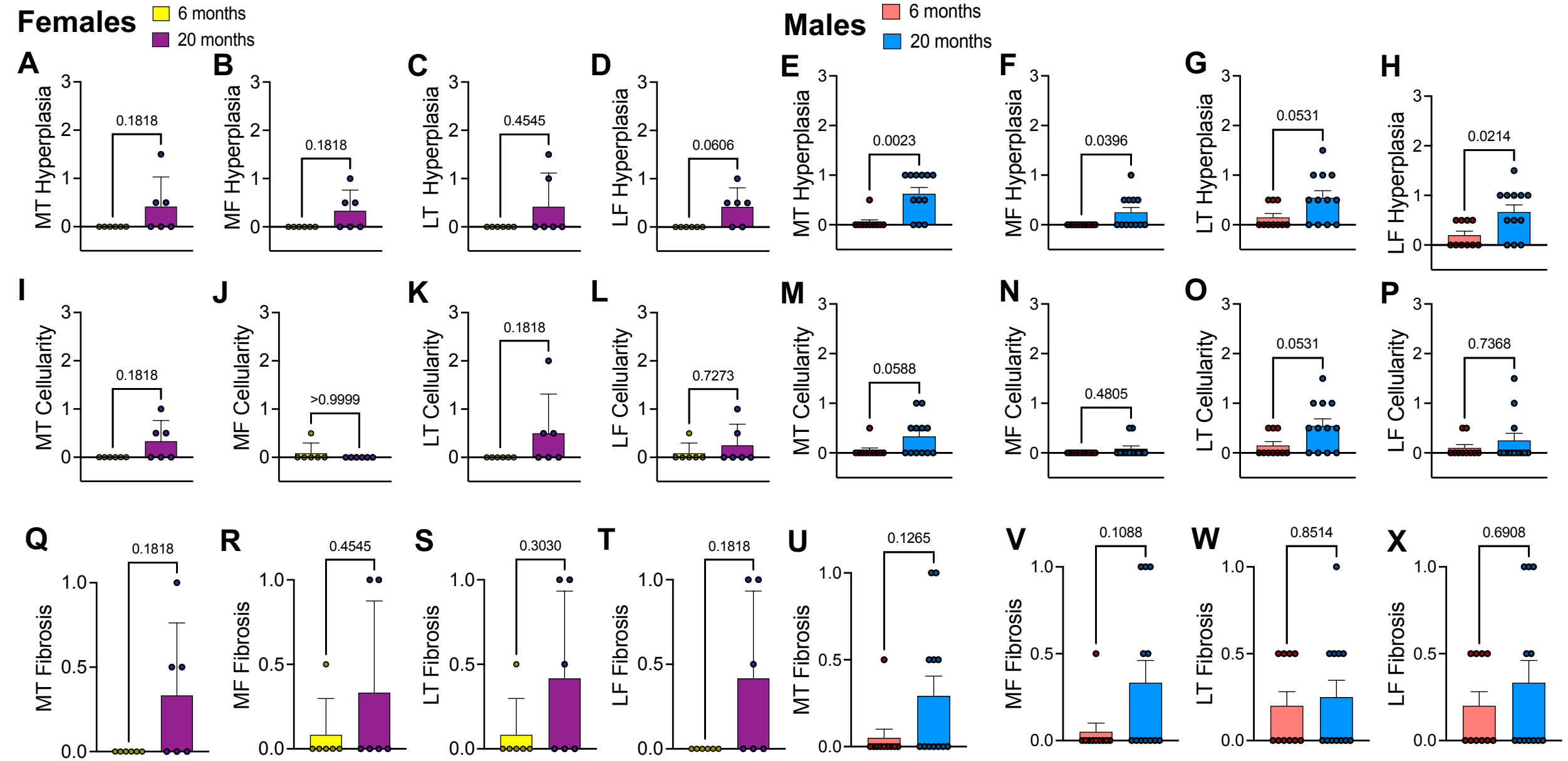


**Suppl. Fig. 5.** Representative Safranin-O images of aged mouse knee osteoarthritis. Representative images of 6-month or 20-month male or female knee joints stained with Safranin-O. Images taken at 2x magnification.

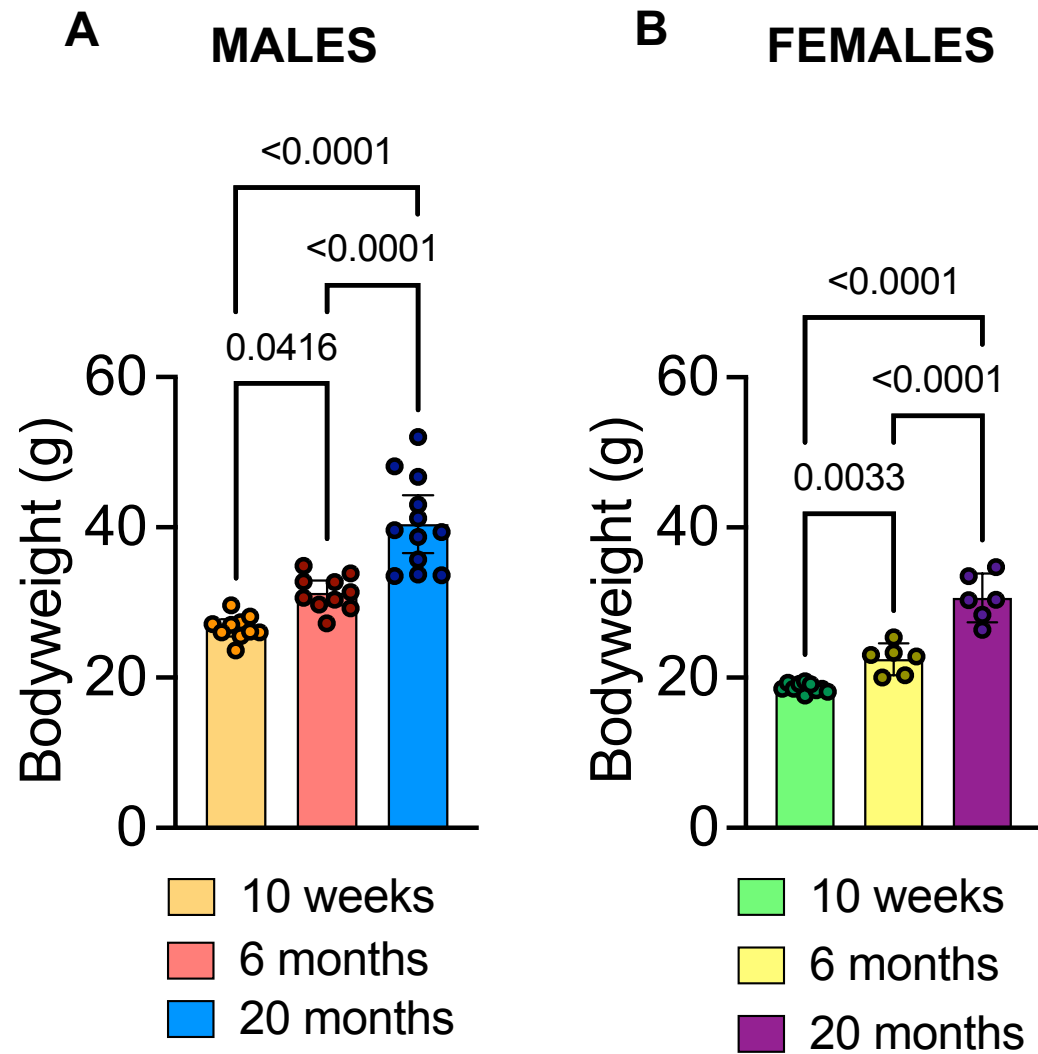
# Male 20 month old mice



**Suppl. Fig. 6.** (A) Range of cartilage damage seen in 20-month old male mice. Knee joints stained with Safranin-O. Images taken at 4x magnification. White numbers on each image show cartilage degeneration score. (B) – (D) Safranin-O stained representative right knee sections from 6- or 20-month old female (B, C) and 20-month old male mouse (D) showing osteophyte width scoring method. A line was drawn along the medial side of the tibia (yellow line). A second line is drawn intersecting that line and the articular surface (black line). Another line (red line) is drawn parallel to the black line at the outer border of the osteophyte. The distance between the red and black lines is defined as the osteophyte width.



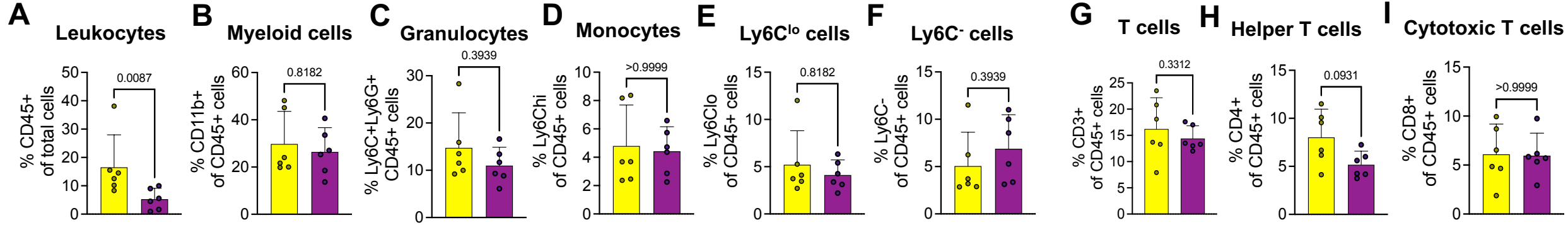
**Suppl. Fig. 7.** Hyperplasia score of four tissue quadrants for females aged 6 or 20 months old (n=6): **(A)** medial tibial (MT) **(B)** medial femoral (MF), **(C)** lateral tibial (LT) and **(D)** lateral femoral (LF) synovium, scored 0-3 per quadrant. **(E) – (H)** Same as in **(A) – (D)** but showing males aged 6 (n=10) or 20 months (n=12). **(I) – (L)** Same as in **(A) – (D)** but showing Cellularity score of four tissue quadrants, scored 0-3 per quadrant. **(M) – (P)** Same as in **(I) – (L)** but showing males aged 6 (n=10) or 20 months (n=12). **(Q) – (T)** Same as in **(A) – (D)** but showing Fibrosis score of four tissue quadrants, scored 0-1 per quadrant. **(U) – (X)** Same as in **(Q) – (T)** but showing males aged 6 (n=10) or 20 months (n=12) old. Mann-Whitney test. Error bars show Mean +/- SEM.



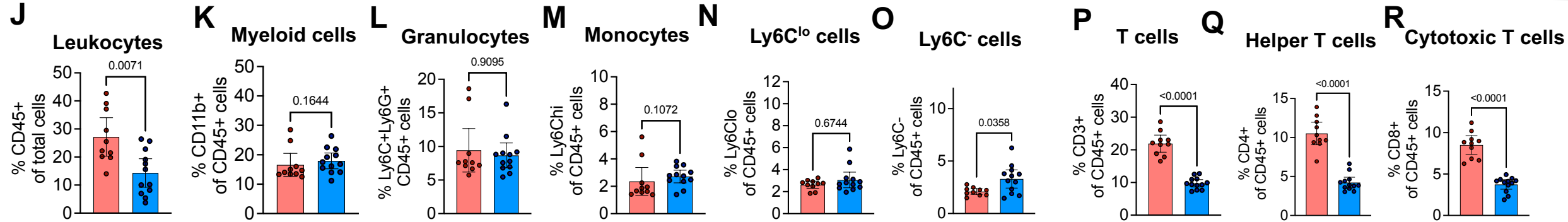
**Suppl. Fig. 8.** (A) Bodyweights of male mice aged 10-weeks, 6-months, or 20-months old in grams. (B) Bodyweights of female mice aged 10-weeks, 6-months, or 20-months old in grams. Statistical analysis by ordinary one-way ANOVA. P values stated on graph. Error bars show Mean +/- SEM.



**Females**  
 6 months (yellow)  
 20 months (purple)



**Males**  
 6 months (red)  
 20 months (blue)



**Suppl. Fig. 9.** Immune cell populations in peripheral blood of aged female and male mice. Female mice (**A**) – (**I**): (**A**) Frequency of CD45+ leukocytes (**B**) CD11b+ myeloid cells (**C**) Ly6G+ granulocytes, (**D**) Ly6Chi monocytes (**E**) Ly6C<sup>lo</sup> cells (**F**) Ly6C<sup>-</sup> cells, (**G**) CD3+ T lymphocytes CD11c+ dendritic cells (**G**) Ly6C-antigen presenting precursor cells (**H**) CD4+ T helper cells, and (**I**) CD8+ cytotoxic T cells in 6-month (n=6), or 20-month (n=6) old female mice. Male mice (**J**) – (**R**) Same as in (**A**) – (**I**) but for 6- and 20-month old male mice peripheral blood. Flow cytometry gating strategy in Suppl. Fig. 4. Statistical analysis by Mann-Whitney test. Significant if p < 0.05. P values stated in graphs. Error bars show Mean +/- SEM.