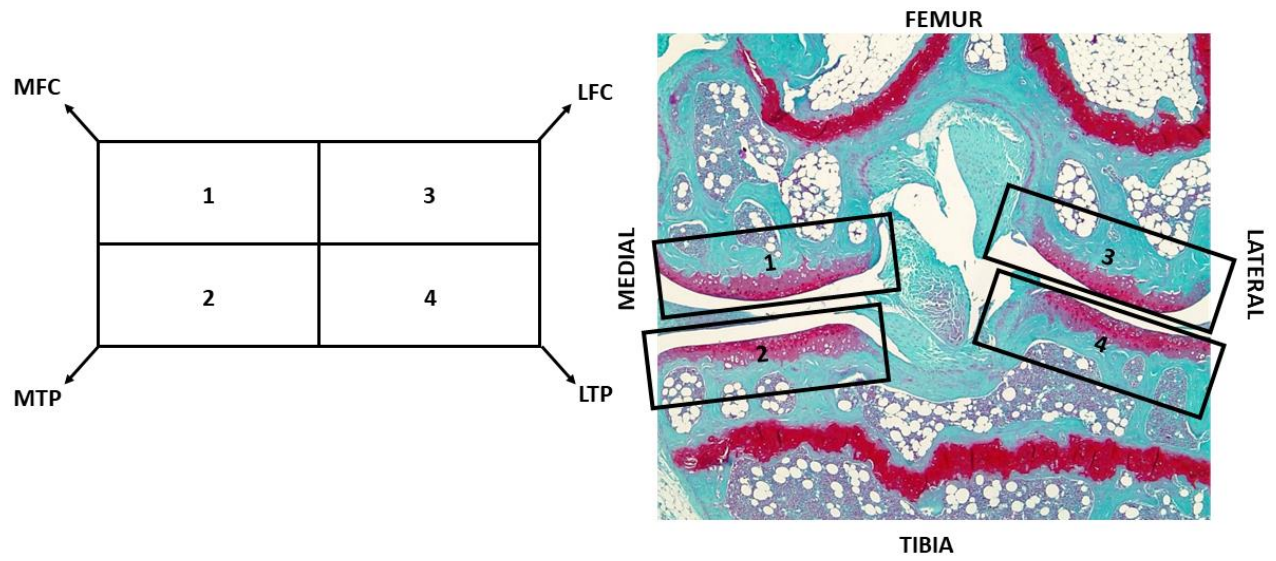
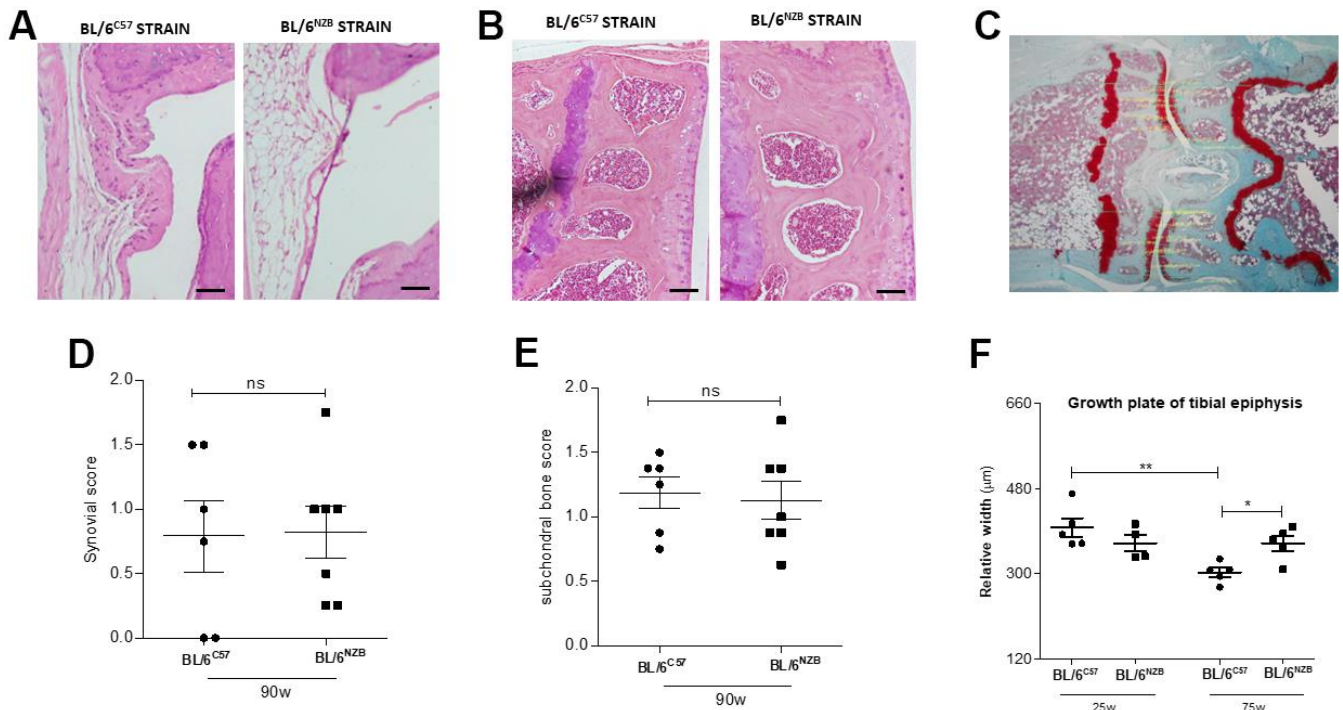


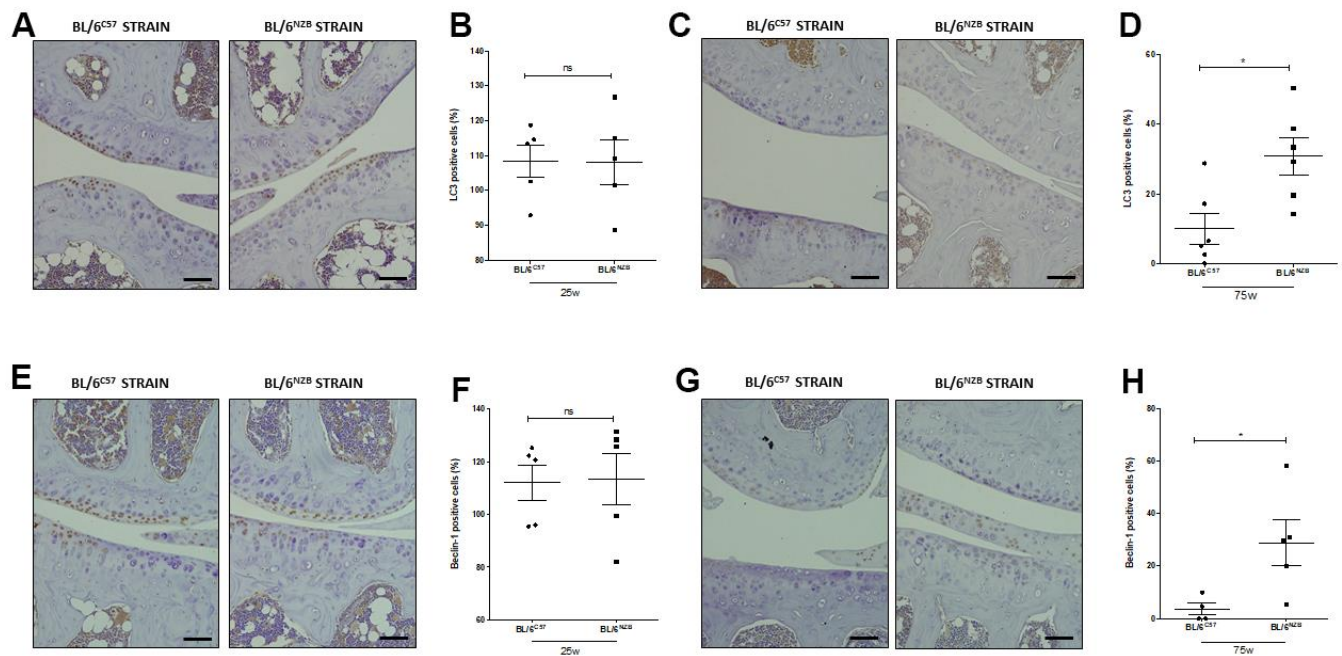
SUPPLEMENTARY FIGURES



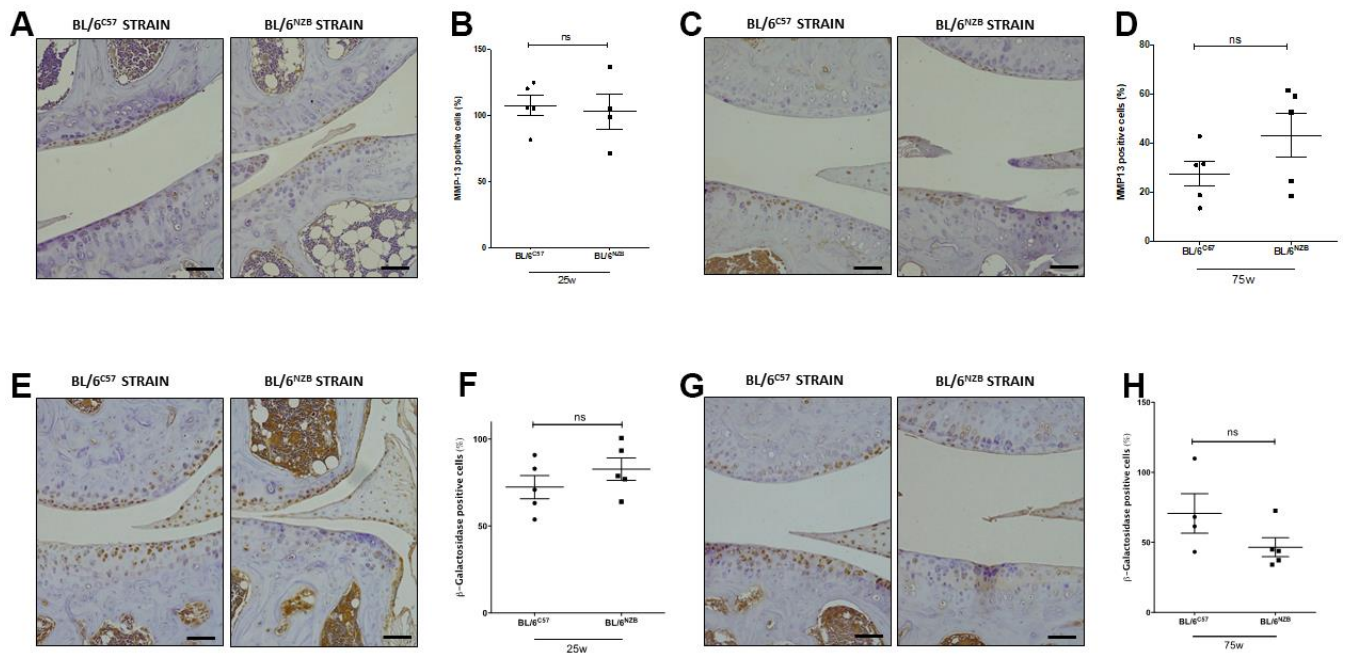
Supplementary Figure 1. Coronal section analysis for Mankin score measurement. TP (tibial plateau) = MTP+LTP; FC (femoral condyle) = MTP+LFC; medial compartment= MTP+MFC; lateral compartment = LTP+LFC; whole joint: medial compartment + lateral compartment.



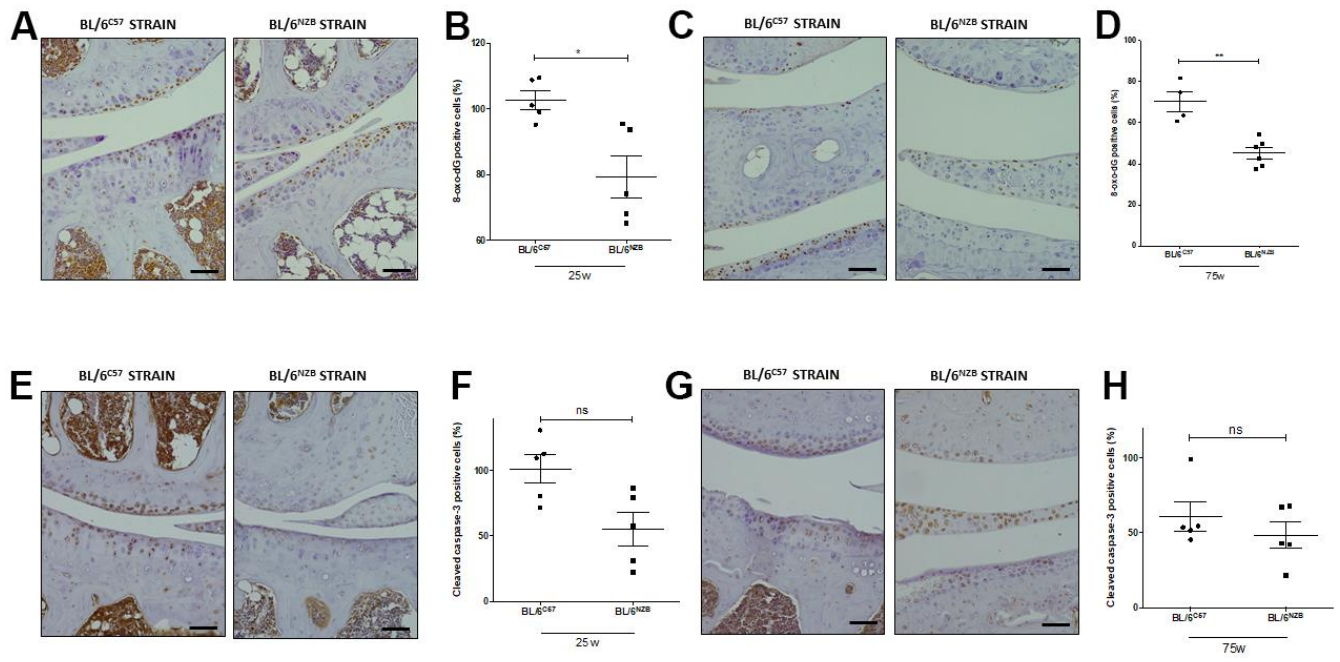
Supplementary Figure 2. Histopathological evaluation of synovial tissue and subchondral bone and histomorphometric analysis of growth plate of tibial epiphysis. Representative images of synovial tissue (A) and subchondral bone (B) from joint sections of BL/6^{CS7} and conplastic (BL/6^{NZB}) mice at 90 weeks of age stained with Hematoxylin-Eosin. Histopathological changes in the synovium (D) and subchondral bone (E) were graded by semi-quantitative scoring system (<https://doi.org/10.1111/j.1365-2559.2006.02508.x>; <https://doi.org/10.1371/journal.pone.0173726>; respectively). Original magnification: 20×. Scale bar, 100 μm. Graphs represent means ± SEM; n=6 in BL/6^{CS7} and n=7 in conplastic (BL/6^{NZB}) mice. (C, F) Histomorphometric analysis of growth plate of tibial epiphysis from joint sections of BL/6^{CS7} and conplastic (BL/6^{NZB}) mice at 25 and 75 weeks. Representative image of analysis performed with Software NIS Elements associated to the microscope NIKON (BX61). Graphs represent means ± SEM; n=5 in BL/6^{CS7} and n=4 in conplastic (BL/6^{NZB}) mice at 25 weeks; n=5 in BL/6^{CS7} and conplastic (BL/6^{NZB}) mice at 75 weeks. ns=not significant, *p<0.05, **p<0.01 by non-parametric Mann-Whitney test.



Supplementary Figure 3. LC3 and Beclin-1 expression in cartilage from mice at 25 and 75 weeks of age. Representative images of medial compartment of knee joints from BL/6^{CS7} and conplastic (BL/6^{NZB}) mice at 25 weeks (A) and 75 weeks (C) of age stained with LC3. Quantitative analysis of LC3-positive cells of knee joints from BL/6^{CS7} and conplastic (BL/6^{NZB}) mice at 25 weeks (B) and 75 weeks (D) of age. 25 weeks: n=5 in BL/6^{CS7} and n=5 conplastic (BL/6^{NZB}) mice; 75 weeks: n=6 in BL/6^{CS7} and n=6 conplastic (BL/6^{NZB}) mice. Representative images of medial compartment of knee joints from BL/6^{CS7} and conplastic (BL/6^{NZB}) mice at 25 weeks (E) 75 weeks (G) of age stained with Beclin-1. Quantitative analysis of Beclin-1-positive cells of knee joints from BL/6^{CS7} and conplastic (BL/6^{NZB}) mice at 25 weeks (F) 75 weeks (H) of age. 25 weeks: n=5 in BL/6^{CS7} and n=5 conplastic (BL/6^{NZB}) mice; 75 weeks: n=4 in BL/6^{CS7} and n=5 conplastic (BL/6^{NZB}) mice. Original magnification: 20×. Scale bar, 50 μm. Graphs represent means ± SEM. ns=not significant, *p<0.05 by non-parametric Mann-Whitney test.



Supplementary Figure 4. Immunohistochemistry for MMP13 and β -Galactosidase in mice at 25 and 75 weeks. Representative images of medial compartment of knee joints from BL/6^{CS7} and conplastic (BL/6^{NZB}) mice at 25 weeks (A) and 75 weeks (C) of age stained with MMP13. Quantitative analysis of MMP13-positive cells of knee joints from BL/6^{CS7} and conplastic (BL/6^{NZB}) mice at 25 weeks (B) and 75 weeks (D) of age. 25 weeks: n=5 in BL/6^{CS7} and n=4 conplastic (BL/6^{NZB}) mice; 75 weeks: n=5 in BL/6^{CS7} and n=5 conplastic (BL/6^{NZB}) mice. Representative images of medial compartment of knee joints from BL/6^{CS7} and conplastic (BL/6^{NZB}) mice at 25 weeks (E) and 75 weeks (G) of age stained with β -Galactosidase. Quantitative analysis of β -Galactosidase-positive cells of knee joints from BL/6^{CS7} and conplastic (BL/6^{NZB}) mice at 25 weeks (F) and 75 weeks (H) of age. 25 weeks: n=5 in BL/6^{CS7} and n=5 conplastic (BL/6^{NZB}) mice; 75 weeks: n=4 in BL/6^{CS7} and n=5 conplastic (BL/6^{NZB}) mice. Original magnification: 20 \times . Scale bar, 50 μ m. Graphs represent means \pm SEM; ns=not significant by non-parametric Mann-Whitney test.



Supplementary Figure 5. 8-oxo-dG cartilage and cleaved caspase-3 expression in conplastic mice at 25 and 75 weeks. Representative images of medial compartment of knee joints from BL/6^{C57} and conplastic (BL/6^{NZB}) mice at 25 weeks (A) and 75 weeks (C) of age stained with 8-oxo-dG. Quantitative analysis of 8-oxo-dG-positive cells of knee joints from BL/6^{C57} and conplastic (BL/6^{NZB}) mice at 25 weeks (B) and 75 weeks (D) of age. 25 weeks: n=5 in BL/6^{C57} and n=5 conplastic (BL/6^{NZB}) mice; 75 weeks: n=4 in BL/6^{C57} and n=6 conplastic (BL/6^{NZB}) mice. Representative images of medial compartment of knee joints from BL/6^{C57} and conplastic (BL/6^{NZB}) mice at 25 week (E) 75 weeks (G) of age stained with cleaved caspase-3. Quantitative analysis of cleaved caspase-3 -positive cells of knee joints from BL/6^{C57} and conplastic (BL/6^{NZB}) mice at 25 weeks (F) and 75 weeks of age (H). 25 weeks: n=5 in BL/6^{C57} and n=5 conplastic (BL/6^{NZB}) mice, 75 weeks: n=5 in BL/6^{C57} and n=5 conplastic (BL/6^{NZB}) mice. Original magnification: 20×. Scale bar, 50 μm. Graphs represent means ± SEM; ns=not significant, *p<0.05, **p<0.01 by non-parametric Mann-Whitney test.