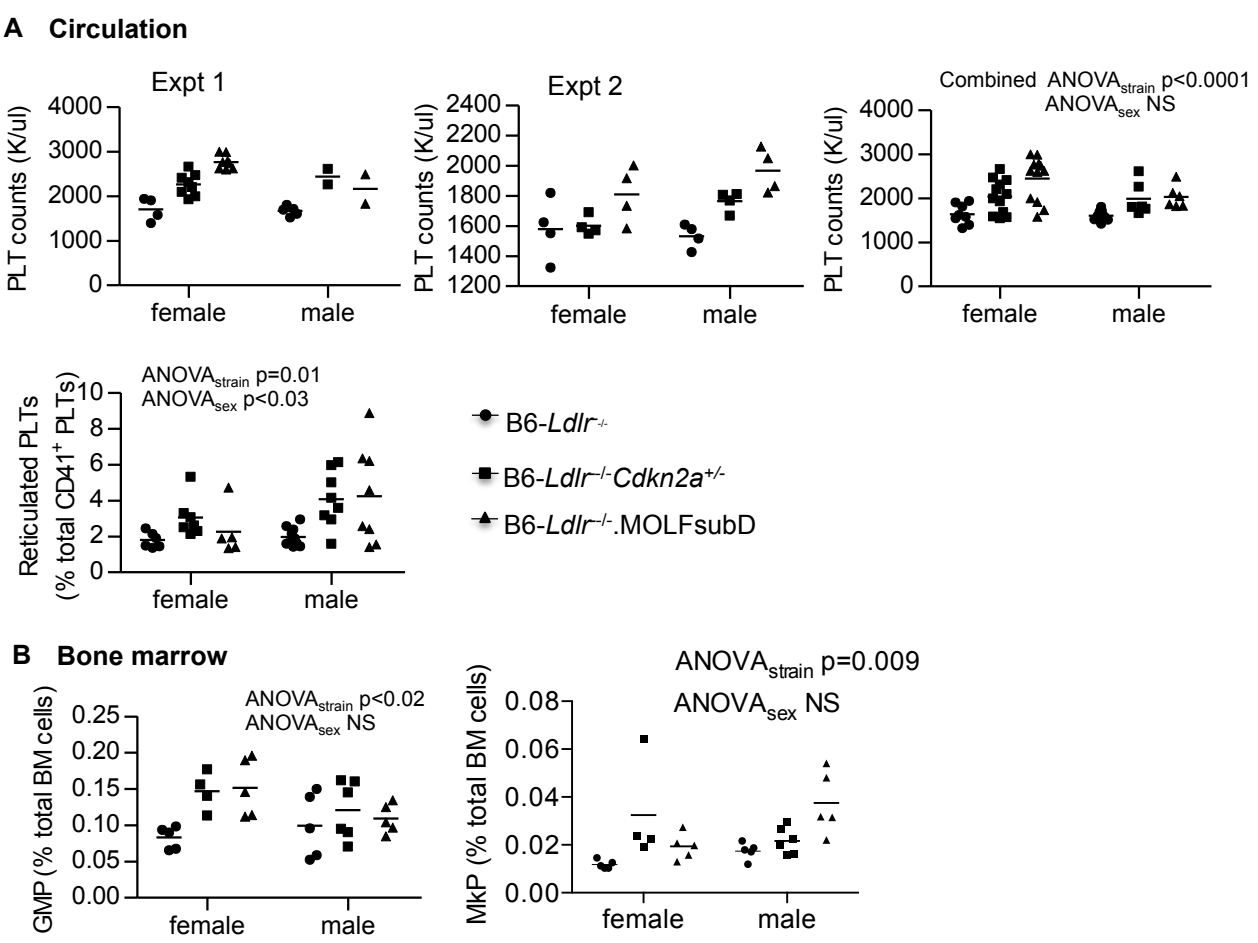
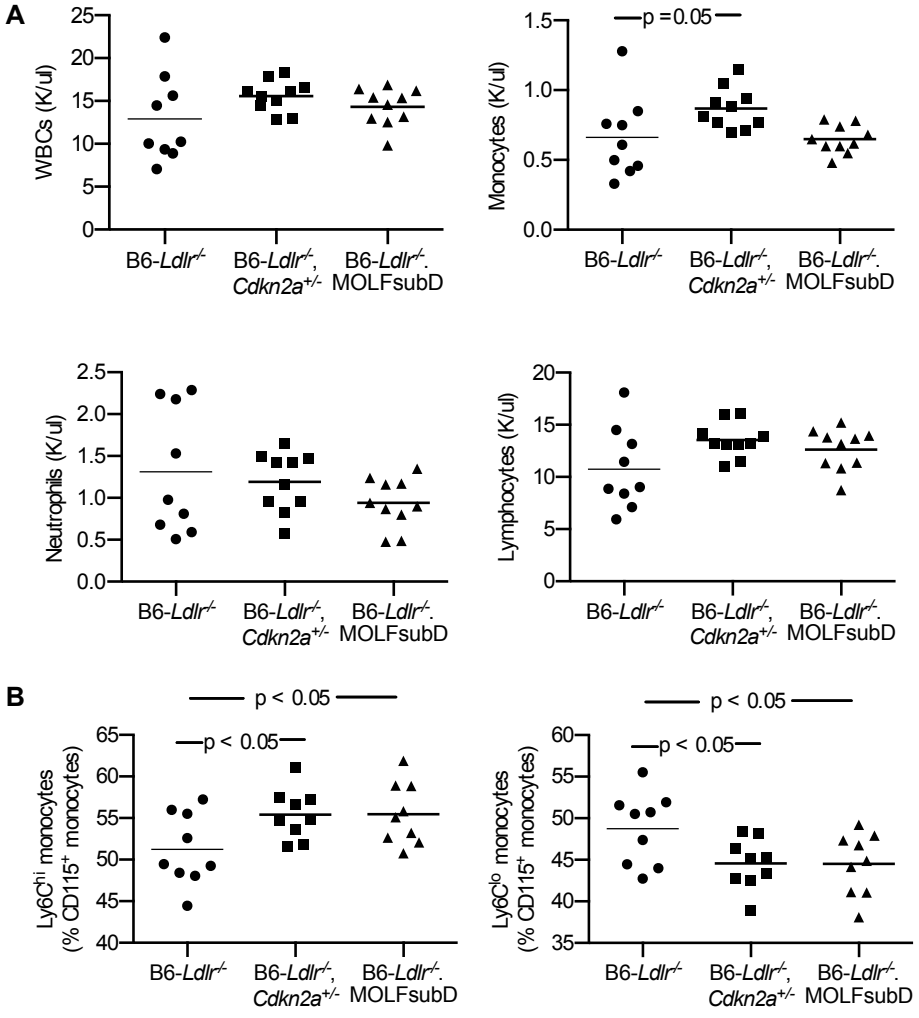
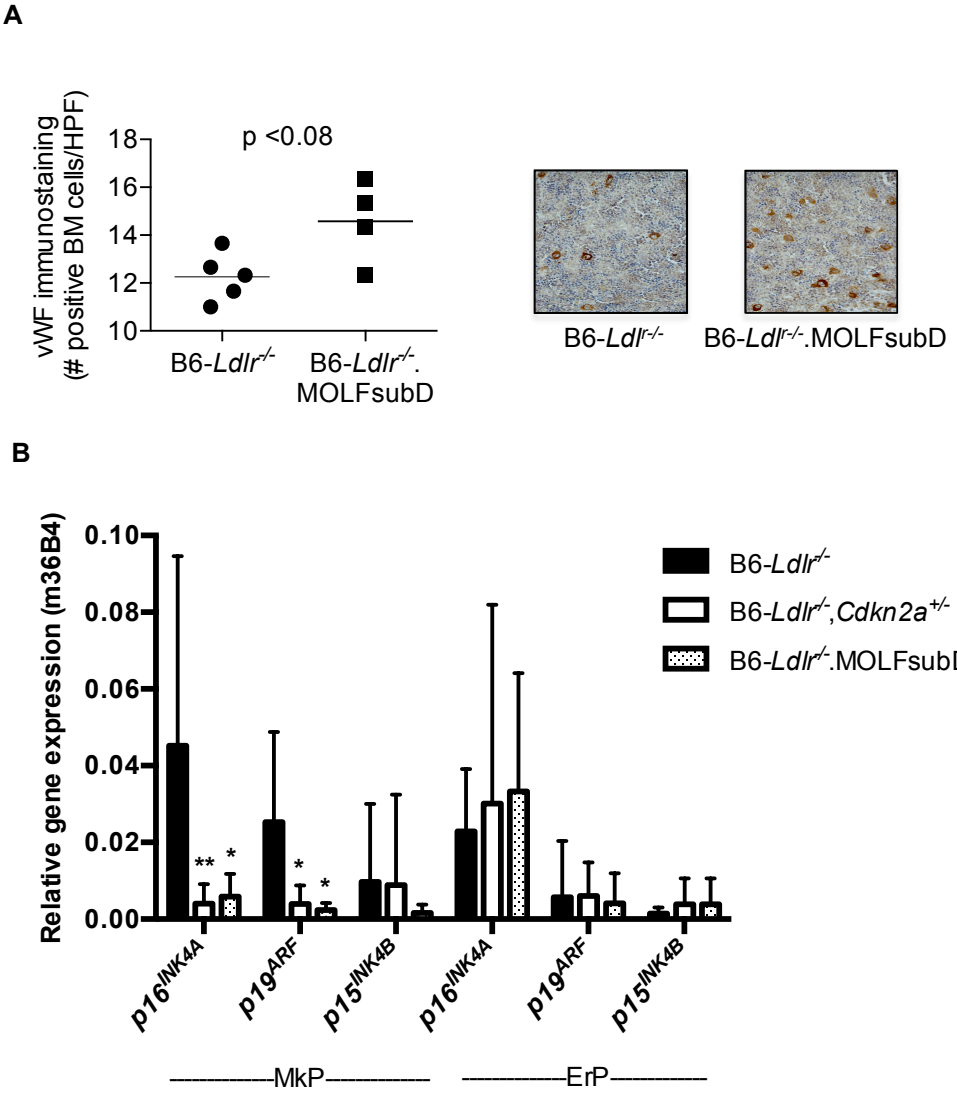
SUPPLEMENTAL MATERIAL



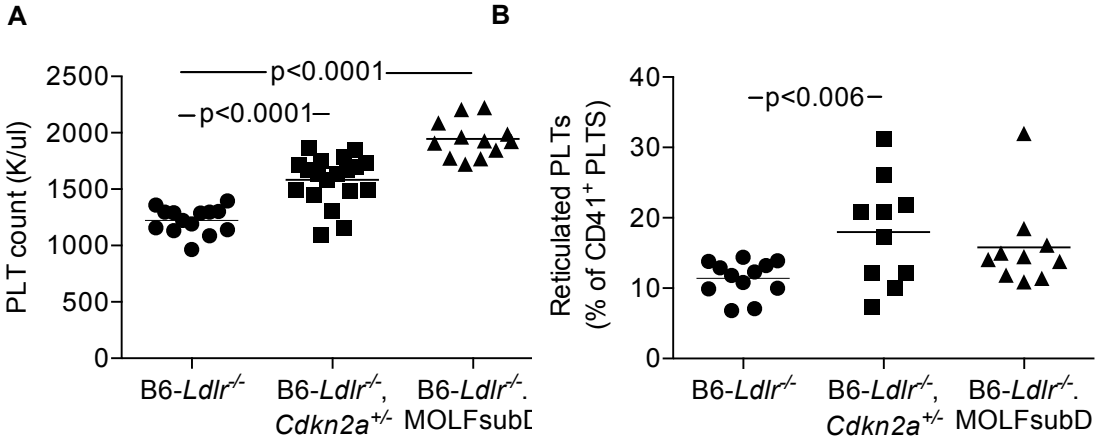
Supplemental Figure 1. Strain-specific differences in PLT counts, stem and progenitor cell profiles are largely independent of sex by two-way ANOVA. A, Circulating PLT counts from two different sets of mice and combined dataset for two-way ANOVA. Reticulated PLT analysis from a single experiment. **B,** BM-derived progenitor subset analyses from a single experiment. Chow diet.



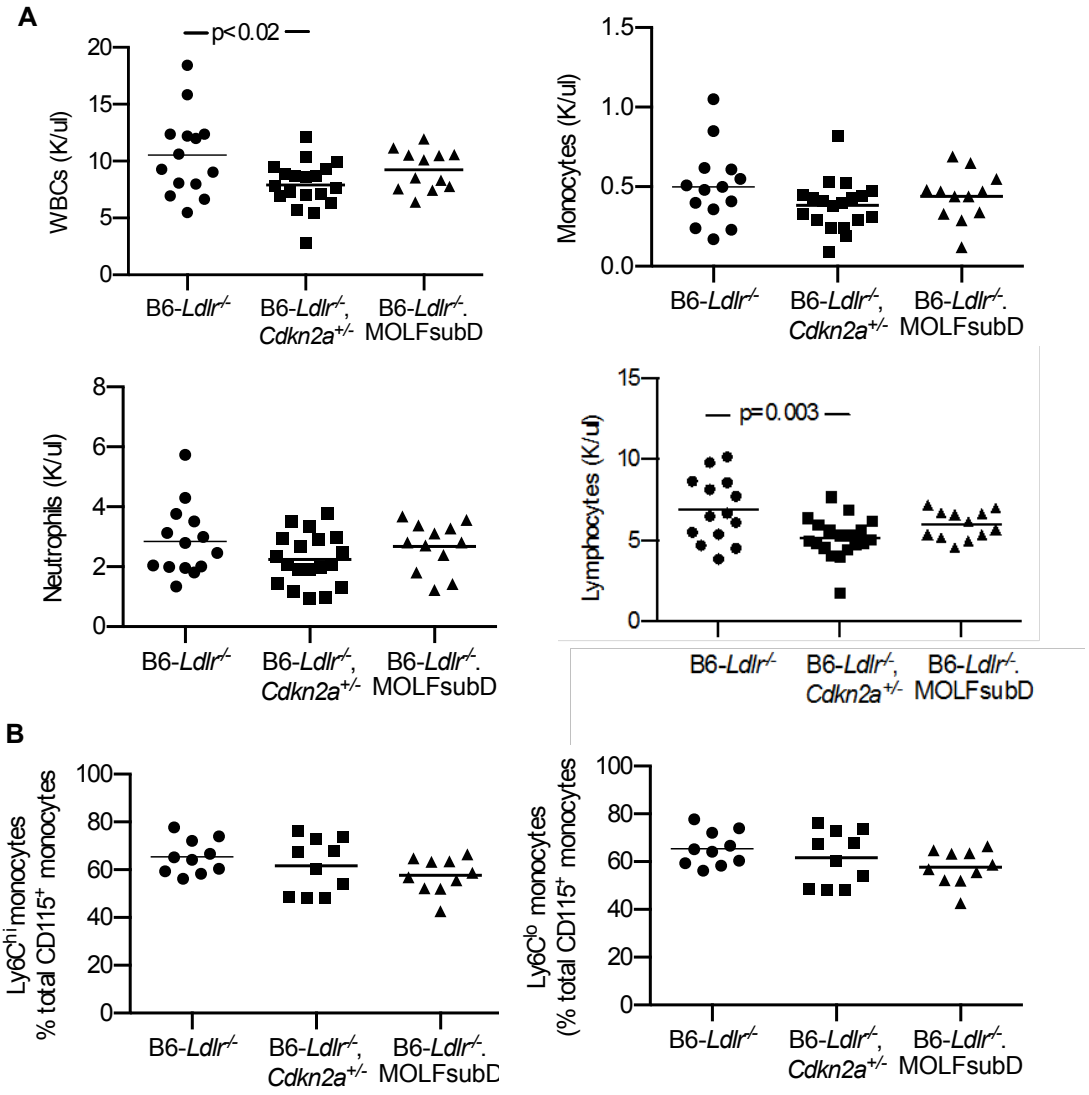
Supplemental Figure 2. Complete blood cell counts and monocyte subset analysis in chow-fed *Cdkn2a*-deficient mice. A, Total white blood cell (WBC), monocyte, neutrophil and lymphocyte counts in EDTA plasma measured with a Forcyte veterinary blood analyzer. **B,** Ly6C^{hi} and Ly6C^{lo} monocyte subsets measured by flow cytometry. Both datasets analyzed by one-way ANOVA.



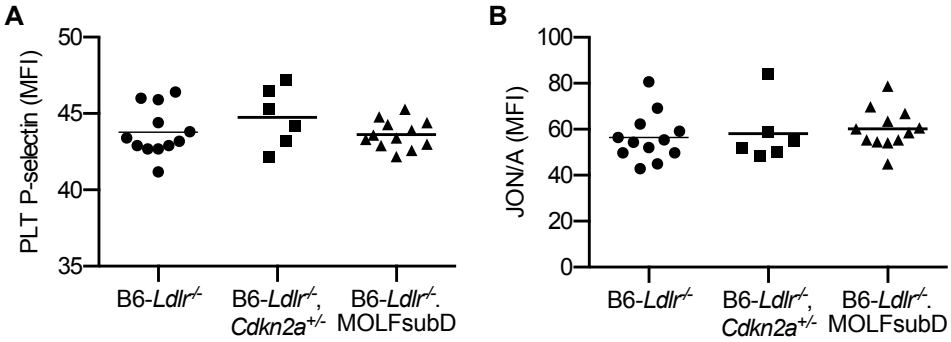
Supplemental Figure 3. vWF immunostaining and *Cdkn2a* transcript expression in BM derived from chow-fed *Cdkn2a*-deficient and *B6-Ldlr*$^{-/-}$ control mice. A, vWF immunostaining (dark brown) depicts the presence of MKs in decalcified bone. N = 4-5 mice/ group. Mann-Whitney test statistic. **B**, Quantitative PCR for transcripts encoded by *Cdkn2a* (*p16*^{INK4A} and *p19*^{ARF}) and *Cdkn2b* (*p15*^{INK4B}) relative to *m36B4*. BM cells were cultured for 7 days in the presence of 30 ng/ml TPO. MkP ($Lin^-Sca1^-c\text{-}Kit^+CD34^{int}FcγRII/III^{int}CD71^-CD41^+$) and ErP ($Lin^-Sca1^-c\text{-}Kit^+CD34^{int}FcγRII/III^{int}CD71^+CD41^-$) cells were isolated by FACS. RNA was isolated using an RNeasy micro kit (Qiagen) according to the manufacturer's protocol. cDNA was synthesized using Maxima First Strand cDNA synthesis kit (Thermo Fisher). Transcript-specific primers have been described[1-3] and were as follows: *p16*^{INK4a} (forward) – CGGTCGTACCCCGATTCAG, (reverse) – GCACCGTAGTTGAGCAGAAGAG; *p19*^{ARF} (forward) – TGAGGCTAGAGAGGATCTTGAGAAG, (reverse) – GTGAACGTTGCCCATCATCATC; *p15*^{INK4b} (catalog #Mm00483241, Applied Biosystems). N = 8 mice/group. Kruskal-Wallis with Dunn's multiple comparison post-hoc tet.



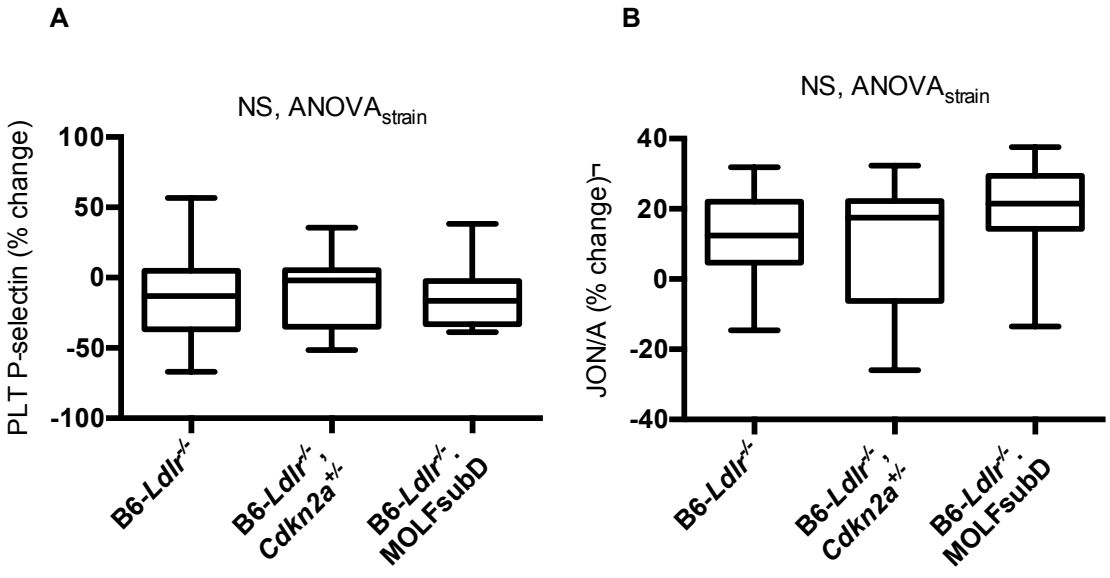
Supplemental Figure 4. Increased circulating PLT counts and reticulated PLTs in 8-week WTD-fed *Cdkn2a*-deficient mice. A, PLT counts in EDTA whole blood. **B,** Reticulated PLTs from acid-citrate-dextrose blood incubated with CD41-APC and thiazole orange nucleic acid-binding dye and analyzed by flow cytometry. One-way ANOVA.



Supplemental Figure 5. Complete blood cell counts and monocyte subset analysis in WTD-fed *Cdkn2a*-deficient mice. A, Total white blood cell (WBC), monocyte and neutrophil counts in EDTA plasma measured with a Forcyte veterinary blood analyzer. **B,** Ly6C^{hi} and Ly6C^{lo} monocyte subsets measured by flow cytometry. Both datasets analyzed by one-way ANOVA.



Supplemental Figure 6. No differences in the surface expression of PLT P-selectin or JON/A in resting PLTs from 8-week WTD-fed mice. Acid-citrate-dextrose whole blood, without stimulation, analyzed by flow cytometry. **A,** Mean fluorescent intensity (MFI) of PLT surface P-selectin. **B,** MFI of PLT surface activated form of JON/A.



Supplemental Figure 7. No differential strain effect of CDK4/6 inhibitor treatment on PLT activation markers. EDTA whole blood incubated ± 0.5 uM PD0332991 for 30 min, then 100 uM AYPGKF for 30 min (to induce PLT activation) and analyzed by flow cytometry. Data are expressed as per cent change ((MFI$_{PD0332991\text{-}treated}$ - MFI$_{untreated}$)/ MFI$_{untreated}$ * 100)). **A,** Per cent change of the mean fluorescent intensity of PLT surface P-selectin. **B,** Per cent change of the mean fluorescent intensity of PLT surface activated form of JON/A. N = 9-20 mice/strain, 5.5 wk WTD feeding.

Supplemental References

1. Krisnamurthy J, Torrice C, Ramsey MR, Kovalev GI, Al-Regaiey K, Su L and Sharpless NE. Ink4a/Arf expression is a biomarker of aging. *J Clin Invest.* 2004:114:1299-1307.

2. Krisnamurthy J, Ramsey MR, Ligon KL, Torrice C, Koh A, Bonner-Weir S and Sharpless NE. P16ink4a induces an age-dependent decline in islet regenerative potential. *Nature.* 2006:443:453-457.

2. Ramsey MR, Krisnamurthy J, Pei XH, Torrice C, Lin W, Carrasco DR, Ligon KL, Xiong Y and Sharpless NE. Expression of p16ink4a compensates for p18ink4c loss in cyclin-dependent kinase 4/6-dependent tumors and tissues. *Cancer Res.* 2007:67:4732-4741.