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<https://doi.org/10.3324/haematol.2023.283858>

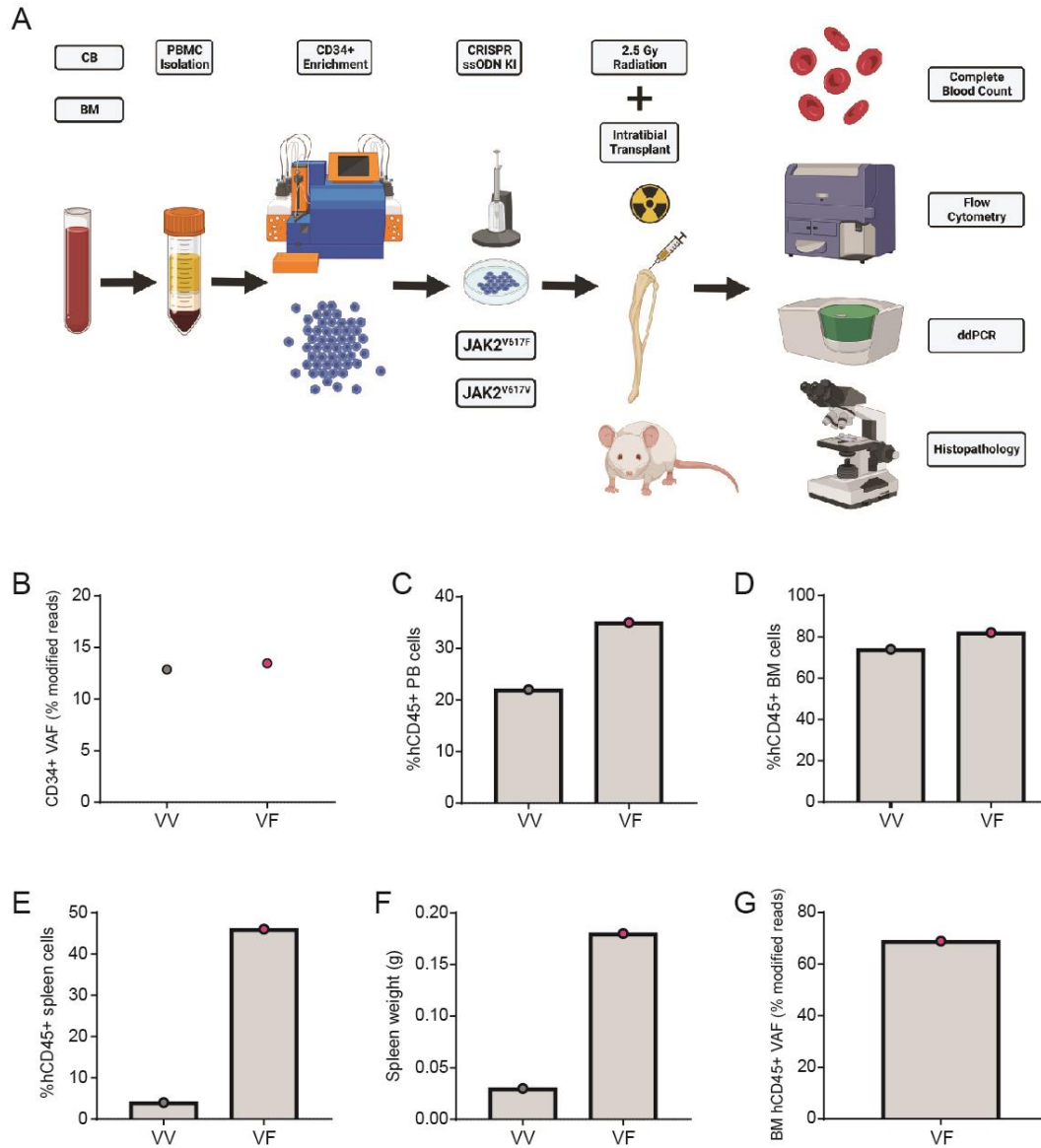
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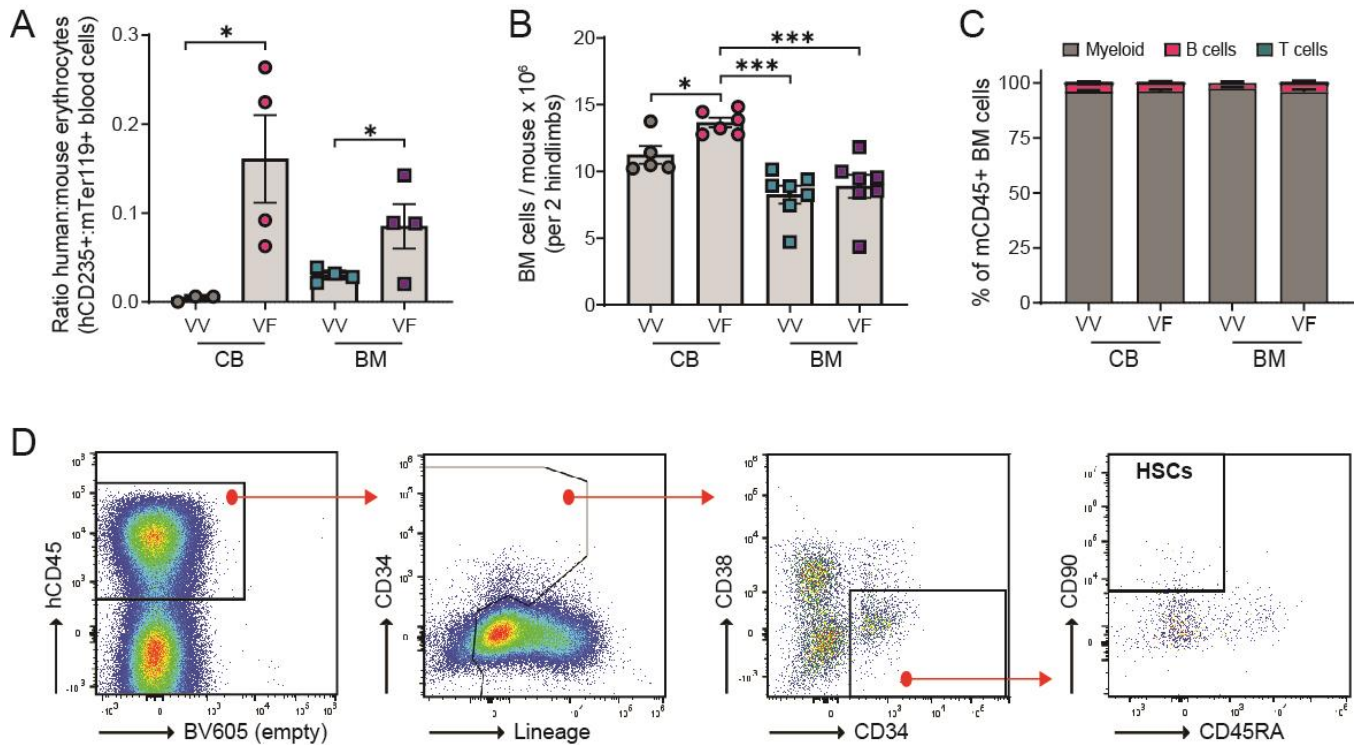
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SUPPLEMENTAL FIGURES



Supplemental Figure 1: *Engineering a Humanized Model of PV*

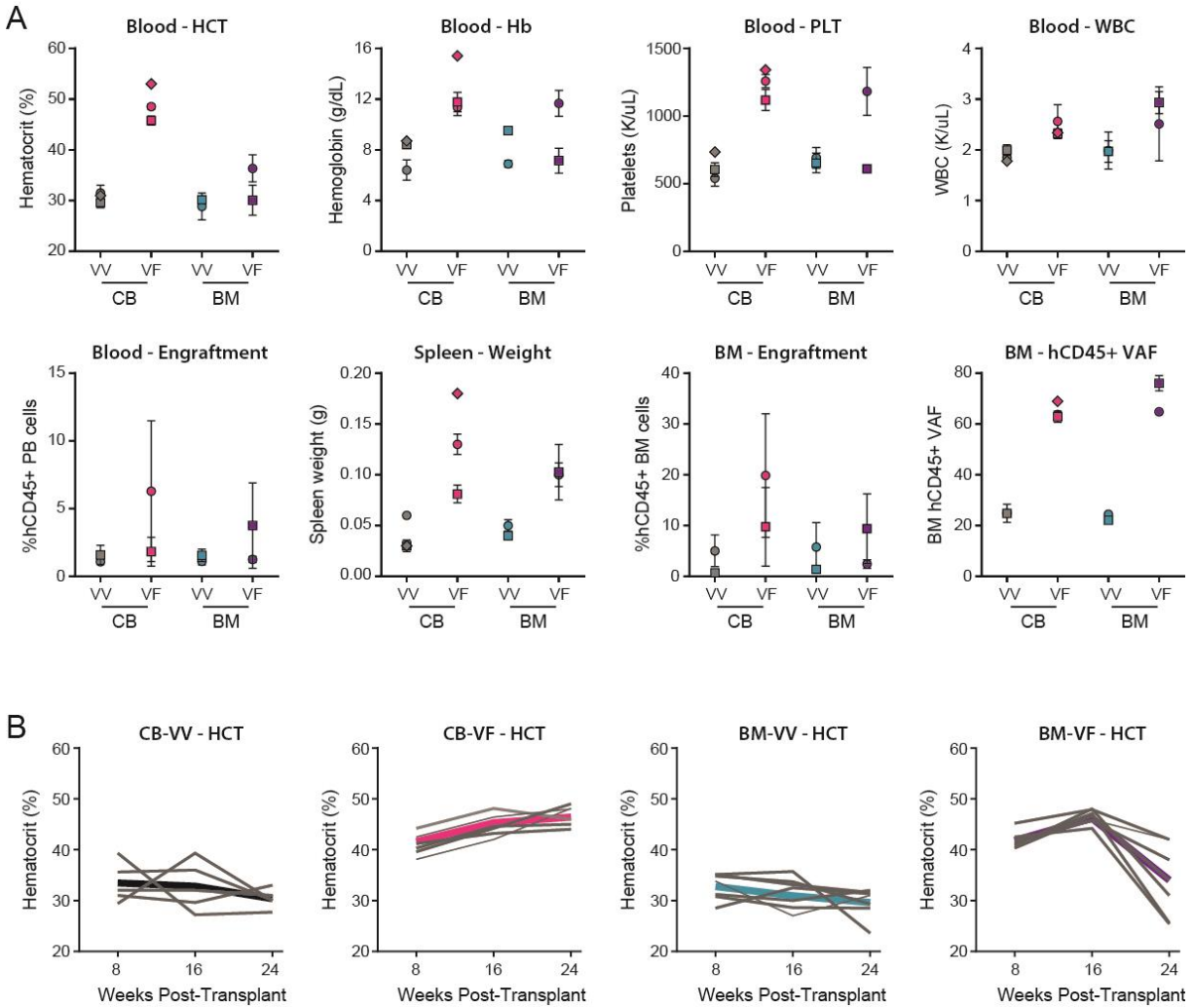
- Schematic showing experimental workflow.
- Knock-in efficiency of VF and VV mutations in CB CD34+ cells determined by NGS.
- Engraftment of human cells in the peripheral blood of NSGS mice 24-weeks post-transplant determined by flow cytometry.
- Engraftment of human cells in the bone marrow of NSGS mice 24-weeks post-transplant determined by flow cytometry.
- Engraftment of human cells in the spleens of NSGS mice determined by flow cytometry.
- Spleen weights of NSGS mice receiving indicated human cells.
- Variant allele frequency of $JAK2^{V617F}$ mutation in BM of NSGS mice determined by ddPCR.



Supplemental Figure 2: Manifestation of MPN Pathologies from a Minimal *JAK2*^{V617F} Mutant Allele Burden

- Ratio of human erythrocytes (hCD235+) to mouse erythrocytes (mTer119+) in the peripheral blood of NSGS mice 24-weeks post-transplant.
- Total bone marrow counts of NSGS mice from indicated groups 24-weeks post-transplant.
- Lineage distribution of mouse hematopoietic cells (mCD45+) in BM of NSGS mice 24-weeks post-transplant.
- Representative flow cytometry gating scheme to identify human HSCs in the BM of NSGS recipient mice.

n=3-7 mice per group, data are compiled from two independent experiments. **p* < 0.05, ****p* < 0.001. Mean ± S.E.M values are shown.



Supplemental Figure 3: Experimental Reproducibility

- A.** Reproducibility of biological features between different experimental cohorts and donor material. Shown are the average values for stated parameters for mice from three distinct experimental cohorts (diamond = pilot study, circle = cohort 1, square = cohort 2).
- B.** Consistency of hematocrit (HCT) levels in NSGS mice between different experimental cohorts and donor material. Shown are the longitudinal HCT values for each mouse transplanted with the indicated donor cells (grey lines) surrounding the average for all mice within that group (thick colored line).

n=1-4 mice per group, data are compiled from three independent experiments. Mean ± S.E.M values are shown.