

Description of Additional Supplementary Files

File name: Supplementary Data.xlsx

Description:

- **Supplementary Data 1: Qualifying *F12* variants.** Qualifying moderately rare ($MAF \leq 1\%$) $FIS=1.0$ variants in *F12* are shown together with predicted variant effect annotation, stratified by dataset. Allele counts ≤ 20 in the All of Us cohort are obscured (**) to comply with NIH reporting regulations.
- **Supplementary Data 2: Associations between *F12* variant carrier status and infection phenotypes in the UK Biobank (N=414,670).** To assess the associations between heterozygous *F12* loss of function and the occurrence of 138 specific infection phenotypes, serial Firth's logistic regression models were generated with adjustment for age, sex, and the first 4 principal components of genetic ancestry. "Any infection" refers to analysis of the aggregate of all 138 phenotypes.
- **Supplementary Data 3: Curated disease phenotypes for UKB and AoU datasets.** Disease phenotypes for VTE, bleeding, and sepsis were generated from ICD-9 and -10 codes; participants with at least one code corresponding to the inclusion criteria for each phenotype were considered cases, and those who met inclusion criteria but also met exclusion criteria at an earlier date were excluded.

File name: Video S1.mp4

Description:

Supplementary Video 1: Platelet and fibrin accumulation at sites of vascular injury. Real-time intravital video microscopy was used to observe platelet and fibrin accumulation in wild-type ($F12^{+/+}$), heterozygous knockout ($F12^{+/-}$), and homozygous knockout ($F12^{-/-}$) mice. Representative videos are shown for one mouse from each group.