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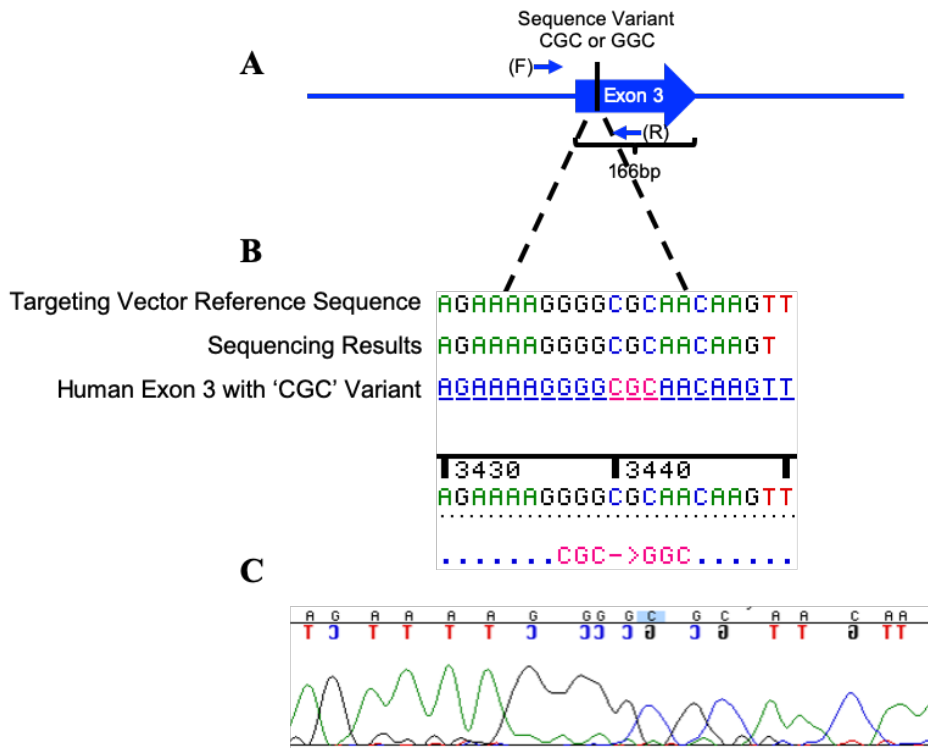
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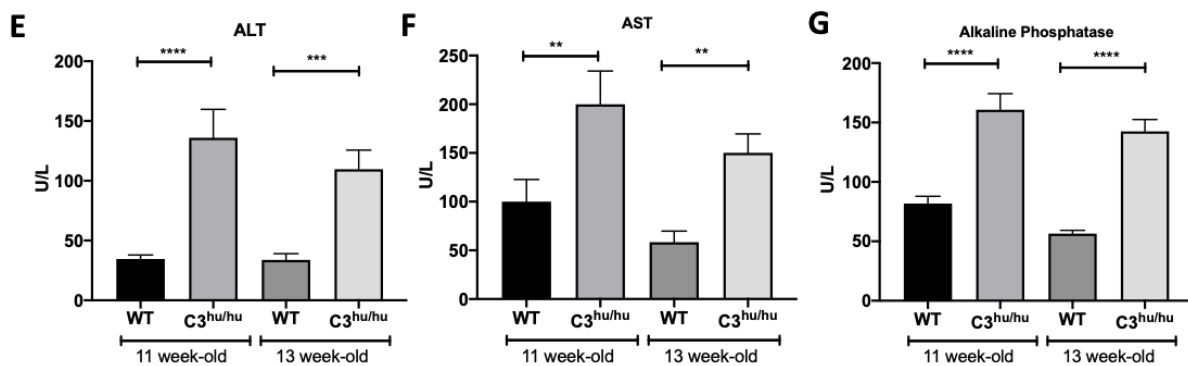
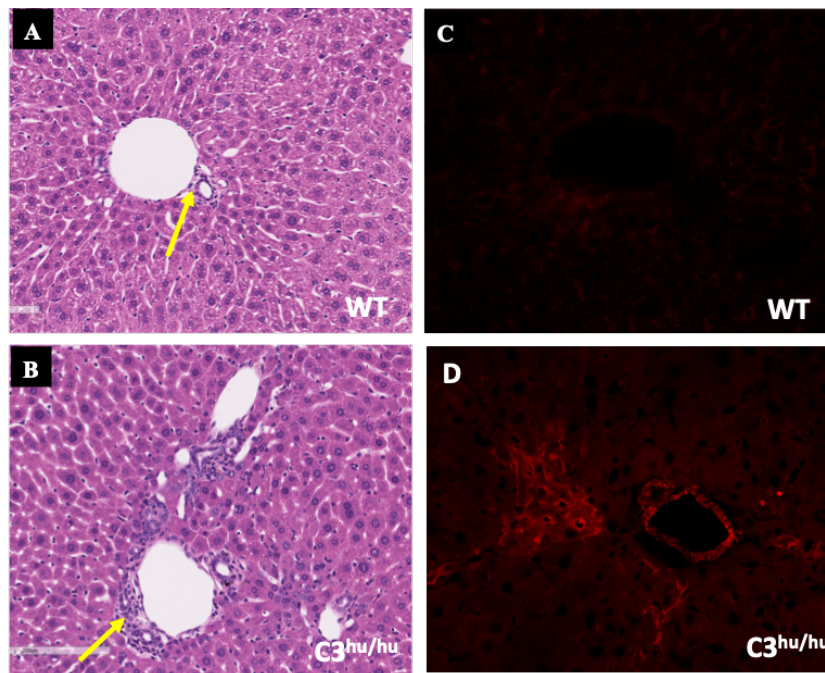
**Supplemental Figure S7:** C5, C3b and CFB mAb effects on C3 and C5 levels in C3<sup>hu/hu</sup> mice.

**Supplemental Figure S1: Sequencing Human C3 Target Vector to Confirm CGC SNP**

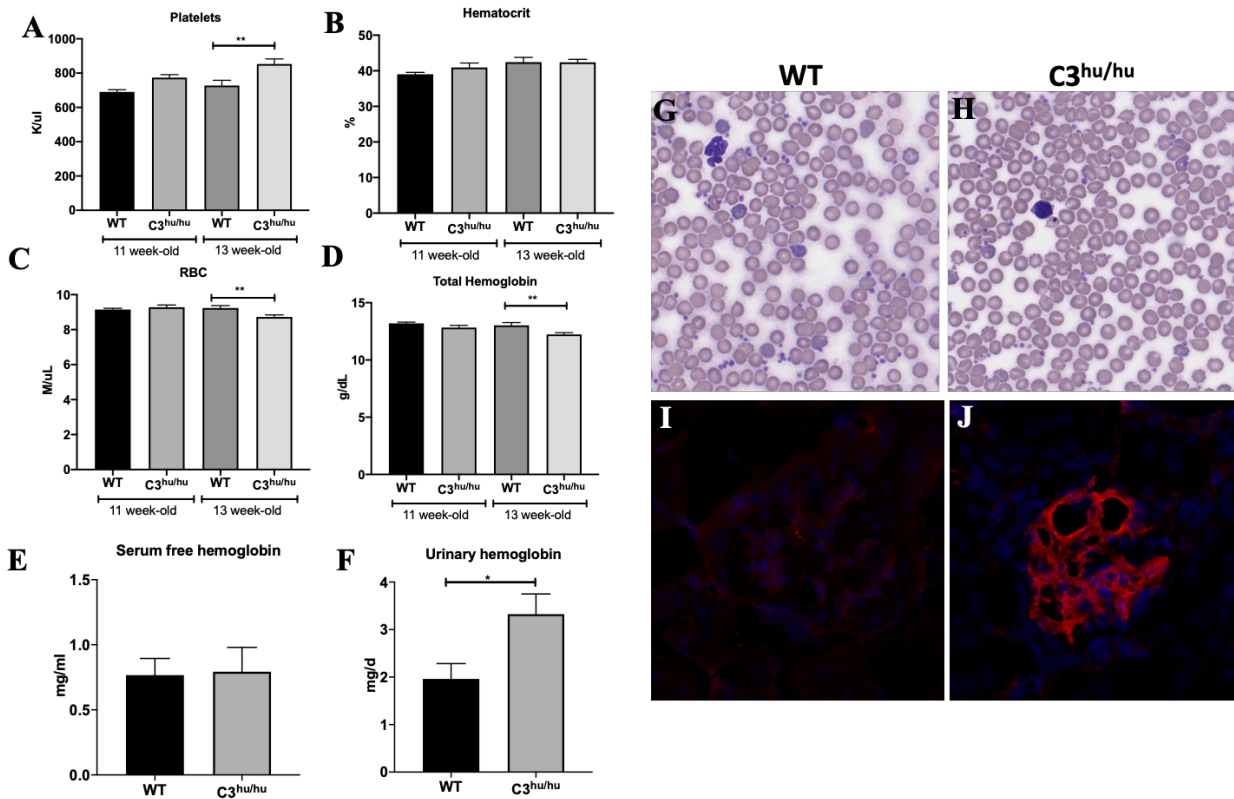
**Variant Coding for Arg102.** A. Human C3, exon 3 schematic showing primer locations to sequence for the 'CGC' or 'GGC' SNP variant. B. Sequencing results from the reverse primer aligned to reference sequences. C. Chromatogram from reverse primer sequence confirming 'CGC' sequence in targeting vector with 'C' SNP highlighted.



**Supplemental Figure S2: Liver pathology in C3<sup>hu/hu</sup> mice:** A: Portal region from a WT mouse (yellow arrow). B: C3<sup>hu/hu</sup> mouse showing inflammation in the portal region (yellow arrow). C & D. C3 deposition in WT and C3<sup>hu/hu</sup> mice respectively. E, F & G. ALT, AST and Alkaline phosphatase respectively in 11-week old WT (n=9). 13-week old WT (n=15). 11-week old C3<sup>hu/hu</sup> (n=10). 13-week old C3<sup>hu/hu</sup> (n=13) mice.

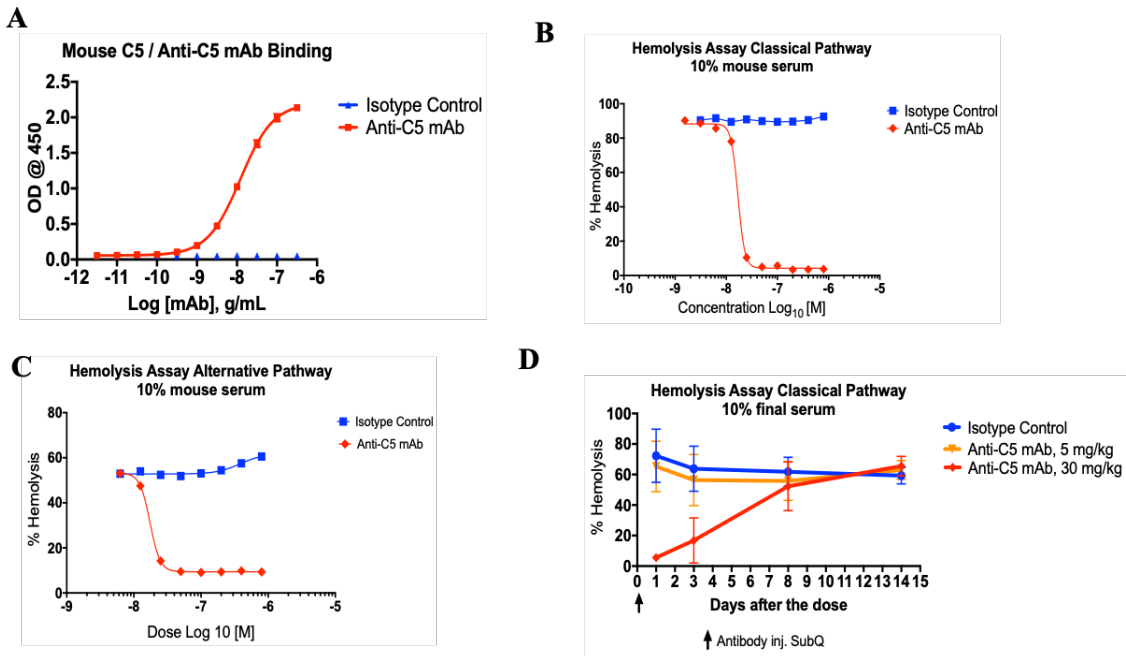


**Supplemental Figure S3: TMA phenotype data.** A, B, C & D: Platelets, hematocrit, RBC & total hemoglobin respectively in 11-week old WT (n=14). 13-week old WT (n=13). 11-week old C3<sup>hu/hu</sup> (n=15). 13-week old C3<sup>hu/hu</sup> (n=29) mice. E. Serum free hemoglobin in 13-week old WT (n=20). 13-week old C3<sup>hu/hu</sup> (n=16). F. Urinary hemoglobin in 13-week old WT (n=10). 13-week old C3<sup>hu/hu</sup> (n=21). G & H. Representative images of blood smears of 13-week old WT (n=8) and C3<sup>hu/hu</sup> (n=7) mice respectively. I & I. Representative images of fibrin deposition of 13-week old WT (n=6) and C3<sup>hu/hu</sup> (n=11) mice respectively.



**Supplemental Figure S4: Binding and functional Characterization of anti-C5 mAb. A:**

Binding of the anti-C5 mAb to mouse C5. B & C: Classical and alternative pathway hemolysis assays, in 10% normal mouse serum in vitro, respectively. D: Ex vivo classical pathway hemolysis activity of serum from normal C57BL6 mice dosed with anti-C5 mAb (n=4) or isotype control (n=4).



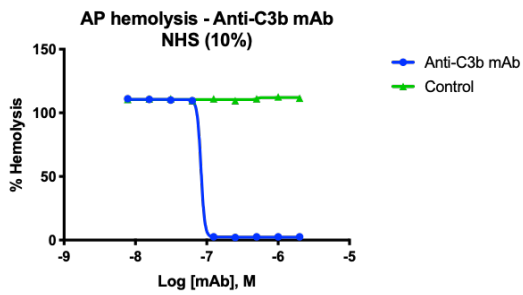
**Supplemental Figure S5: Functional characterization of anti-C3b and anti-CFB mAbs. A &**

**B:** Graphs showing alternative pathway hemolysis and classical pathway hemolysis with anti-

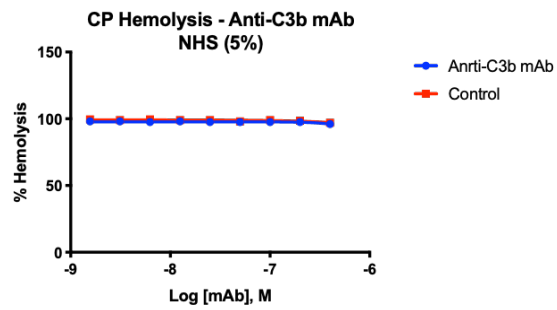
C3b mAb or Control mAb, respectively. **C:** Graph showing alternative pathway hemolysis with

anti-CFB mAb or Control mAb. NHS: Normal human serum. NMS: Normal mouse serum.

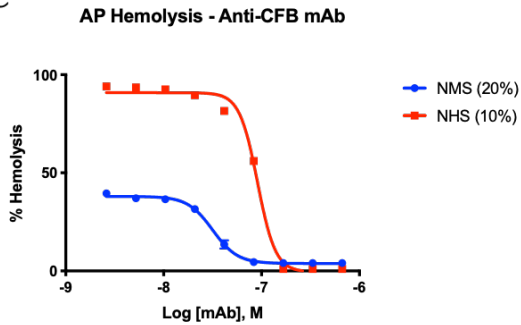
**A**



**B**



**C**



**Supplemental Figure S6: C3b and CFB mAb effects on kidney function in C3<sup>hu/hu</sup> mice. A.**

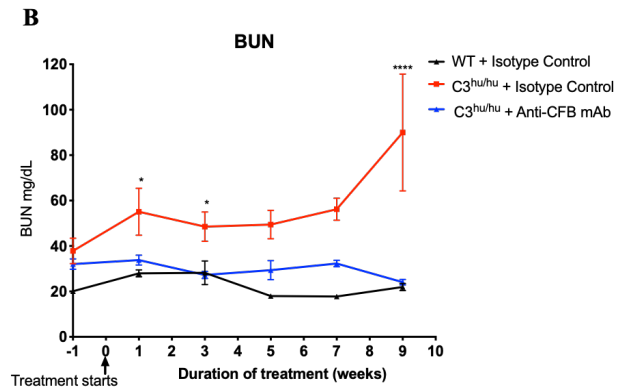
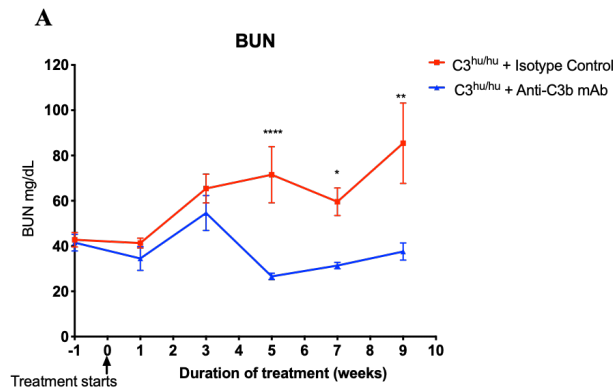
BUN of C3<sup>hu/hu</sup> mice treated with isotype control or anti-C3b mAb. \*P<0.05, \*\*P<0.01,

\*\*\*\*P<0.0001, C3<sup>hu/hu</sup> + anti-C3b mAb vs. C3<sup>hu/hu</sup> + isotype control B. BUN of WT mice treated

with isotype control and C3<sup>hu/hu</sup> mice treated with isotype control or anti-CFB mAb. For the

experiment in E, treatment stopped after 16 weeks. \*P<0.05, \*\*\*\*P<0.0001, – C3<sup>hu/hu</sup> + anti-

CFB mAb vs. C3<sup>hu/hu</sup> + isotype control.



**Supplemental Figure S7: C5, C3b and CFB mAb effects on C3 and C5 levels in C3<sup>hu/hu</sup>**

**mice.** A. Serum human C3 levels in C3<sup>hu/hu</sup> + Isotype Control (n=14) and C3<sup>hu/hu</sup> + anti-C5 mAb (n=15). B. Serum mouse C5 levels in C3<sup>hu/hu</sup> + Isotype Control (n=10) and C3<sup>hu/hu</sup> + anti-C5 mAb (n=11). C. Serum human C3 levels in C3<sup>hu/hu</sup> + Isotype Control (n=11) and C3<sup>hu/hu</sup> + anti-C3b mAb (n=14). D. Serum mouse C5 levels in C3<sup>hu/hu</sup> + Isotype Control (n=11) and C3<sup>hu/hu</sup> + anti-C3b mAb (n=14). E. Serum human C3 levels in C3<sup>hu/hu</sup> + Isotype Control (n=14) and C3<sup>hu/hu</sup> + anti-CFB mAb (n=16). F. Serum mouse C5 levels in C3<sup>hu/hu</sup> + Isotype Control (n=14) and C3<sup>hu/hu</sup> + anti-CFB mAb (n=16). Note: Values from WT mice from a different experiment shown as reference.

