## Supplemental material

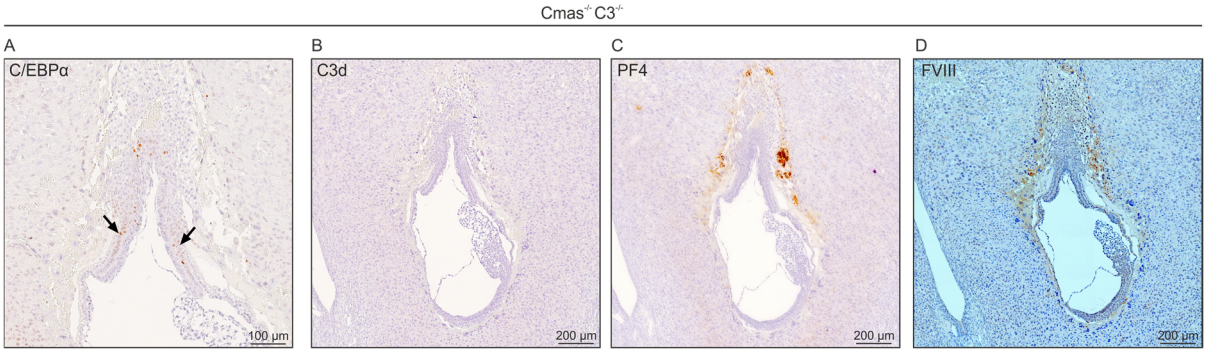



**Figure S1: Loss of C3 rescues excessive thrombosis and placental development in *Cmas*$^{-/-}$ mice.** (**A-C**) Representative images of C/EBPα (A), C3d (B), PF4 (C) and FVIII (D) immunostaining of *Cmas*$^{-/-}$; *C3*$^{-/-}$ placenta sections at E8.5. Arrows in A point towards the chorionic plate. For the number of individually analysed implants, see Table S1.

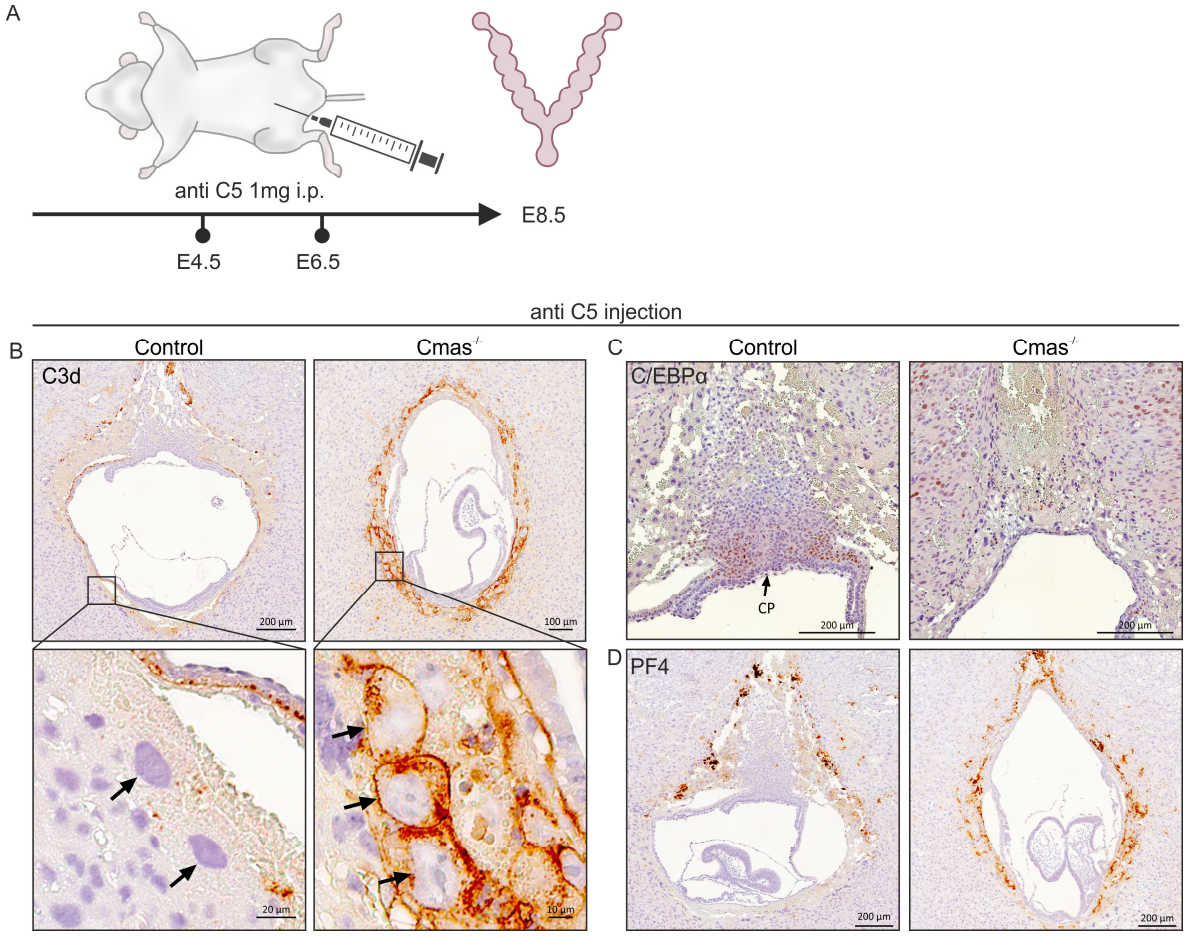



**Figure S2: C5 blockade does not reduce excessive thrombosis in *Cmas*$^{-/-}$ implants.** (A) Treatment regimen for C5 blockade. C5 activation was blocked by intraperitoneal injection of 1 mg anti-C5 (BB5.1) at E4.5 and E6.5 in 4 individual experiments. (**B-D**) Representative images of C3d (B), C/EBPα (C) and PF4 (D) immunostaining of *Cmas*$^{-/-}$ pregnancies under C5 blockade at E8.5. For the number of individually analysed implants, see Table S1.

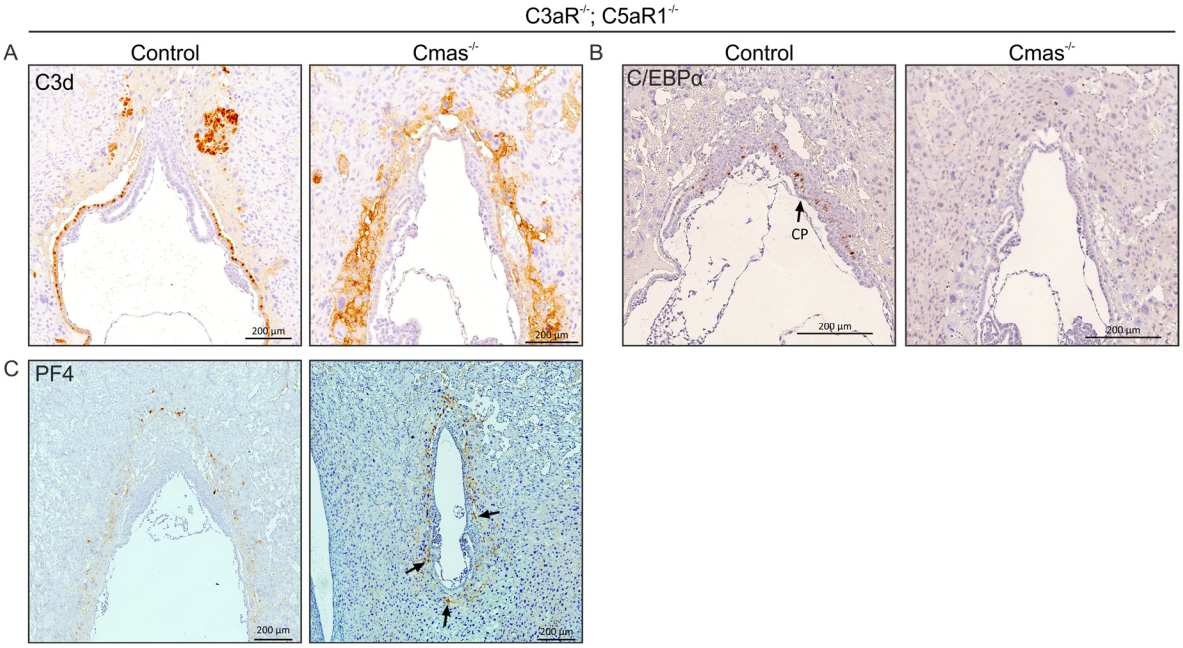
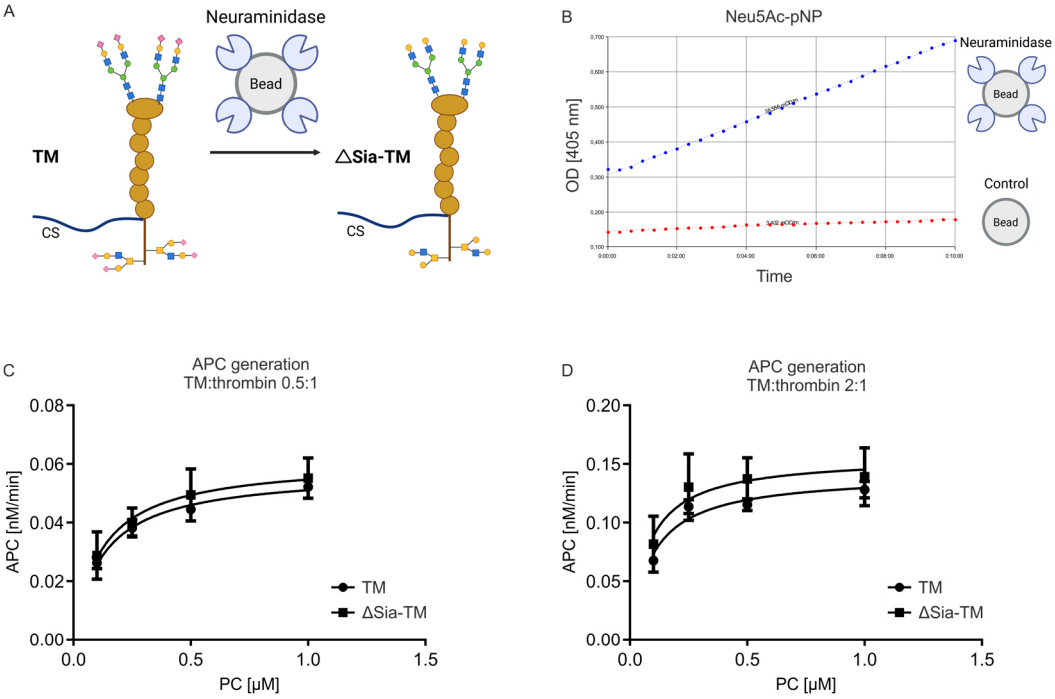



**Figure S3: Impaired anaphylatoxin signaling does not rescue the phenotype of *Cmas*$^{-/-}$ mice.** (**A-C**) Representative images of C3d (A), C/EBPα (B) and PF4 (C) immunostaining of *Cmas*$^{-/-}$; *C3aR*$^{-/-}$; *C5aR1*$^{-/-}$ pregnancies under C5 blockade at E8.5. For the number of individually analysed implants, see Table S1.




E

| TM:thrombin 1:1 | | |
|---|---|---|
| | TM | ΔSia-TM |
| kcat | 0,04739 | 0,05394 |
| Std. Error kcat | 0,002543 | 0,006772 |
| | | |
| Km | 0,109 | 0,15 |
| Std. Error Km | 0,02349 | 0,06551 |
| | | |
| $R^2$ | 0,9127 | 0,7551 |

| TM:thrombin 0.5:1 | | |
|---|---|---|
| | TM | ΔSia-TM |
| kcat | 0,0287 | 0,03062 |
| Std. Error kcat | 0,0008651 | 0,002898 |
| | | |
| Km | 0,1245 | 0,1201 |
| Std. Error Km | 0,01418 | 0,04366 |
| | | |
| $R^2$ | 0,9738 | 0,7806 |

| TM:thrombin 2:1 | | |
|---|---|---|
| | TM | ΔSia-TM |
| kcat | 0,07076 | 0,07817 |
| Std. Error kcat | 0,003653 | 0,008498 |
| | | |
| Km | 0,09302 | 0,0767 |
| Std. Error Km | 0,02081 | 0,03986 |
| | | |
| $R^2$ | 0,8991 | 0,5993 |

**Figure S4: Generation of desialylated TM. (A)** Schematic representation of bead-coupled neuraminidase induced desialylation of TM. Created in BioRender. Abeln, M. (2026) https://BioRender.com/tk2cnmv **(B)** Neuraminidase activity as measured as increase in OD [405 nm] through hydrolysis of Neu5Ac-pNP. Schematics created in BioRender. Abeln, M. (2026) https://BioRender.com/mnjr479 **(C-D)** APC generation kinetics of thrombin in 0.5:1 (C) and 2:1 (D) ratio with with TM and ΔSia-TM. Data are presented as mean ± SD of duplicates. **(E)** Enzyme kinetic parameters of APC generation by TM or ΔSia-TM in a complex with thrombin.

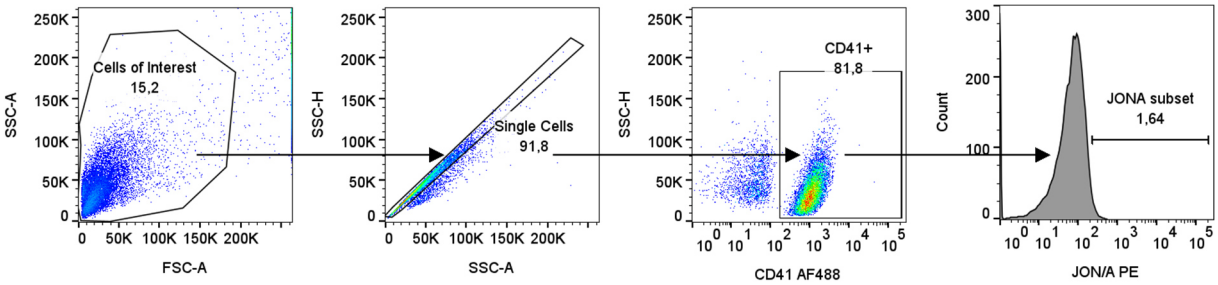



**Figure S5: Gating strategy for the flow cytometry analysis of active αIIbβ3 (JON/A).** After selection of cells of interest and exclusion of doublets, CD41-positive platelets were gated, and JON/A-positive events were quantified as a measure of integrin αIIbβ3 activation.

**Table S1:** Total numbers of analysed implants and uteri (brackets) in IHC and HE staining.

| | | ***Cmas*** | **FVIII** | **PF4** | **C3d** | **Properdin** | **vWF** | **CD62P** | **HE** | **Serotonin** | **beta3** | **TM** | **caspase 3** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Cmas*** | E8.5 | KO | 13(8) | 8(5) | 13(6) | 9(7) | | 20(9) | | 13(6) | 10 (4) | 8 (3) | 9 (4) |
| | | ctrl | 15(5) | 5(5) | 9(6) | 17(7) | | 4(4) | | 9(6) | 8 (4) | 9 (3) | 9 (4) |
| ***Cmas*** **;** ***C3*** **-/-** | E8.5 | KO | 8(3) | 5(3) | 5(3) | | | | | | | | |
| | | ctrl | 11(3) | 9(3) | 9(3) | | | | | | | | |
| ***Cmas*** **;** ***Par4*** **-/-** | E8.5 | KO | 6(4) | 6(4) | 6(4) | 4(4) | 6(5) | | 7(4) | 6(4) | 7 (4) | | |
| | | ctrl | 5(4) | 10(4) | 10(4) | 12(4) | 9(5) | | 10(4) | 5(4) | 6 (4) | | |
| ***Cmas*** **anti-GPIba** | 2x | KO | 6(2) | | 6(2) | 4(2) | | | 6(2) | 5(2) | 5 (2) | | 4 (2) |
| | | ctrl | 4(3) | | 10(3) | 3(2) | | | 10(3) | 3(2) | 3 (2) | | 7 (2) |
| | 1x | KO | | | | | | | | | | | 9 (4) |
| | | ctrl | | | | | | | | | | | 13 (5) |
| ***Cmas*** **anti-C5** | E8.5 | KO | | 7(2) | 7(2) | | | | | | | | |
| | | ctrl | | 7(2) | 7(2) | | | | | | | | |
| ***Cmas*** **;** ***C3ar*** **-/-;** ***C5aR1*** **-/-** | E8.5 | KO | | 8(3) | 11(4) | | | | | | | | |
| | | ctrl | | 3(3) | 7(4) | | | | | | | | |

Table S2: Primary and secondary antibodies used in IHC experiments.

| Reagent | Host species | Label | Manufacturer | Catalog no. | Blocking reagent | Dilution |
|---|---|---|---|---|---|---|
| **anti-Factor VIII** | Rabbit | - | Bioss, Woburn, USA | BS-2974R | 1% BSA in PBS | 1:1000 |
| **anti-Platelet factor 4** | Rat | - | R&D Systems, Minneapolis, USA | MAB595 | 1% BSA in PBS | 1:2000 |
| **anti-TER-119** | Rat | - | R&D Systems, Minneapolis, USA | MAB1125 | 1% BSA in PBS | 1:5000 |
| **anti-C3d** | Goat | - | R&D Systems, Minneapolis, USA | AF2655 | 1% BSA in PBS | 1:2000 |
| **anti-CD62P** | Rabbit | - | biorbyt, Cambridge, United Kingdom | BYT-ORB382723-100 | 5 % skimmed milk/PBS | 1:1000 |
| **anti-Ly6G** | Rat | - | BioXCell, Lebanon, USA | BP0075-1 | 1% BSA in PBS | 1:500.000 |
| **anti-vWF** | Rabbit | - | Dako (Agilent), Glostrup, Denmark | P 0226 | 5 % skimmed milk/PBS | 1:100 |
| **anti-Properdin** | Goat | - | Complement Technologies, Tyler, USA | A239 | 1% BSA in PBS | 1:10.000 |
| **anti-C/EBPα** | Rabbit | - | Cell Signaling Technology, Danvers, USA | 8178 | 1% BSA in PBS | 1:50 |
| **anti-uPAR** | Rabbit | - | Bioss, Woburn, USA | bs-1927R | 1% BSA in PBS | 1:1500 |
| **anti-Serotonin (5-HT)** | Rat | - | Novus Biologicals (biotechne), Centennial, USA | NB1065037SS | 1% BSA in PBS | 1:250 |
| **beta3** | Rabbit | - | Novus Biologicals (biotechne), Centennial, USA | NBP2-67416 | 1% BSA in PBS | 1:10.000 |
| **TM** | Rabbit | - | Abcam, Cambridge, UK | ab230010 | 1% BSA in PBS | 1:16.000 |
| **cl caspase 3** | Rabbit | - | Cell Signaling Technology, Danvers, USA | # 9664 | 1% BSA in PBS | 1:1000 |
| **JON/A** | Rat | PE | Emfret Analytics, Würzburg, Germany | M023-2 | | |
| **anti-rabbit IgG** | Goat | HRP-Polymer | Vector Laboratories, Newark, USA | VEC-MP-7451-15 | - | - |
| **anti-goat IgG** | Horse | HRP-Polymer | Vector Laboratories, Newark, USA | VEC-MP-7405-15 | - | - |
| **anti-rat IgG** | Goat | HRP-Polymer | Vector Laboratories, Newark, USA | VEC-MP-7444-15 | - | - |