

A rat model of severe VWD by elimination of the VWF gene using CRISPR/Cas9

Jessica Garcia MD¹ | Veronica H. Flood MD^{2,3}  | Sandra L. Haberichter PhD³ | Scot A. Fahs³ | Jeremy G. Mattson³ | Aron M. Geurts PhD³ | Mark Zogg⁴ | Hartmut Weiler PhD³ | Qizhen Shi MD, PhD^{2,3} | Robert R. Montgomery MD^{2,3}

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Attention, la **Figure 2** originale contient des panels C et D, mais nous vous demandons de commenter seulement les panels A et B représentés ici.

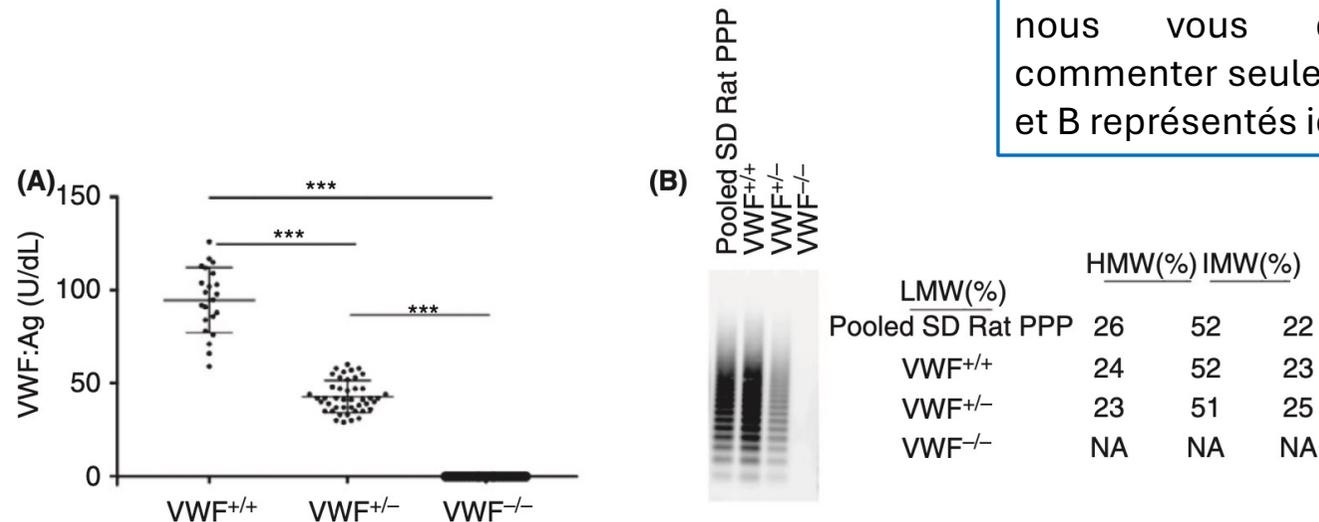


FIGURE 2 Rats with full length deletion of the von Willebrand factor (VWF) gene have undetectable VWF antigen, VWF multimers, collagen IV binding, and factor VIII activity. Blood draws (0.5 mL) were obtained from the tail artery of 6- to 10-week-old Sprague-Dawley rats to obtain platelet poor plasma. (A) VWF antigen (VWF:Ag) is not detectable in VWF^{-/-} rats and reduced in VWF^{+/-} rats when compared to VWF^{+/+} rats. (B) VWF multimers are absent in VWF^{-/-} rats and reduced concentration in in VWF^{+/-} rats when compared to VWF^{+/+} rats.

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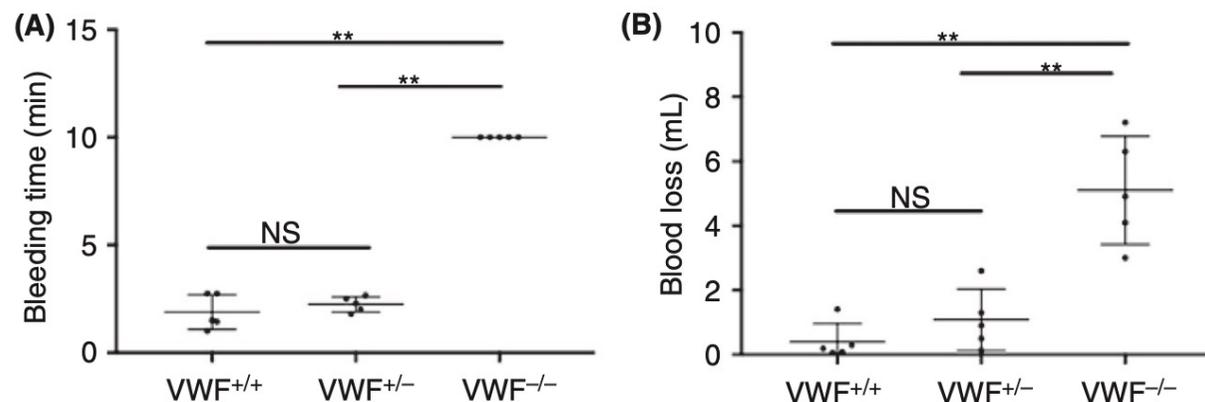


FIGURE 3 Increased bleeding in von Willebrand factor (VWF)^{-/-} rats after lateral tail vein transection. Anesthetized 20- to 24-week-old Sprague-Dawley rats' lateral tail veins were transected at a diameter of 6.4 mm and a depth of 2.0 mm using a template. (A) Measurement of cessation of bleeding over time, and (B) amount of blood loss in mL, for wild-type (VWF^{+/+}), heterozygous (VWF^{+/-}), and homozygous VWF deficient (VWF^{-/-}) rats by tail bleeding assay. VWF^{-/-} rats bled longer and lost greater quantities of blood when compared to VWF[±] and VWF^{+/+} rats. Fisher's exact test was used to compare bleeding times of VWF^{-/-} rats to VWF[±] and VWF^{+/+} rats. Mann-Whitney test was used to compare blood loss in all genotypes. Error bars denote 1 standard deviation. N ≥ 5 for each genotype. Results were pooled from 5 independent experiments. *P<0.05, **P<0.01, ***P<0.001. P = 0.22 for blood loss when VWF +/- is compared to VWF +/+ and P = 0.63 for bleeding time when VWF +/- is compared to VWF +/+