ARTICLE - Coagulation & its Disorders

The IgG-degrading enzyme, Imlifidase, restores the therapeutic activity of FVIII in inhibitor-positive hemophilia A mice.

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Supplemental data

Supplemental Figure S1

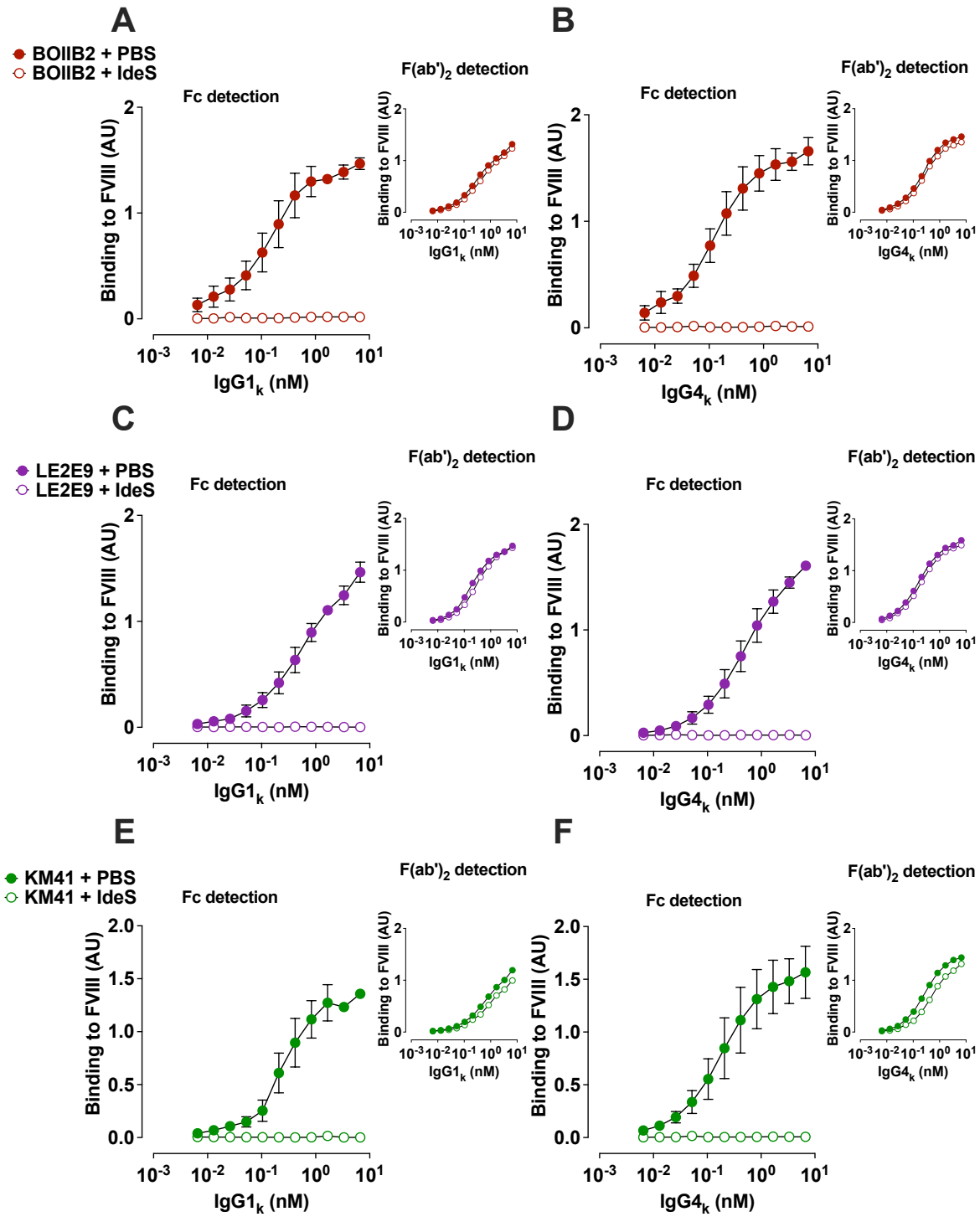

Figure S1: Cleavage of human monoclonal anti-FVIII IgG by IdeS. Binding of BOIIB2 (panels A and B), LE2E9 (panels C and D), and KM41 (panels E and F) IgG to FVIII following cleavage by IdeS. $IgG1_k$ (panels A, C, and E) and $IgG4_k$ (panels B, D, and F) at 1.66 µM were

incubated alone or with IdeS (0.14 μM) for 24 hr at 37°C. The binding of IgG (main graphs) and $F(ab')_2$ fragments (insets) to FVIII was validated by ELISA. Results are expressed in arbitrary units (AU, representative of 2 experiments) from optical density measured at 492 nm.

Supplemental Figure S2

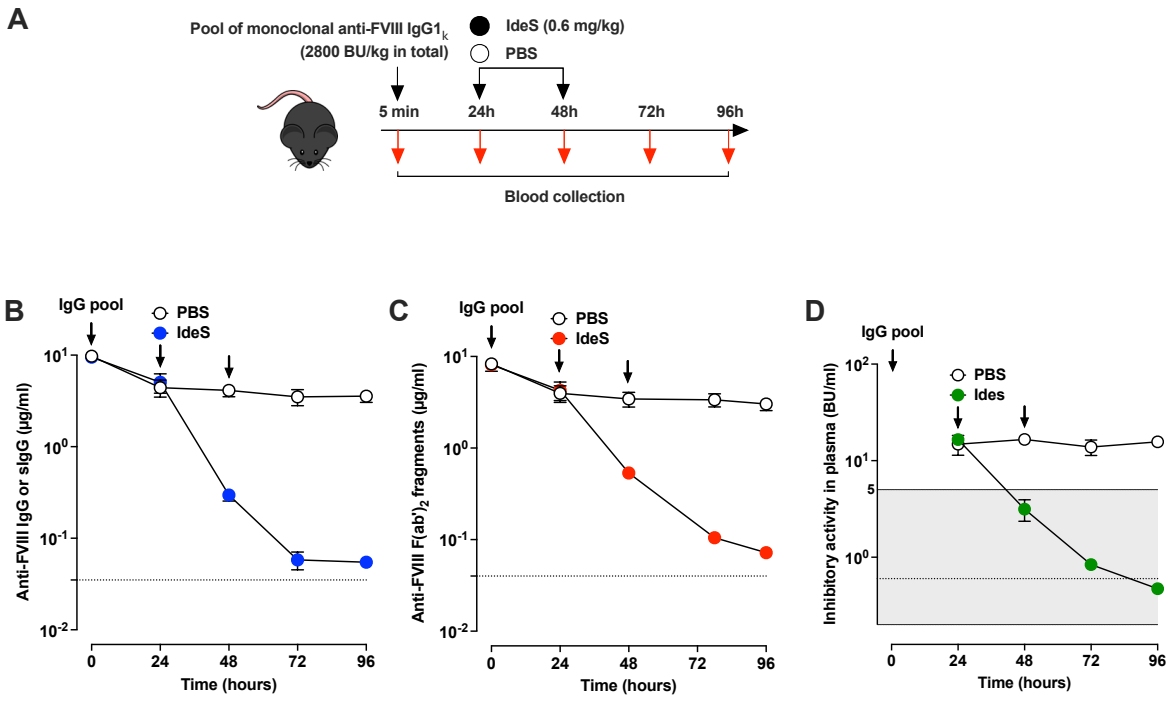

Figure S2. IdeS-mediated elimination of a pool of monoclonal anti-FVIII IgG in inhibitor-positive HA mice. Panel A. HA mice (n=4 per group) were passively immunized with a pool of monoclonal IgG1$_k$ (BOIIB2, KM41, LE2E9, and BO2C11 at equimolar amounts of 3.4 µg for a total of 2800 BU/kg to reach 15±3 BU/mL after 24 hr, and injected twice with IdeS (0.6 mg/kg or 0.29 µM) or PBS 24 hr and 48 hr later. **Panels B, C and D.** The levels of intact IgG and/or scIgG (panel B, IgG concentration at 24 hr: 31.5±1.1 nM), the levels of F(ab')$_2$ fragments (panel C) and the inhibitory titers (panel D) were determined over time by ELISA and Bethesda assay (mean±SD). The dotted lines represent the respective detection thresholds: 0.03 µg/mL, 0.08 µg/mL and 0.6 BU/mL. The grey zone in panel D depicts inhibitory titers below 5 BU/ml, a titer that is compatible with the hemostatic efficacy of exogenous FVIII.