Supplementary Information

Rescuing AAV gene transfer from neutralizing antibodies with an IgG-degrading enzyme

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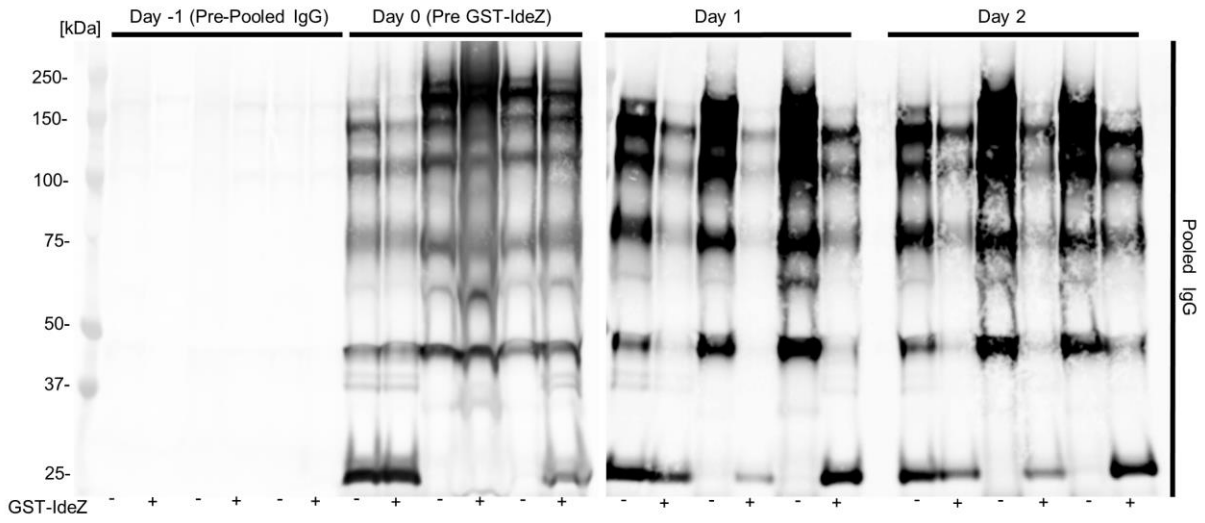
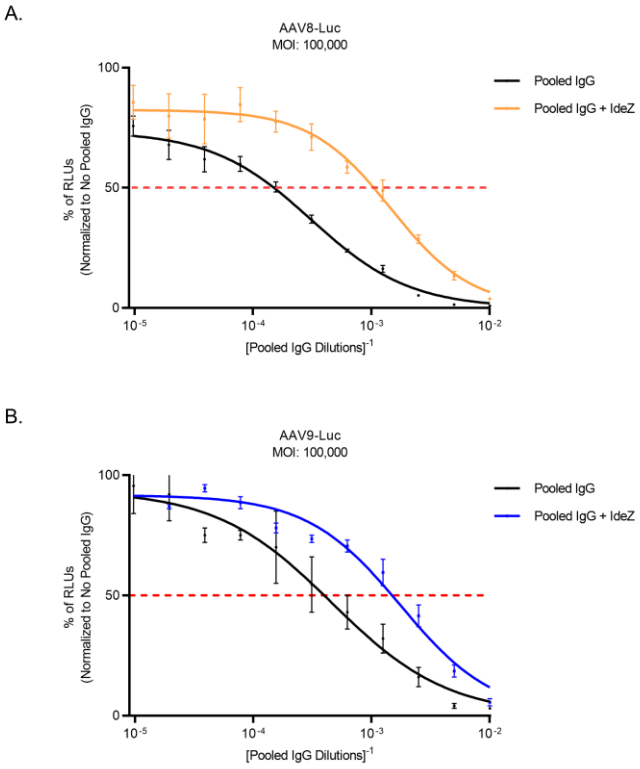
Supplementary Figures

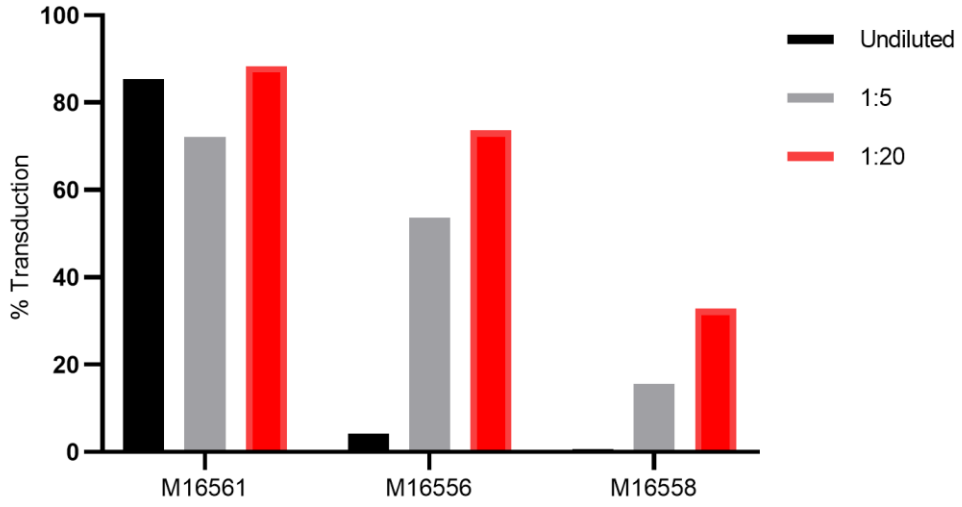


Supplemental Fig 1. Kinetic analysis of IdeZ mediated cleavage of pooled human IgG *in vivo*. Mice were injected intraperitoneally with pooled human IgG. The same mice were injected intravenously 24 hours later with PBS (-) or recombinant GST-IdeZ (2.5 mg/kg) (+). Blood samples were taken 24 and 48 hours post injection and analyzed by SDS-PAGE under reducing conditions and probed with human IgG specific antibodies to analyze IgG cleavage.

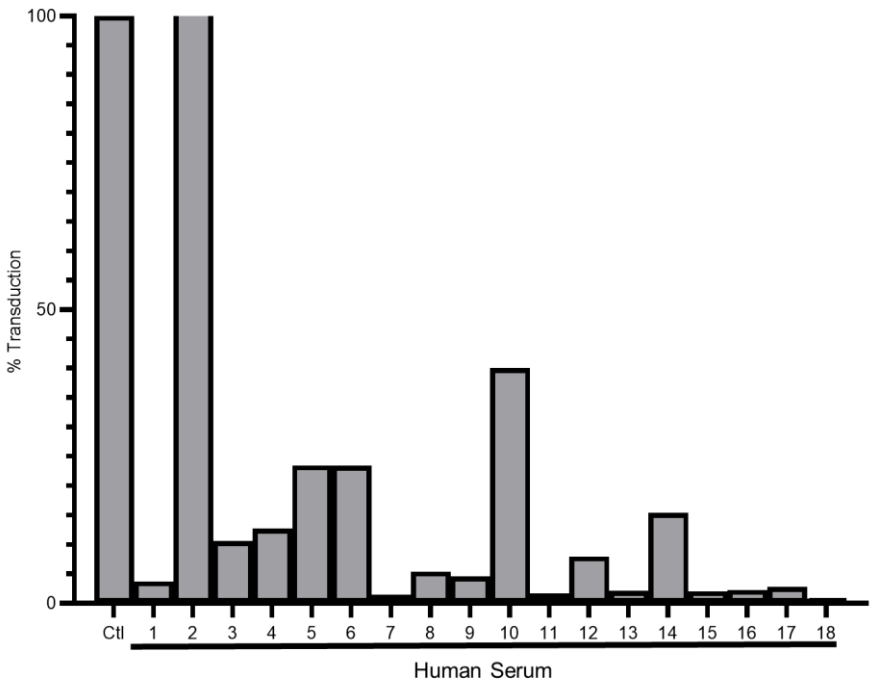


Supplemental Fig 2. IdeZ mitigates human IgG mediated neutralization of AAV8 and AAV9 *in vitro*.

Pooled human IgG was treated with PBS or GST-IdeZ (1ug). Samples were then serially diluted in twofold increments from 1:100 to 1:102,400 and then co-incubated with AAV8-Luc (**A**), or AAV9-Luc (**B**) *in vitro* (100,000 vg/cell). The dotted red line represents NAb-mediated inhibition of AAV8/9 transduction by 50%. Solid lines represent relative transduction efficiencies of AAV8/9 incubated with IgG (black) and AAV8/9 incubated with IgG treated with GST-IdeZ (yellow,blue) at different dilutions. Error bars represent SEM (AAV8, $n = 3$) (AAV9, n=2).



Supplemental Fig 3. AAV9 neutralization profile of NHP sera. NHP sera from three individual animals (M16561, M16556, M16558) were diluted from 1:5 to 1:20 and then coincubated with AAV9-Luc *in vitro* (100,000 vg/cell). Transduction levels were normalized to no serum control.



Supplemental Fig 4. AAV9 neutralization profile of human sera. Human sera from 18 individuals was diluted 1:5 and then coincubated with AAV9-Luc *in vitro* (100,000 vg/cell). Transduction levels were normalized to no serum control. Luciferase activity was determined at 24 hrs post-transduction. Detailed methods are described in Tse *et al.*, PNAS, 2017.

Supplemental Table 1. Demographic analysis of human serum used in this study.

Serum #	Lot #	Gender	Age	Race
1	BRH1499625	Male	37	Hispanic
2	BRH1499636	Male	32	Black
3	BRH1499659	Female	22	Black
4	BRH1499617	Male	32	Black
5	BRH1499665	Female	35	Hispanic
6	BRH1499637	Male	37	Caucasian
7	BRH1536076	Male	11	Caucasian
8	BRH1499666	Female	27	Black
9	BRH1499685	Female	35	Caucasian
10	BRH1499676	Female	35	Caucasian
11	BRH1499638	Male	30	Caucasian
12	BRH1499620	Male	21	Hispanic
13	BRH1536073	Female	16	Black
14	BRH1499645	Male	34	Caucasian
15	BRH1499679	Female	33	Caucasian
16	BRH1499647	Male	35	Caucasian
17	BRH1499669	Female	23	Hispanic
18	BRH1499660	Female	35	Hispanic