OMTM, Volume *26*

Supplemental information

AAV-monoclonal antibody expression protects mice from Ebola virus without impeding the endogenous antibody response to heterologous challenge

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Supplementary Figures

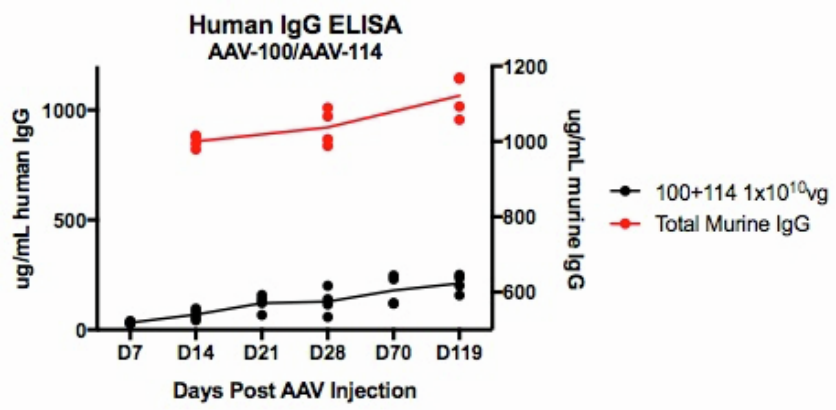

Figure S1. Comparison of human IgG expression to total murine IgG. BALB/c female mice (n=4/ group) were injected IM with $1x10^{10}$ vg of AAV6.2FF-100/114 (equimolar amounts) and human IgG as well as murine IgG was quantified from serum over 17 weeks.

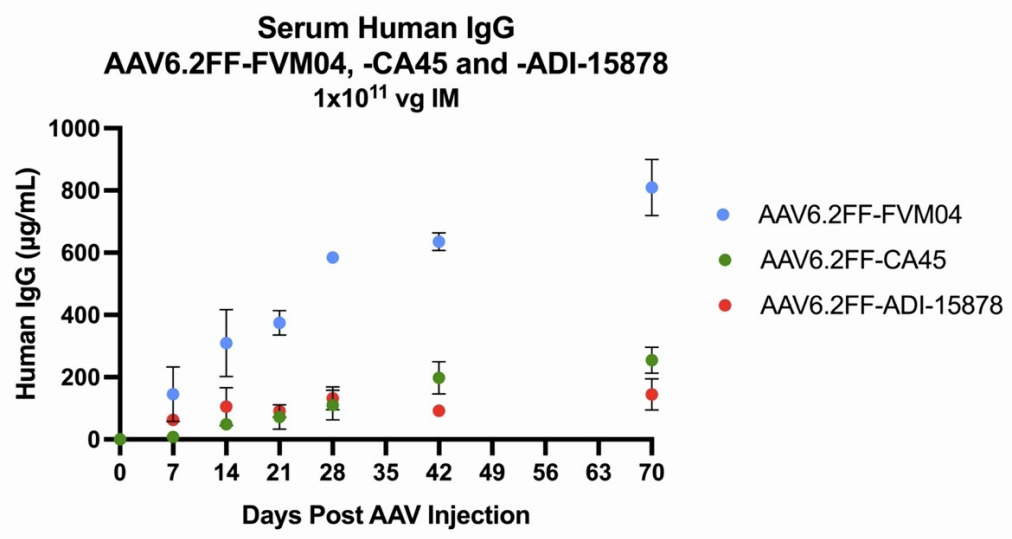

Figure S2. Serum human IgG concentrations in mice injected intramuscularly with AAV6.2FF vectors expressing mAbs FVM04, CA45, and ADI-15878. BALB/c female mice (n=4/ group) were injected IM with $1x10^{11}$ vg of either AAV6.2FF-FVM04, AAV6.2FF-CA45, or AAV6.2FF-ADI-15878, and human IgG was quantified from serum for 10 weeks. The mean and SD are shown.

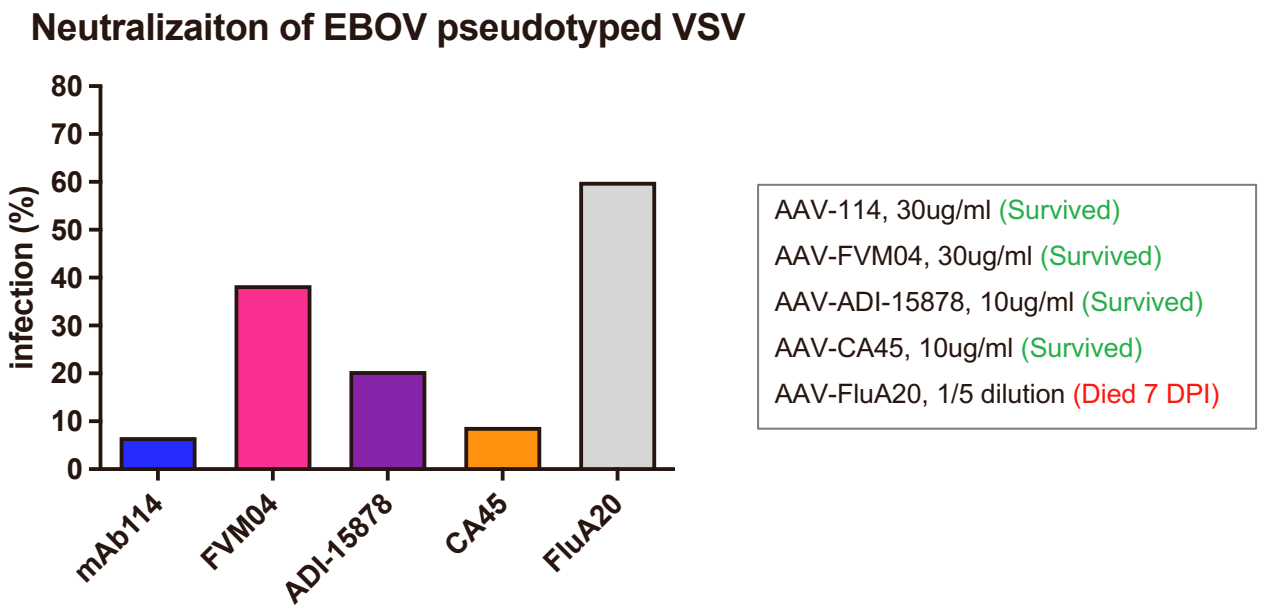

Figure S3. Neutralizing activity of serum harvested from mice that were transduced with AAV-mAbs and survived MA-EBOV challenge. We performed virus neutralizing assays using EBOV GP pseudotyped VSV and the limited serum available from mice that received AAV-mAbs mAb114, FVM04, ADI-15878 and CA45 and survived MA-EBOV challenge. Serum from the mouse that was treated with the control AAV showed ~60% infection, meaning that it inhibited infection by about 40%. This is considered background neutralization attributable to non-specific factors in the serum. Note that the comparison between the control AAV and the experimental AAVs is imperfect, since the volume of sample changed depending on the concentration of IgG. AAV-114, AAV-15878, and AAV-CA45 are clearly producing neutralizing antibody. AAV-FVM04 does seem to show some neutralizing activity, although it is minimal compared to what one would expect based on the survival curves. In general, these data support the notion that the quantity of mAb in the serum is the best correlate of protection.

Table S1. IC50 values for the human mAbs expressed from AAV6.2FF

Monoclonal Antibody	IC50	Reference
5D2	IC50 not available; however, efficacy in mice and guinea pigs has been tested. Mice: 100 μg given -1 dpi = 87% survival 100 μg given +1 dpi = 100% survival 12.5 μg given +1 dpi = 100% survival Guinea Pigs: 5 mg given +1 dpi = 0% survival	PLoS Negl Trop Dis 2012; 6(3): e1575
2G4	IC50 not available; however, efficacy in mice and guinea pigs has been tested. Mice: 100 μg given -1 dpi = 7% survival 100 μg given +1 dpi = 60% survival Guinea Pigs: 5 mg given +1 dpi = 60% survival	PLoS Negl Trop Dis 2012; 6(3): e1575
mAb100	0.461 nM (0.06 ug/ml)	*Science* 2016; 351(6279): 1339-42
mAb114	0.692 nM (0.09 ug/ml)	*Science* 2016; 351(6279): 1339-42
FVM04	0.385 nM (0.05 ug/ml)	*J Virol* 2016; 90(1): 279-91
ADI-15878	≤ 1 nM	*Cell* 2017; 169(5): 878-890.e15
CA45	1.4-0.6 nM	*Cell* 2017; 169(5): 891-904.e15
*dpi = day post-infection		

Table S2. AAV vector doses used in this study reported as vector genomes per kg (vg/kg)

AAV vector genomes (vg) administered	Conversion to vg/kg
$4x10^{11}$ vg	$2x10^{13}$ vg/kg
$1x10^{11}$ vg	$5x10^{12}$ vg/kg
$5x10^{10}$ vg	$2.5x10^{12}$ vg/kg
$2.5x10^{10}$ vg	$1.25x10^{12}$ vg/kg
$1x10^{10}$ vg	$5x10^{11}$ vg/kg
$8x10^{9}$ vg	$4x10^{11}$ vg/kg
$5x10^{9}$ vg	$2.5x10^{11}$ vg/kg