

**Supplementary Table S3. Specific productivity and genomic DNA analysis for selected MWs**

Vector	MW #	Productivity <sup>a</sup> (vg/cell), n	Copies/cell <sup>b</sup> FVIII	Rep	Puro
AAVrh8R/5.1	35	$1.0 \times 10^5 \pm 1.9 \times 10^4$ (H) (5)	52	47	48
AAVrh8R/5.1	272	$5.8 \times 10^3 \pm 1.0 \times 10^3$ (M) (2)	15	18	17
AAVrh8R/5.1	418	$1.5 \times 10^4 \pm 4.7 \times 10^3$ (M) (7)	191	191	202
AAVrh8R/opt-5.1 <sup>c</sup>	14	$5.1 \times 10^4 \pm 2.5 \times 10^4$ (H) (8)	1072	1115	1016
AAVrh8R/opt-5.1 <sup>c</sup>	27	$2.9 \times 10^4 \pm 9.6 \times 10^3$ (M) (7)	56	51	52
AAV8/5.1	287	$2.4 \times 10^5 \pm 5.0 \times 10^4$ (H) (8)	212	208	182
AAV8/5.1	342	$8.2 \times 10^5 \pm 3.9 \times 10^4$ (H) (8)	61	61	66
AAVrh8R/5.4	61	$1.2 \times 10^4 \pm 1.1 \times 10^4$ (M) (9)	184	179	169
AAVrh8R/5.4	163	$5.1 \times 10^4 \pm 2.1 \times 10^4$ (H) (6)	196	181	162
AAV2/SEAP-4.3 <sup>d</sup>	156	$2.1 \times 10^5 \pm 9.5 \times 10^4$ (H) (10)	0	48	48
	HELAS3		0	0	0

<sup>a</sup>Vector production in 20 mL shaker flask cultures was measured by qPCR using FVIII-A2 primer/probe set. H, high-producing MWs are defined as  $\geq 5.0 \times 10^4$  vg/cell; M, medium producer as  $5.0 \times 10^3$  to  $5.0 \times 10^4$  vg/cell. N, number of independent measurements.

<sup>b</sup>Copy numbers of FVIII (FVIII-A2 primer/probe set), *rep* and *puro*<sup>R</sup> genes by qPCR (levels normalized to E6 gene in HeLaS3 cells [11 copies per HeLaS3 genome]).

<sup>c</sup>MWs containing mTTR202opt-HI-FVIII expression cassette.

<sup>d</sup>Published data.<sup>26</sup>