

**Table S1:** CSF nucleated cell counts in MPS I dogs following vector injection (Cells/ $\mu$ L)

Animal No.	Day post IT vector				
	0	7	21	51	81
549	1	ND	2	0	0
550	2	ND	11 <sup>a</sup>	BC	2
552	0	ND	ND	2	2
553	2	ND	1485 <sup>c</sup>	2	2
554	0	ND	14 <sup>b</sup>	1	2
562	2	BC	1	0	0
563	BC	1	29 <sup>b</sup>	1	0
564	1	1	4	0	0

ND = not done, BC = Blood contamination of CSF sample (>500 erythrocytes/ $\mu$ L), IT=intrathecal.

Normative range  $\leq 5$  cells/ $\mu$ L.

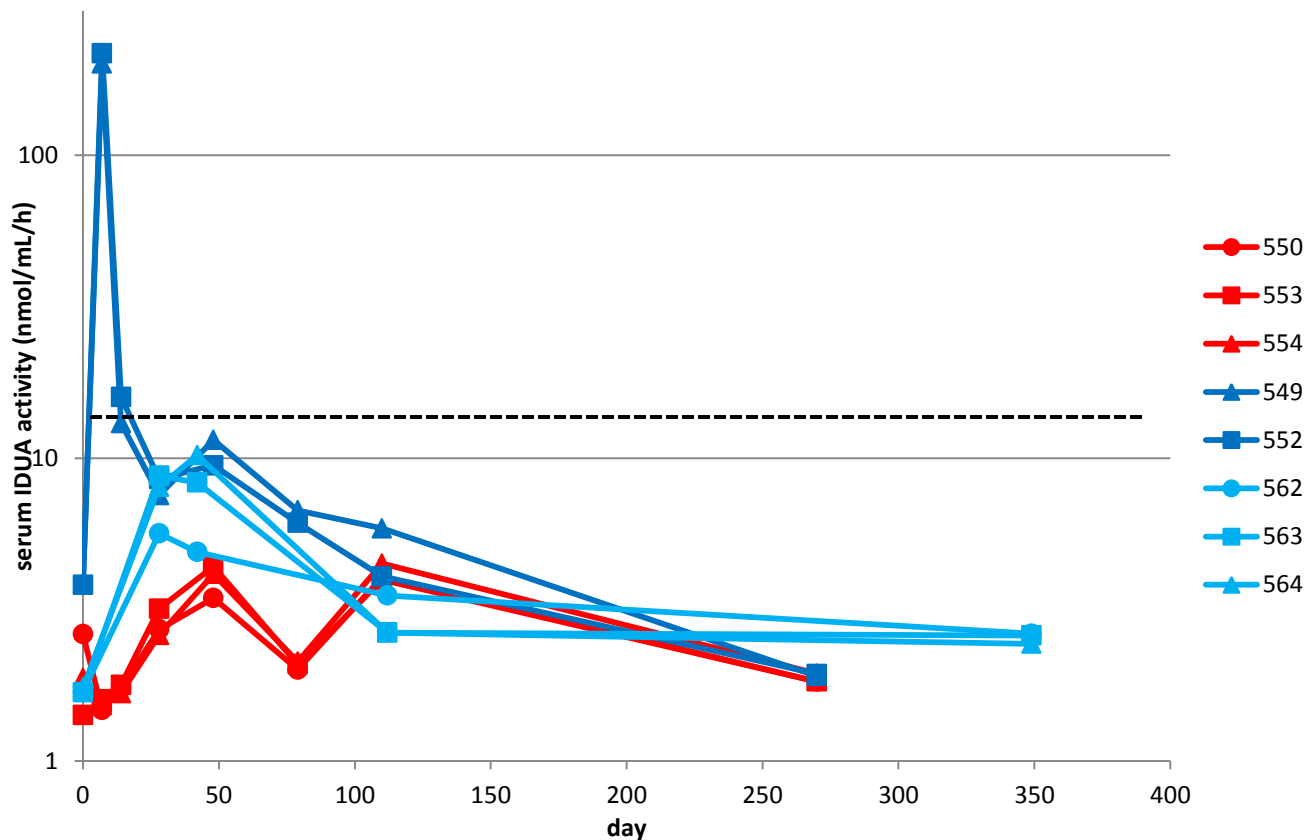
- 317 erythrocytes/ $\mu$ L
- >70% lymphocytes
- >70% monocytes

**Table S2: Vector biodistribution<sup>a</sup>**

	I-550	I-553	I-554	I-549	I-552	I-562	I-563	I-564
Frontal cortex	0.207224	0.032837	0.037931	0.195879	0.311028	0.053383	0.014606	0.41984
Temporal cortex	0.324461	0.015715	0.042556	0.682856	0.024615	0.075457	0.539041	0.541367
Occipital cortex	0.240198	0.03092	0.068607	0.585868	0.158689	0.006249	0.021576	0.724321
Hippocampus	0.007486	0.032587	0.058214	0.008692	0.336849	0.01288	0.056152	0.065506
Medulla	0.156078	0.012703	0.004936	0.063498	0.194763	0.294345	0.032355	0.020695
Cerebellum	0.022631	0.014178	0.010712	0.061944	0.046369	0.025023	0.026128	0.02586
Spinal cord cervical	0.257116	0.034117	0.014234	0.165666	0.509951	0.510722	0.046194	0.093024
Spinal cord thoracic	0.43775	0.063695	0.02829	0.359055	0.140467	0.120746	0.079992	0.100718
Spinal cord lumbar	0.190243	0.03037	0.116436	0.460682	0.313737	0.225627	0.241252	0.263238
Heart	0.001076	<0.0005 <sup>b</sup>	0.001983	0.00145	0.001454	0.02967	0.005545	0.005753
Lung	0.000879	0.002424	0.001887	0.000491	0.000538	0.000667	0.001105	0.001883
Liver	0.001304	0.004242	0.001918	0.010545	0.206071	0.030681	0.006334	0.028654
Spleen	0.002579	0.001543	0.001228	0.002596	0.002229	0.044439	0.003144	0.008972

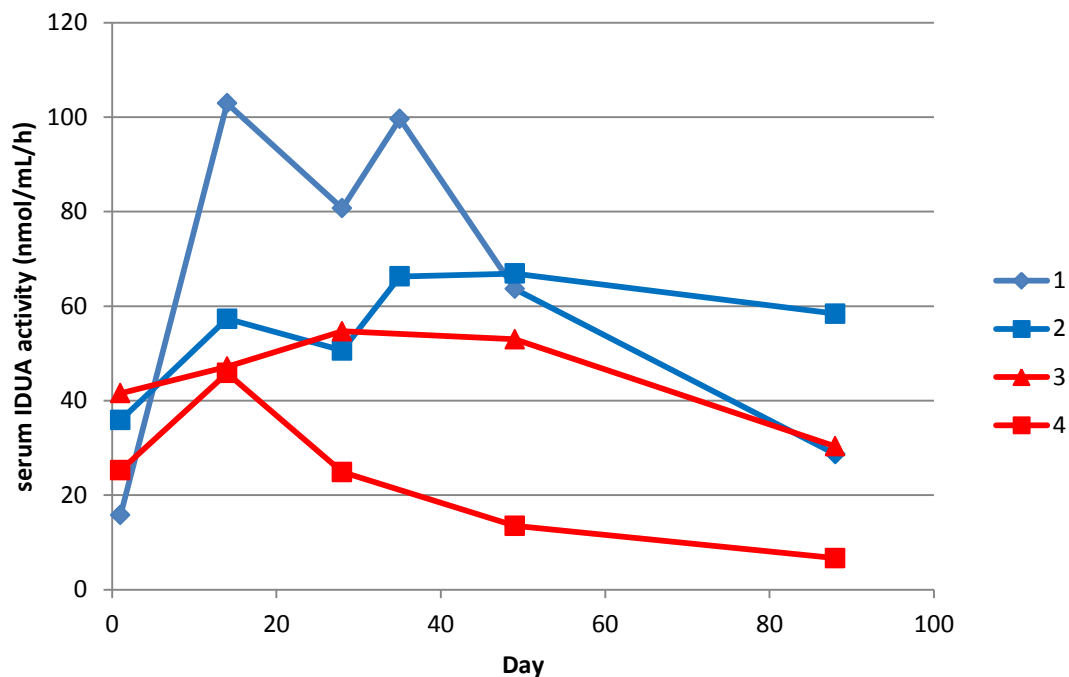
a. Values are genome copies (GC) per diploid genome. The assay does not distinguish between the AAV8 and AAV9 vectors.

b. Limit of detection



**Fig S1:** Serum IDUA activity in MPS I dogs.

MPS I dogs were treated with an intravenous injection of an AAV8 vector encoding canine IDUA under control of a liver specific promoter on postnatal day 1 (I-549, I-552) or postnatal day 7 (I-562, I-563, I-564) followed by intrathecal injection of an AAV9 vector at one month of age. Serum was serially collected from treated animals and assayed for IDUA enzyme activity. The dotted line indicates normal serum IDUA activity.



**Fig S2.** Serum IDUA activity in rhesus monkeys.

Newborn rhesus macaques were administered an AAV8 vector intravenously expressing human IDUA (animal 1 and 2) or human factor IX (3 and 4). All four were administered an intrathecal injection of an AAV9 vector expressing human IDUA at one month of age. Serum was serially collected from treated animals and assayed for IDUA enzyme activity.