

## Supplementary Data

**Supplementary Table S1. Certificate of analysis for vectors**

<i>Test</i>	<i>Method</i>	<i>Specification</i>	<i>AAV8.TBG.mLDLR</i>	<i>AAV8.TBG.hLDLR—lot 1</i>	<i>AAV8.TBG.hLDLR—lot 2</i>
Purity	SDS-PAGE	90–100% VP	97% VP1, 2, 3	92% VP1, 2, 3	100% VP1, 2, 3
Titer (GC/mL)	qPCR	$>1.0 \times 10^{13}$	$2.36 \times 10^{13}$	$2.2 \times 10^{13}$	$3.17 \times 10^{13}$
Infectious titer (IU/mL)	TCID <sub>50</sub> /qPCR	Report result	$7.22 \times 10^{10}$	$3.17 \times 10^{10}$	$8.08 \times 10^{10}$
GC:IU ratio	TCID <sub>50</sub> /qPCR	GC:IU ratio 1–1,000	327	694	392
Endotoxin (EU/mL)	LAL assay	<0.5	<0.5	<0.5	<0.5
Sterility method suitability	Bacteriostasis/fungistasis	Growth of all spiked organisms	Pass	Pass	Pass
Sterility	Direct culture 21 CFR 610.12	No growth observed	No growth observed	No growth observed	No growth observed

**Supplementary Table S2.** *Profile of cytokines and chemokines analyzed from peripheral blood*

*Cytokine analytes*

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G-CSF	IL-3	IL-13	IL-9
Eotaxin	IL-5	LIX	MIP-1 $\beta$
GM-CSF	IL-6	IL-15	M-CSF
IFN- $\gamma$	IL-7	IL-17	MIP-2
IL-1 $\alpha$	IL-10	IP-10	MIG
IL-1 $\beta$	IL-12p40	KC	RANTES
IL-2	IL-12p70	MCP-1	VEGF
IL-4	LIF	MIP-1 $\alpha$	TNF- $\alpha$

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**Supplementary Table S3. Tissues harvested at necropsy**

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*Tissues collected*

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Aorta	Liver, left and right lobe	Pancreas
Blood	Liver, left and median lobe	Small intestine
Bone, left leg	Liver	Salivary gland
Brain	Lungs	Spleen
Esophagus	Lymph node, inguinal	Stomach
Heart	Lymph node, lumbar	Testicle
Kidney, left	Muscle, gastrocnemius	Trachea
Large intestine	Ovary	Gross lesions (if any)

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**Supplementary Table S4. IFN- $\gamma$  ELISPOT to AAV8 Capsid and hLDLR Transgene in Splenocytes from DKO Mice**

Sex	Mouse ID	Medium	SFU/10 <sup>6</sup> splenocytes								SFU/10 <sup>3</sup> cells PMA + ION
			AAV8 capsid			hLDLR					
			A	B	C	A	B	C	D	E	
Male	377	13	13	20	23	15	38	8	23	18	83
	378	15	15	43	<b>93</b>	33	18	23	18	38	94
	384	23	33	33	55	40	<b>73</b>	35	40	30	93
	385	13	15	20	23	18	20	8	20	23	64
	386 (686)	23	38	68	<b>153</b>	20	35	20	30	28	81
	393	23	13	58	<b>80</b>	23	28	40	40	10	68
	394	15	20	20	35	15	33	23	30	20	70
Female	337	8	15	20	<b>70</b>	13	15	10	15	5	41
	356 (956)	15	10	5	35	15	5	10	8	5	41
	342	5	3	5	8	8	15	5	8	20	43
	343	5	15	15	10	8	10	13	13	5	41
	330	13	25	23	<b>63</b>	13	33	10	3	10	42
	875 (675)	13	33	33	<b>70</b>	15	18	13	10	5	49
	309	23	45	33	<b>103</b>	20	<b>98</b>	18	60	25	41

Mice administered i.v. with  $6.0 \times 10^{13}$  GC/kg of AAV8.TBG.hLDLR were necropsied on day 14 post vector administration. Splenocytes were isolated and IFN- $\gamma$  ELISPOT performed to study T-cell responses to the AAV8 capsid and hLDLR transgene. The table shows average SFU from two replicates per stimulant. Positive ELISPOT counts were defined as >55 SFU per million lymphocytes, with values three times over background. AAV8 capsid and hLDLR transgene pools that scored positive are shown in bold. Parentheses indicate the retagged ear tag number for mouse ID. Positive control: PMA/I: mixture of phorbol 12-myristate 13-acetate/ionomycin.