

### **Associated Protocol 3: Serum ELISAs**

**ANIMALS.** All mice experiments were approved by the Broad Institute IACUC. Wild-type adult C57BL/6J mice (000664) were purchased from the Jackson Laboratory. All mice were housed in a room maintained on a 12 h light and dark cycle with *ad libitum* access to standard rodent diet and water. Animals were randomly assigned to various experimental groups.

**RETRO-ORBITAL INJECTIONS.** 50 mL of VLPs (containing  $4 \times 10^{11}$  or  $7 \times 10^{11}$  VLPs) were centrifuged for 10 min at 15,000 *g* to remove debris. The clarified supernatant was diluted to 120 mL in 0.9% NaCl (Fresenius Kabi; 918610) right before injection.  $1 \times 10^{11}$  viral genomes (vg) of total AAV was diluted to 120 mL in 0.9% NaCl (Fresenius Kabi; 918610) right before injection. Anesthesia was induced with 4% isoflurane. Following induction, as measured by unresponsiveness to bilateral toe pinch, the right eye was protruded by gentle pressure on the skin, and an insulin syringe was advanced, with the bevel facing away from the eye, into the retrobulbar sinus where VLP or AAV mix was slowly injected. One drop of Proparacaine Hydrochloride Ophthalmic Solution (Patterson Veterinary; 07-885-9765) was then applied to the eye as an analgesic. Genomic DNA was purified from various tissue using Agencourt DNAdvance kits (Beckman Coulter; A48705) following the manufacturer's instructions.

**SERUM Pcsk9 MEASUREMENTS.** To track serum levels of Pcsk9 blood was collected using a submandibular bleed in a serum separator tube. Serum was separated by centrifugation at 2000 *g* for 15 min and stored at  $-80^{\circ}\text{C}$ . Pcsk9 levels were determined by ELISA using the Mouse Proprotein Con- vertase 9/PCSK9 Quantikine ELISA Kit (R&D Systems; MPC900) following the manufacturer's instructions.