

Expanded View Figures

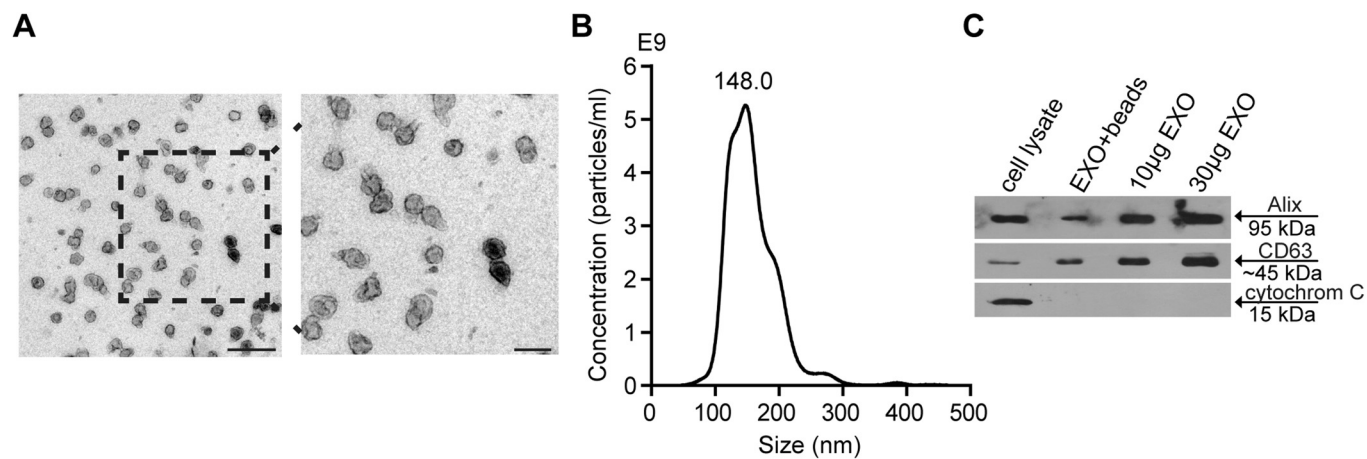


Figure EV1. Characterization of murine myotube-derived exosomes and CP05-based binding assay.

(A) Representative transmission electron microscopic (TEM) images of exosomes derived from murine myotubes (scale bar = 200 nm for right panel and 500 nm for the left). (B) Size distribution of exosomes derived from murine myotubes with nanoparticle tracking analysis (NTA). (C) Western blot to examine the binding of murine myotube-derived exosomes (EXO) to CP05-coated beads. The loading was specified in the figure.

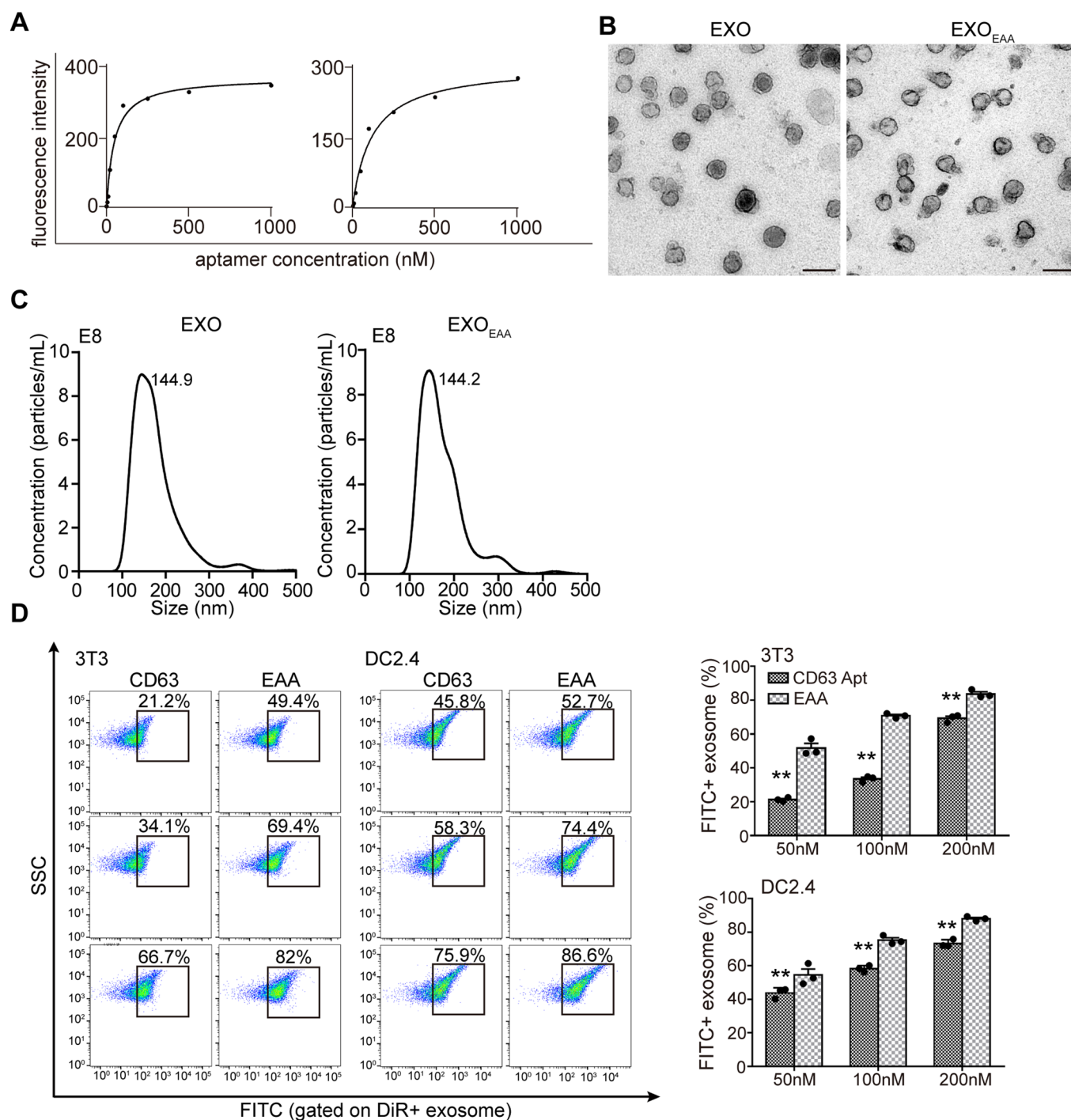


Figure EV2. Characterization of murine myotube-derived exosomes modified with EAA and binding assay for EAA with different exosomes.

(A) Measurement of binding affinity of EAA or CD63 aptamer to exosomes derived from mouse serum with flow cytometry. (B) Representative TEM images of murine myotube-derived exosomes modified with EAA (EXO_{EAA}) (scale bar = 200 nm). (C) Size distribution of EXO and EXO_{EAA} with nanoparticle tracking analysis (NTA). (D) Flow cytometric and quantitative analysis of binding efficiency of EAA or CD63 aptamer to exosomes across different concentrations (n = 3). Exosomes were derived from murine 3T3 and DC2.4 cells. Data information: Data represent different numbers (n) of biological replicates. The data with error bars are shown as mean ± SEM. (D) Statistical significance was determined using two-tailed t test. **P < 0.001.

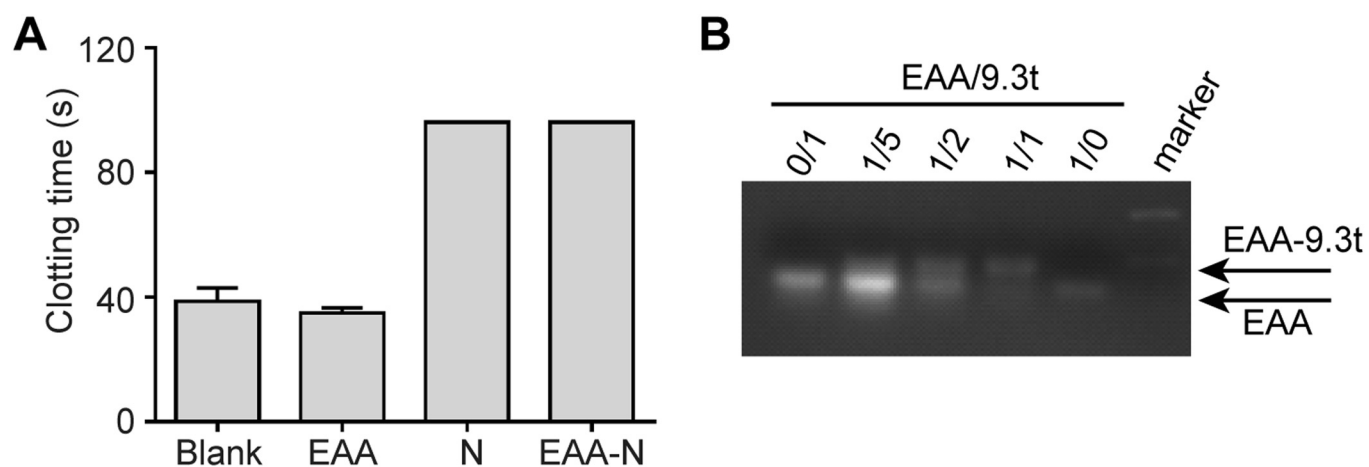


Figure EV3. In vitro evaluation of EAA-NU172's activity and optimization of binding ratio of EAA to 9.3t RNA aptamers.

(A) Measurement of the clotting time of rat plasma after the addition of thrombin in the presence of EAA, NU172 (N) or EAA-NU172 (EAA-N) ($n = 3$). Data represent different numbers (n) of biological replicates. The data with error bars are shown as mean $\pm$ SEM. (B) Agarose gel for mobility shift assay to determine the binding of EAA-linker to linker-9.3t at different molar ratios.

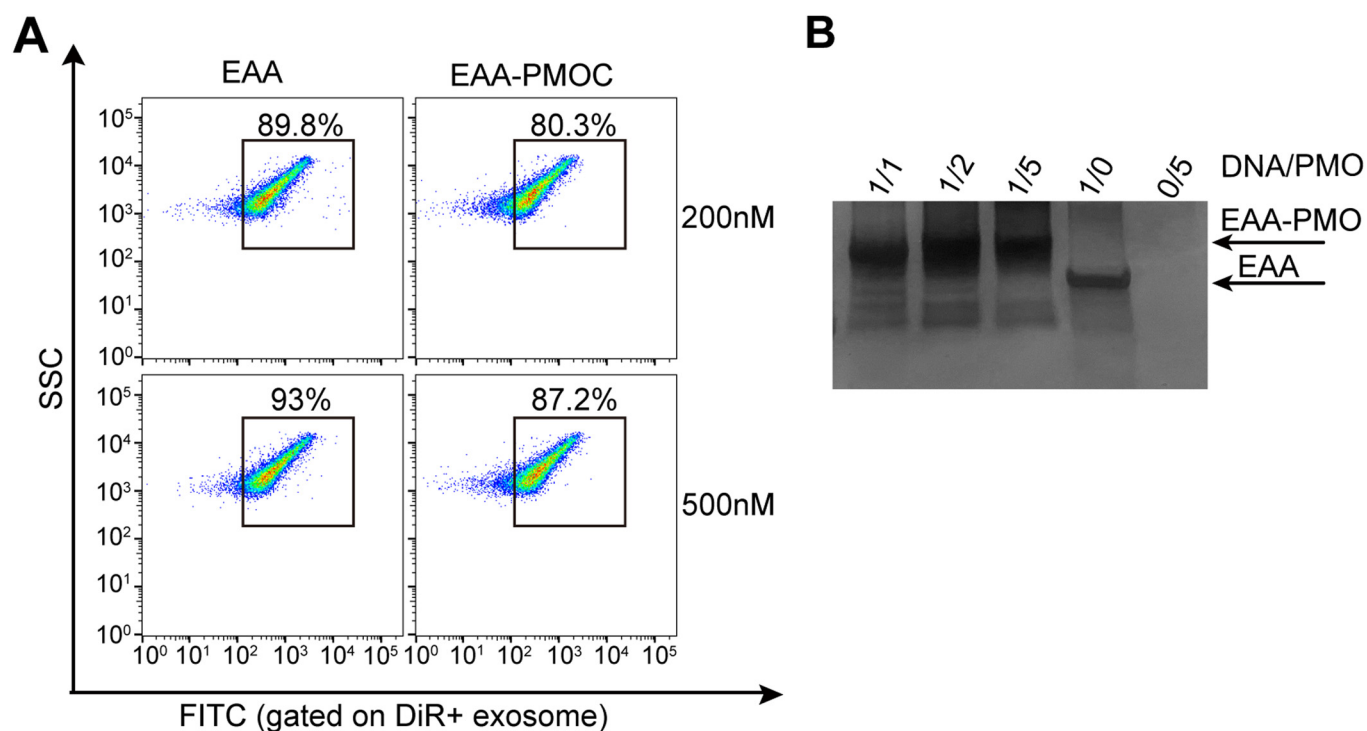


Figure EV4. Evaluation of binding efficiency of EAA-PMOC to exosomes and optimization of binding of EAA-PMOC to PMO.

(A) Flow cytometric analysis of binding efficiency of EAA-PMOC to exosomes derived from murine myotubes at two different concentrations. EAA-PMOC refers to EAA fused with a PMO- Complementary sequence. Aptamers were labeled with FITC and exosomes were labeled with DiR. (B) Silver staining for mobility shift assay to determine the binding of EAA-PMOC to PMO at different molar ratios.

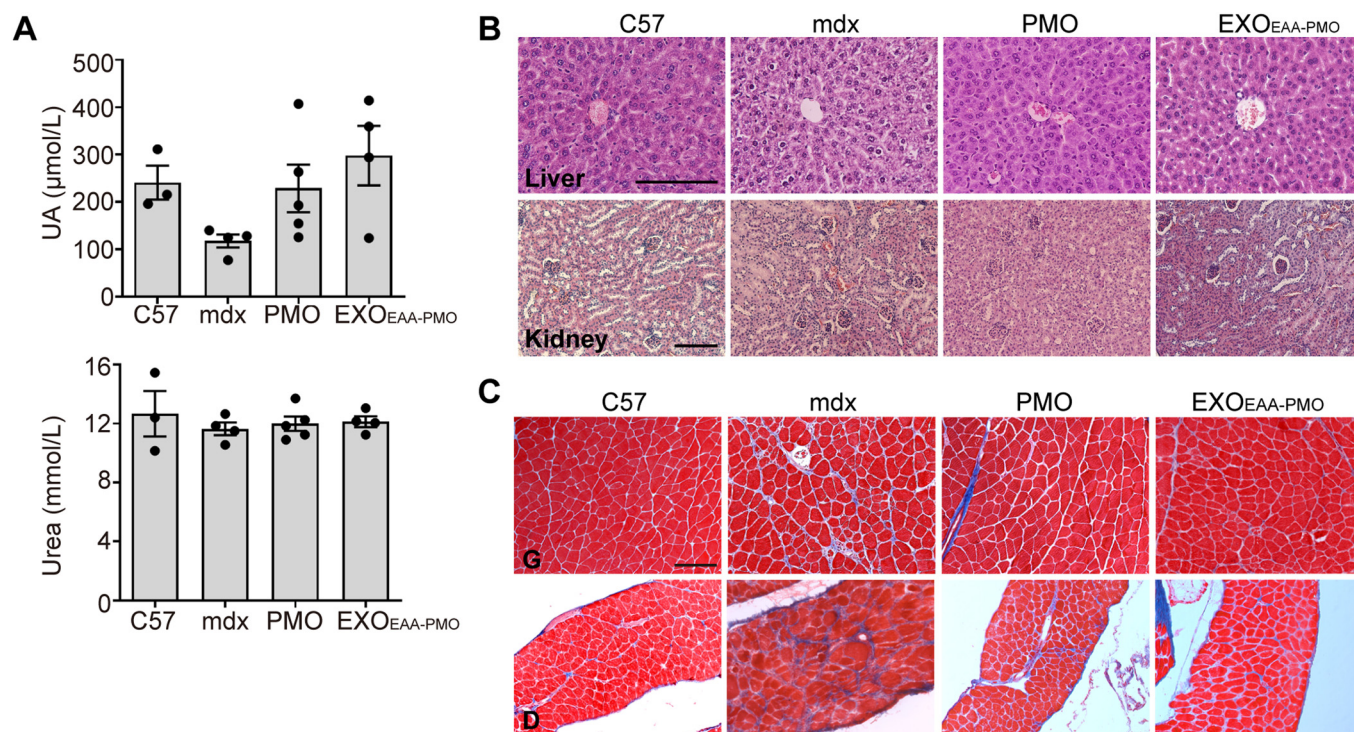


Figure EV5. Biochemical and histological examination of *mdx* mice treated with EXO_{EAA-PMO}.

EXO_{EAA-PMO} at the PMO dose of 25 mg/kg were administered into adult *mdx* mice for three times weekly intravenously and tissues were harvested 2 weeks after last injection. (A) Analysis of biochemical indicators for kidney function in *mdx* mice treated with PMO ($n = 5$), EXO_{EAA-PMO} ($n = 4$), untreated *mdx* ($n = 4$) and C57BL/6 controls ($n = 3$). (B) H&E staining of liver and kidney from *mdx* mice treated with EXO_{EAA-PMO} (scale bar = 100 μm). (C) Collagen deposition analysis in gastrocnemius (G) and quadriceps (Q) from treated *mdx* mice (scale bar = 100 μm). Data information: In (A), the data represent different numbers (n) of biological replicates. The data with error bars are shown as mean $\pm$ SEM.