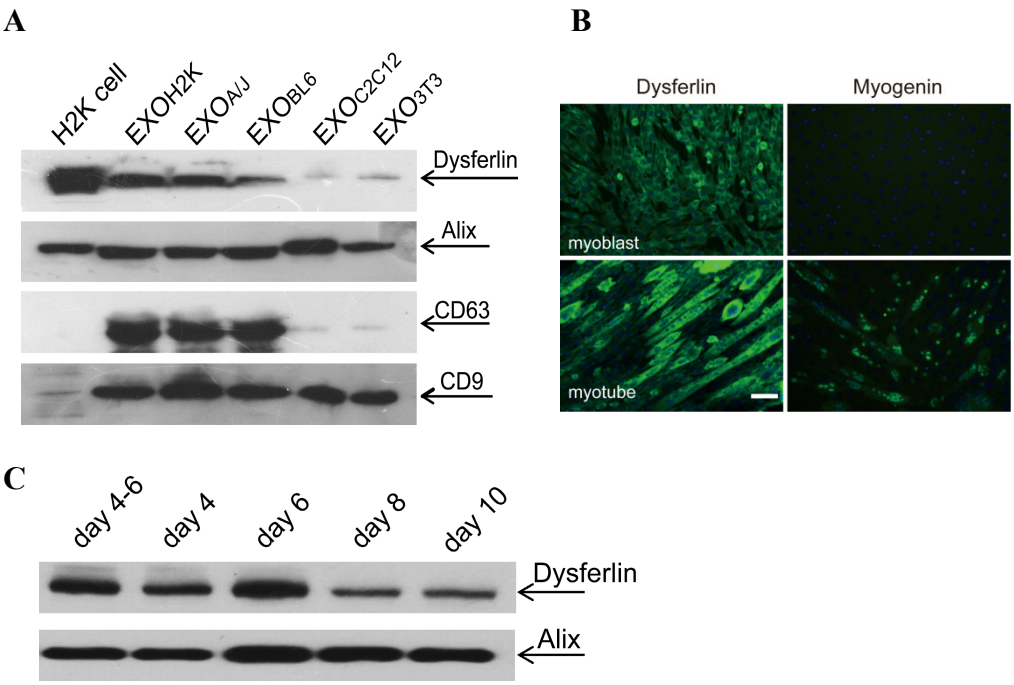
Supplementary Material

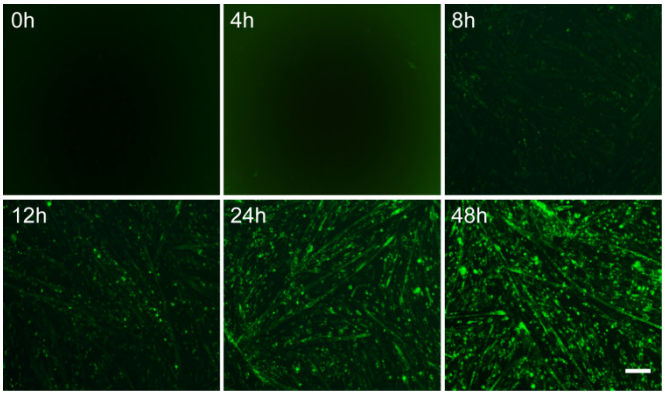
Supplementary Figure 1



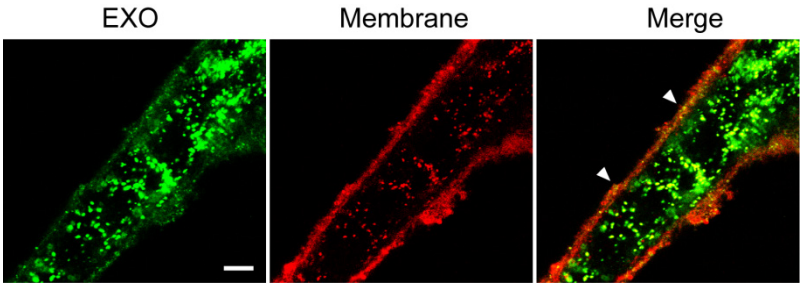
Supplementary Figure 1. Examination of dysferlin protein in exosomes derived from different murine myoblasts and differentiated myotubes. (**A**) Western blot to examine levels of dysferlin protein in exosomes derived from different murine myoblasts. 50 or 100 μg total protein from cell lysates or exosomes was loaded. EXO_{H2K}, $EXO_{A/J}$, EXO_{BL6}, EXO_{C2C12} and EXO_{3T3} refer to exosomes derived from immortalized H2K, A/J, BL6, C2C12 and 3T3 cells, respectively. H2K cell means immortalized H2K cell lysates. (**B**) Immunostaining of dysferlin and myogenin in H_2K myoblasts and myotubes. Nucleic were counterstained with DAPI (blue) (scale bar =100 μm). (**C**) Western blot to examine levels of dysferlin protein in exosomes derived from differentiated myotubes at different time-points after induction. 20 μg total protein from exosomes was loaded and Alix was used as an exosomal marker.

Supplementary Figure 2

A

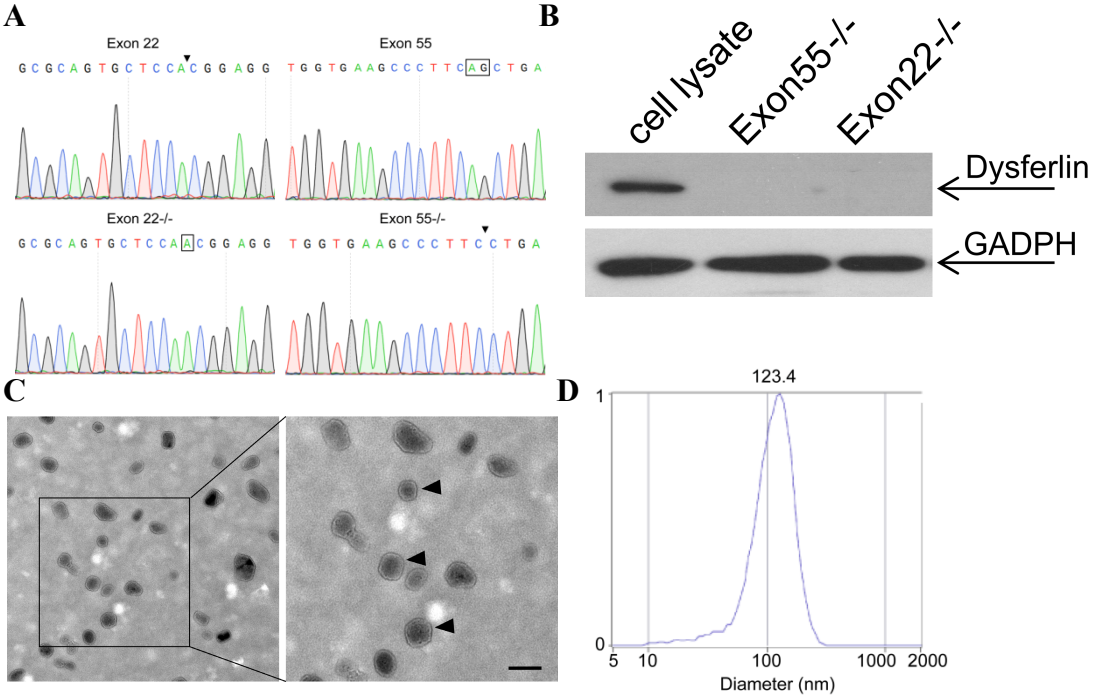


B



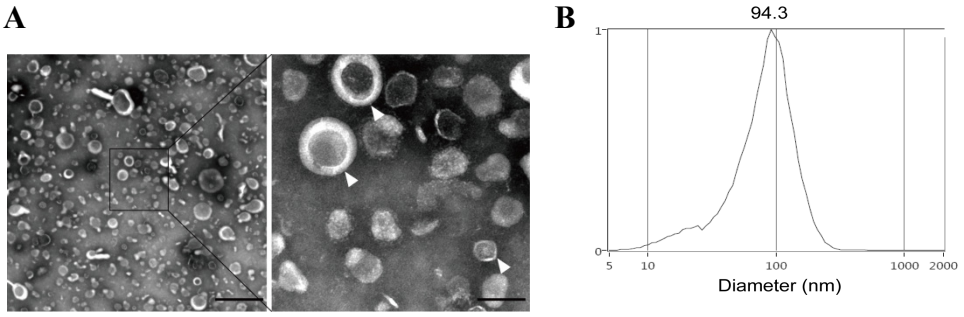
Supplementary Figure 2. Cellular uptake and localization of PKH67-labelled EXOdysf in murine H2K DYSF$^{-/-}$ myotubes. (**A**) Cellular uptake of PKH67-labelled EXOdysf in DYSF$^{-/-}$ myotubes at different time-points after the addition of 5 µg PKH67-labelled EXOdysf (scale bar =40 µm). (**B**) Confocal fluorescence microscopic images to show the localization of PKH67-labelled EXOdysf in DYSF$^{-/-}$ myotubes. The membrane dye FM4-64 was used to label membrane (red). Arrowheads point to exosomes localized on the membrane (scale bar =20 µm).

Supplementary Figure 3



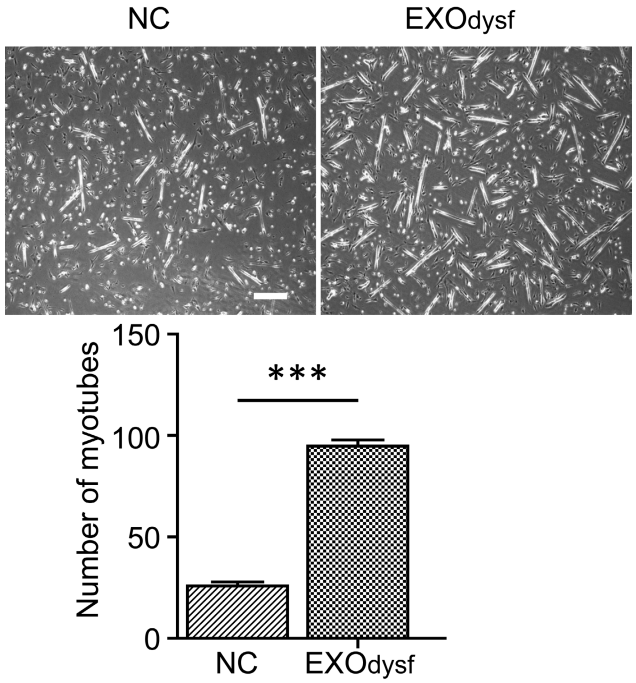
Supplementary Figure 3. Characterization of human *dysferlin* gene knock-out myoblasts and human serum exosomes. (**A**) Gene sequencing for human *dysferlin* gene exon 22 and 55 knock-out myoblasts. (**B**) Western blot to confirm the expression of dysferlin in human *dysferlin* exon 22 (Exon $22^{-/-}$) and exon 55 (Exon $55^{-/-}$). 30 µg total protein from cell lysates was loaded and GAPDH was used as a loading control. (**C**) Representative transmission electron microscopy (TEM) image of exosomes from human serum (scale bar = 100 nm). Arrowheads point to the sauce-cup shape of exosomes. (**D**) Analysis of size distribution of exosomes from human serum with Nano Particle Tracking and Zeta potential distribution Analyzer (NTA) system.

Supplementary Figure 4



Supplementary Figure 4. Characterization of exosomes derived from human urine. (**A**) Representative TEM images of human urine exosomes (scale bar =500 nm (left) or 100 nm (right)). Arrowheads point to the sauce-cup shape of exosomes. (**B**) Analysis of size distribution of human urine exosomes with the NTA system.

Supplementary Figure 5



Supplementary Figure 5. Measurement of myotubes formed in EXOdysf-treated DYSF$^{-/-}$ myoblasts (EXOdysf). A significant increase in the number of myotubes formed was observed in EXOdysf-treated DYSF$^{-/-}$ myoblasts compared to untreated myoblasts (NC) (n=15, two-tailed test, ***P<0.001) (scale bar = 40 μm).