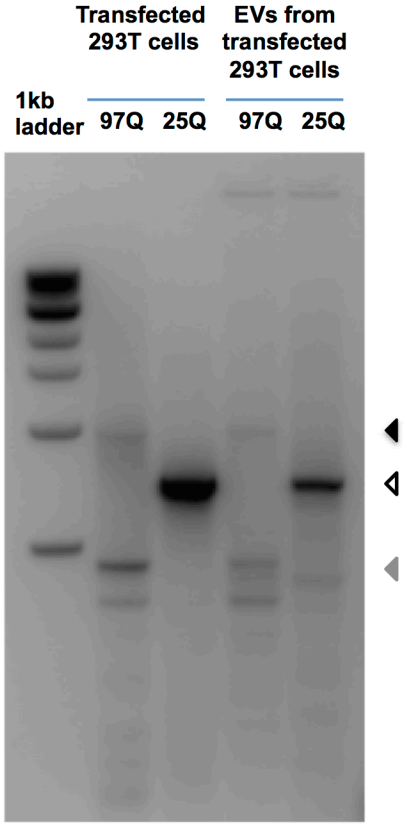
Supplemental Figure 1



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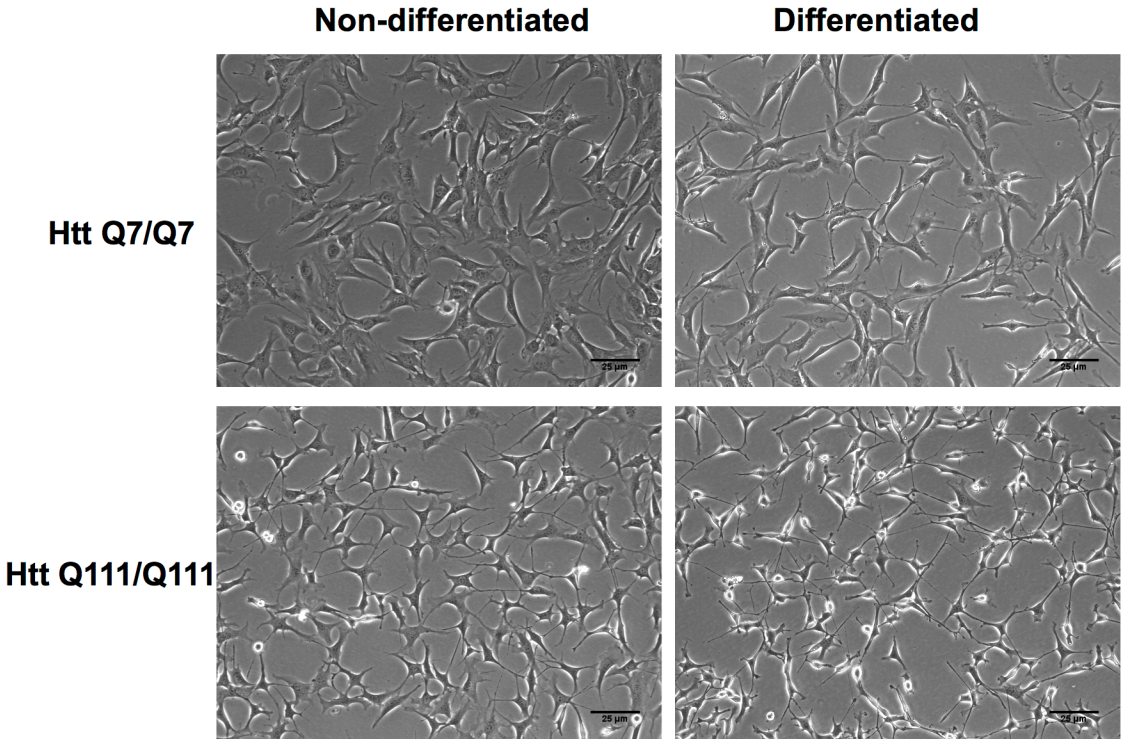
Supplemental Figure 2



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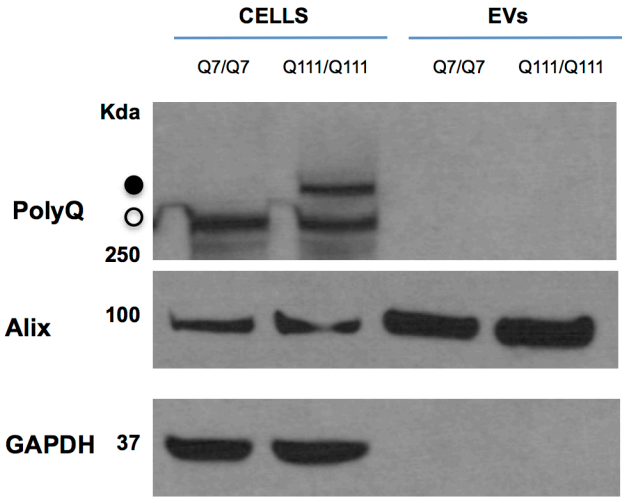
Supplemental Figure 3



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Supplemental figure S1. RT-PCR of polyQ-GFP RNA with different repeat lengths from transduced 293T cells and EVs. 293T cells were transduced using lentiviral vectors encoding GFP (not shown), Htt^{ex1}-25Q-GFP, and Htt^{ex1}-97Q-GFP. Two weeks later (equivalent to about 6 passages) RNA from cells and EVs was extracted using the miRNeasy mini kit. RT-PCR products were analyzed on 1 % agarose gel using 1 kb Quick-Load ladder. [Open arrowhead—25Q-GFP; solid arrowhead—97Q-GFP; gray arrowhead—GFP RNAs.]

Supplemental figure S2. Bright field image showing striatal neuron-like STHdhQ7/Q7 and STHdhQ111/Q111 cells 12 h after differentiation. Immortalized mouse striatal cell lines, STHdhQ111/Q111 and STHdhQ7/Q7 were normally cultured in high glucose DMEM (Corning) plus 10 % FBS and 40 mg/ml of G418 at 33^{o}C. After neuronal differentiation, which was induced by incubation with a dopamine cocktail of α-FGF (10 ng/ml), 3-IBMX (240 μM), forskolin (48.6 μM), and dopamine (5 μM) (Sigma) in DMEM/F12 for 12 h, cells develop long neuron-like processes with STHdhQ7/Q7 appearing to have larger soma than the STHdh Q111/Q111 cells.

Supplemental figure S3. HTT protein was detected in the STHdh111/111 cells but not in the EVs from these cells. Striatal cells were allowed to attach for 6 h before being differentiated. Cells and EVs in conditioned media were harvested from both striatal cell lines 48 h after differentiation. Western blots were performed for both striatal cells and EV lysates using monoclonal 3B5H10 antibody. The HTT protein (approx. 350 kDa) was found in STHdh111/111 cells, but was not detectable in STHdh7/7 cells, consistent with the low levels of HTT protein in the latter (Krauss et al. 2013). No HTT immunoreactive proteins were found in the EVs from these cell lines. Open circle = non-specific protein; solid circle = HTT protein.

Supplementary Table 1. Average Ct value of all genes and conditions used to calculate the HTT RNA loading into EVs

	RNA	Average Ct value[a]	Standard deviation
Q7/Q7 cells	Hdh	23.52	0.66
	HPRT	21.73	0.50
	ActB	16.83	0.26
Q7/Q7 EVs	Hdh	29.66	0.78
	HPRT	26.28	1.96
	ActB	20.80	1.62
Q111/Q111 cells	Hdh	24.05	0.65
	HPRT	21.91	0.55
	ActB	17.32	0.55
Q111/Q111 EVs	Hdh	28.10	0.82
	HPRT	28.10	0.82
	ActB	19.96	1.16

[a] Average Ct value of n=3 experiments with duplicate measurements