



**Figure 8 - figure supplement 1: Impact of polyQ flanking regions on mHtt degradation and proteolysis**

**A.** Fluorescence images of MSNs co-transfected with the mHtt variants, YFP, and CCT1. Images were taken 1 day (top row) and 4 days (bottom row) after transfection. Data are representative of at least three independent experiments. Scale bar is 20  $\mu\text{m}$ .

**B.** Radiogram gels of  $^{35}\text{S}$  pulse-chase measuring soluble protein degradation of mHtt-Ex1 variants in transfected ST14a cells.

**C. – D.** Quantified data of Ex1 and  $\Delta\text{P}$  degradation from four independent experiments each, demonstrating the robust degradation data.

**E.** Quantification of protein degradation of mHtt variants. Data compiled from four independent experiments each. Data fitted with GraphPad Prism software using the non-linear regression fit.

**F. i.** Schematic of trypsin digestion experiment: Ex1 and  $\Delta\text{P}$  oligomers were generated *in vitro*, then digested with increasing concentrations of trypsin protease. Protease-digested reactions were run in an SDS-PAGE gel and probed for N17. **ii.** SDS-PAGE gel of trypsin-digested Ex1 and  $\Delta\text{P}$  oligomers immunoprobed for N17. **iii.** Quantification of N17 signal intensity from SDS PAGE gel in (ii).