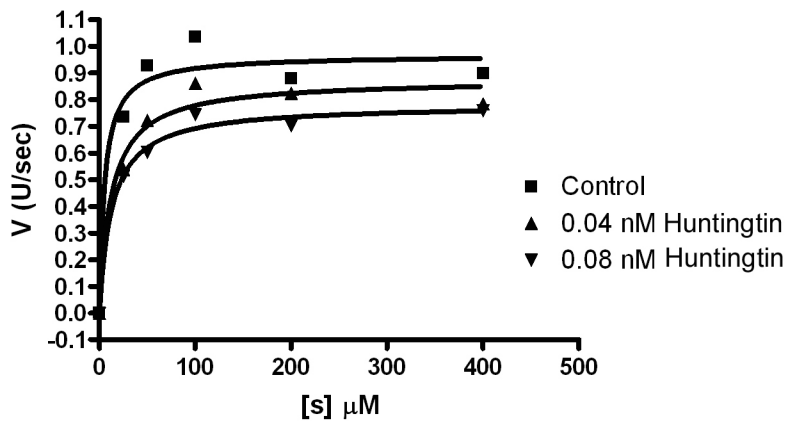


**A****B**

	Control	0.04 nM	0.08 nM
Michaelis-Menten			
Best-fit values			
VMAX	0.97	0.88	0.78
KM	5.56	12.53	13.04
Std. Error			
VMAX	0.062	0.048	0.026
KM	4.05	4.47	2.74

**Fig. S1**

Figure S1. Concentration-dependent inhibition of caspase-3 by huntingtin. (A) Plot for the inhibitory effects of huntingtin on velocities ( $V$ ) of caspase-3 – catalyzed reactions at various concentrations of substrate, DEVD-AFC ( $[S]$ ). Recombinant Caspase-3 (Chemicon) was used in a final concentration of 0.391 nM. Huntingtin was generated by reticulocyte coupled transcription/translation system and dialyzed through 100 kDa Spectra/Por CE membranes (Spectrum Lab, Inc., CA) to reduce the amount of hemoglobin. Dialysates of reticulocyte extracts not expressing huntingtin were used as the controls (■). Due to the limited amount of protein from *in vitro* translated products and dialyze preparation, the highest concentration of huntingtin only reached 0.08 nM (▲). Huntingtin was pre-incubated with caspase-3 for 15 min before adding substrate and measured for 45 min at 37°C. As demonstrated using this fluorogenic assay, huntingtin inhibited caspase-3 activity (Figure S1A) in a concentration-dependent manner. In these experiments, huntingtin increased caspase-3 enzymatic  $K_m$  value and reduced  $V_{max}$  (Figure S1B). This data is representative of three independent experiments.