2019-10-30

Allele-selective lowering of mutant HTT protein by HTTLC3 linker compounds

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10.1038/s41586-019-1722-1
Nature
Springer Science and Business Media LLC

Model and treatment	Readout and figures	Compound effects
cultured primary cortical neurons, from mice ($Hdh^{Q7/Q140}$)	the mHTT level by Western-blot (Fig. 2a&d)	10O5: 26.0±3.3% lowering
		8F20: 40.1±12.6% lowering
		AN1: 35.7±2.8% lowering
		AN2: 34.0±6.2% lowering
primary human HD patient fibroblasts (Q49)	the mHTT level by HTRF (Fig. 3a)	10O5: 45.1±4.0% lowering
		8F20: 44.8±4.9 lowering
		AN1: 46.1±6.2% lowering
		AN2: 54.8±7.5% lowering
primary human HD patient fibroblasts (Q55)	the mHTT level by HTRF (Fig. 3a)	10O5: 34.3±5.4% lowering
		8F20: 28.7±3.6% lowering
		AN1: 26.5±7.0% lowering
		AN2: 39.3±4.8% lowering
primary human HD patient fibroblasts (Q68)	the mHTT level by HTRF (Fig. 3a)	10O5: 20.9±2.7% lowering
		8F20: 22.9±5.3% lowering
		AN1: 26.4±2.8% lowering
		AN2: 18.1±5.1% lowering
HD patient iPSC-derived neurons (Q47)	the mHTT level by HTRF (Ext. Data. Fig. 5c)	10O5: 31.4±3.2% lowering
		8F20: 28.9±3.7% lowering
		AN1: 39.3±3.2% lowering
		AN2: 40.5±2.8% lowering
	surface area of each neuron by Tuj1 staining (Fig. 5a)	10O5: 69.5±1.6% rescue
		8F20: 51.6±3.1% rescue
		AN1: 58.8±4.9% rescue
		AN2: 64.4±2.7% rescue
immortalized human HD patient fibroblasts (Q47)	the mHTT level by HTRF (Fig. 3b)	10O5: 30.2±4.5% lowering
		8F20: 22±4.8% lowering
		AN1: 42.0±3.9% lowering
		AN2: 41.4±5.1% lowering
icv-injected mice ($Hdh^{Q7/Q140}$)	the mHTT level by Western-blot (Ext. Data Fig. 9a)	10O5: 43.3±2.2% lowering
		8F20: 9.1±5.3% lowering (n.s.)
		AN1: 29.9±2.9% lowering
		AN2: 30.3±7.4% lowering
ip-injected mice ($Hdh^{Q7/Q140}$)	the cortical mHTT by Western-blot (Ext. Data Fig. 9b)	10O5: 24.8±4.2% lowering
		AN2: 36.6±7.4% lowering
	the striatal mHTT by Western-blot (Ext. Data Fig. 9c)	10O5: 22.9±2.3% lowering
		AN2: 26.3±5.5% lowering
	the cortical HTT by MASS-SPEC (Ext. Data Fig. 11b)	10O5: 18.1±2.4% lowering
		AN2: 25.2±3.2% lowering
	latency to fall by rotarod tests (Fig. 5d)	10O5: (60.8% averaged rescue)
		AN2: (64.3% averaged rescue)
	passing time by balance beam tests (Fig. 5e)	10O5: (77.2% averaged rescue)
		AN2: (92.8% averaged rescue)
	gripping force tests (Fig. 5f)	10O5: (43.6% averaged rescue)
		AN2: (52.4% averaged rescue)