Researchers find a protein involved in Huntington's disease motor deficits

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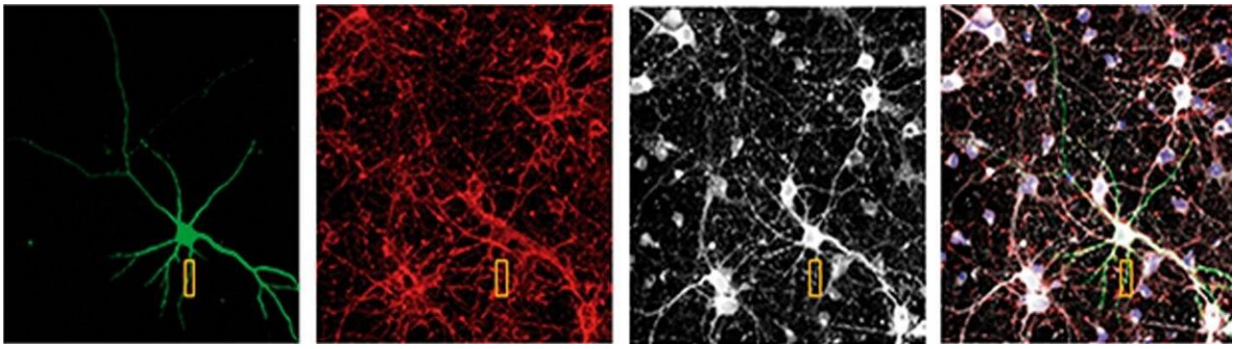

Overexpression of exon-1 mhtt increases RTP801 protein levels in dendrites and in synaptic spines. Yellow rectangles show digital zoom of dendrites with spines and yellow arrows show RTP801 staining at the puncta. Credit: Universidad de Barcelona

Huntington's disease is caused by a mutation in the Huntingtin gen. Patients show involuntary movements, cognitive deficits and specific psychiatric disorders resulting from the degeneration and death of medium spiny striatal neurons. A study led by researchers of the Institute of Neurosciences of the UB (UBNeuro) describes the toxic role of the protein RTP801 in this pathology, and specifically, how it affects motor deficits.

"This protein was identified in Parkinson's disease, and we have described it in Huntington's, another movement disorder. When the

expression of this protein is regulated downward, we prevent motor deficits from appearing," says Cristina Malagelada, researcher at UBNeuro and one of the authors of the study, published in the journal *Cell Death and Disease*.

Using mice models, cultured primary neurons and postmortem brain samples of patients with Huntington's, the team studied whether the protein RTP801 is involved in the deficits in motor learning. The results of the study provide high levels of this protein in the synapsis of the striatum, both in mice models and human samples.

"The main result of the study is that the protein RTP801 contributes to the damaging effect of the mutated huntingtin in mice striatal synaptic spines that model Huntington's disease," says Esther Pérez Navarro, researcher at UBNeuro and author of the study.

In the study, researchers saw that provoking a decrease of the RTP801 protein restored the crucial protein levels that are dysregulated in this pathology: Akt kinase, RICTOR and TrkB. "These results validate RTP801 as a therapeutic target in Huntington's disease. The design of molecules or therapeutic strategies to modulate levels of the protein RTP801 will be very important to find an efficient treatment to work on this disease," concludes Malagelada.

More information: Núria Martín-Flores et al. Synaptic RTP801 contributes to motor-learning dysfunction in Huntington's disease, *Cell Death & Disease* (2020). DOI: 10.1038/s41419-020-02775-5

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