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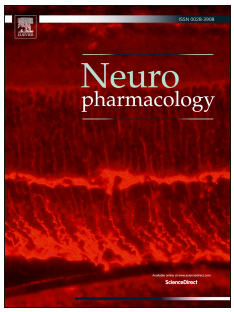

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Huntingtin protein: A new option for fixing the Huntington's disease countdown clock

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Abstract

Huntington's disease is a dreadful, incurable disorder. It springs from the autosomal dominant mutation in the first exon of the *HTT* gene, which encodes for the huntingtin protein (HTT) and results in progressive neurodegeneration. Thus far, all the attempted approaches to tackle the mutant HTT-induced toxicity causing this disease have failed. The mutant protein comes with the aberrantly expanded poly-glutamine tract. It is primarily to blame for the build-up of β-amyloid-like HTT aggregates, deleterious once broadened beyond the critical ~35-37 repeats threshold. Recent experimental findings have provided valuable information on the molecular basis underlying this HTT-driven neurodegeneration. These findings indicate that the poly-glutamine siding regions and many post-translation modifications either abet or counter the poly-glutamine tract. This review provides an overall, up-to-date insight into HTT biophysics and structural biology, particularly discussing novel pharmacological options to specifically target the mutated protein and thus inhibit its functions and toxicity.

Keywords: Huntingtin; Aptamers; Biophysics; Huntington's disease; Oligonucleotide