# Ku70 shown to be critical regulator of DNA damage in Huntington's disease

May 3 2010

Ku70, a component of the DNA repair complex, is shown to be a new critical player in the DNA damage-linked pathologies of Huntington's disease (HD), according to a study in the May 3 issue of the *Journal of Cell Biology*.

DNA repair defends against naturally occurring or disease-related DNA damage during the long lifespan of neurons. Impairments to this process underlie "polyQ" diseases, a major group of hereditary neurodegenerative disorders that includes HD. Understanding the multiple pathogenic pathways that lead to such DNA repair dysfunction is key for the development of new therapies.

In this study, Hitoshi Okazawa and colleagues report that expression of mutant huntingtin (Htt)—the protein responsible for HD—in neurons causes double-strand breaks (DSBs) in genomic DNA and impairs DNA repair. The researchers identify Ku70 as a mediator of the DNA repair dysfunction in mutant Htt-expressing neurons—mutant Htt interacts with Ku70, impairing its function in nonhomologous end joining, which consequently increases DSB accumulation. Boosting Ku70 levels rescues mutant Htt-induced neurodegeneration in a mouse model of HD, suggesting that Ku70 is a critical regulator of DNA damage in HD pathology.

**More information:** Enokido, Y., et al. 2010. J. Cell Biol. doi:10.1083/jcb.200905138

Provided by Rockefeller University