Molecular basis for neurodegeneration in Ataxia telangiectasia

14 April 2008

An upcoming paper from Dr. David Wassarman (University of Wisconsin School of Medicine and Public Health) in the May 1 issue of G&D lends new insight into the pathogenesis of neurodegeneration in Ataxia telangiectasia.

Ataxia telangiectasia (A-T) is a rare, genetic immunodeficiency disease that affects multiple organ systems and is characterized by neurodegeneration and cancer predisposition. A-T is caused by recessive mutations in the ataxia telangiectasia mutated (ATM) gene.

While existing animal models have established how ATM mutations contribute to genomic instability and cancer susceptibility, Dr. Wassarman's paper reveals how ATM mutations cause neurodegeneration.

The scientists generated a Drosophila model of A-T, in which neurodeneneration occurs in the absence of induced DNA damage – as it does in human A-T patients. Thus, Dr. Wassarman's model most faithfully recapitulates neurodegeneration associated with the human disease.

Using this model, Dr. Wassarman and colleagues determined ATM
functions normally to prevent neurons from re-entering the cell cycle.

"At the end of the day, ATM-dependent arrest of cell growth is critical for both neuron function and tumor suppression," explains Dr. Wassarman. Furthermore, he is excited by the findings, as they "point to possible therapeutic potential of CDC25 and other cell cycle inhibitors" to treat A-T as well as other neurodegenerative disorders.

Source: Cold Spring Harbor Laboratory