

# Detector of DNA damage: Structure of a repair factor revealed

June 19 2012

---

Double-stranded breaks in cellular DNA can trigger tumorigenesis. Researchers from Ludwig-Maximilians-Universitaet (LMU) in Munich, Germany, have determined the structure of a protein involved in the repair and signaling of DNA double-strand breaks. The work throws new light on the origins of neurodegenerative diseases and certain tumor types.

Agents such as radiation or [environmental toxins](#) can cause double-stranded breaks in genomic DNA, which facilitate the development of tumors or the neurodegenerative disorders ataxia telangiectasia (AT) and AT-like disease (ATLD). Hence efficient repair mechanisms are essential for [cell survival](#) and function. The so-called MRN complex is an important component of one such system, and its structure has just been elucidated by a team led by Professor Karl-Peter Hopfner of LMU's Gene Center.

The MRN complex consists of the nuclease Mre11, the ATPase Rad50 and the protein Nbs1. Nbs1 is responsible for recruiting the protein ATM, which plays a central role in early stages of the cellular response to [DNA damage](#), to the site of damage. "How the MRN complex actually recognizes double-stranded breaks is still not clear," says Hopfner. He and his colleagues therefore set out to clarify the issue by analyzing the structures of mutant, functionally defective versions of the complex.

"We found that pairs of Mre11 molecules form a flexible dimer, which

is stabilized by Nbs1." Mutations in different subunits of the complex are associated with distinct syndromes, marked by a predisposition to certain cancers, sensitivity to radiation or neurodegeneration. Hopfner's results help to explain these differences. For instance, the mutation linked to ATLD lies within the zone of contact between Mre11 and Nbs1, and may inhibit activation of ATM by weakening their interaction.

Provided by Ludwig Maximilian University of Munich

Citation: Detector of DNA damage: Structure of a repair factor revealed (2012, June 19)  
retrieved 27 April 2024 from  
<https://medicalxpress.com/news/2012-06-detector-dna-factor-revealed.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.