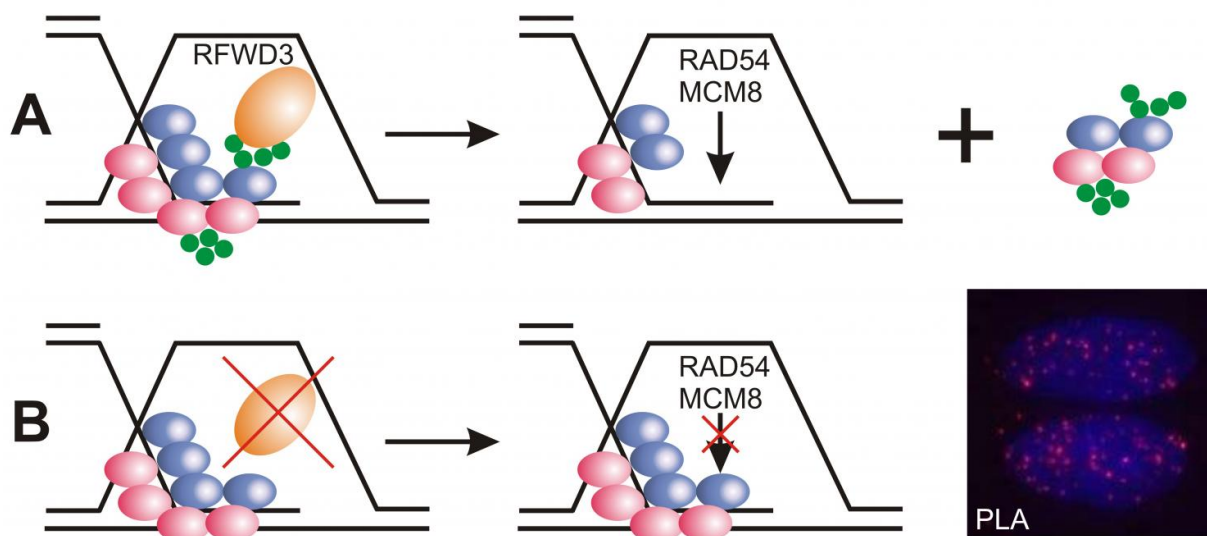


Study identifies new gene mutation associated with defective DNA repair and Fanconi anemia

July 10 2017



A: The enzyme RFWD3 helps target other proteins on single-stranded DNA for degradation. B: Cells lacking RFWD3 show DNA repair defects. Credit: (Figure modified from Inano et al.)

Fanconi anemia is a rare genetic disease characterized by hematologic symptoms that include low platelet count and unusually large red blood cells. Mutations in nearly 20 genes have been identified as causative for Fanconi anemia, all of which encode proteins involved in DNA repair mechanisms. The failure to repair DNA is also considered the source of

increased cancer risk in individuals with Fanconi anemia. Ongoing efforts to identify additional genes and pathways linked to this disease may also reveal potential susceptibility genes for hereditary cancers.

This week in the *JCI*, a team led by Detlev Schindler at the University of Wurzburg describes classical Fanconi anemia-like symptoms in a 12 year-old individual without mutations in any known Fanconi anemia genes. Sequencing of this individual's genome detected missense mutations in both alleles of the gene *RFWD3*, which encodes an enzyme that helps target other proteins for degradation.

This patient's cells were more sensitive to chromosome breakage and showed other indicators of increased susceptibility to DNA damage compared to cells from healthy individuals. Cells lacking *RFWD3* or harboring the patient's mutation showed similar DNA repair defects, which were rescued by expression of wild-type *RFWD3*. Moreover, *RFWD3*-deficient mice exhibited a phenotype that resembled other mouse models of Fanconi anemia. Together, these findings support the identification of *RFWD3* as a Fanconi anemia gene.

Schindler and collaborators further describe the mechanisms by which *RFWD3* mediates DNA repair in two recently-published studies in *Molecular Cell*. Future explorations of this enzyme may reveal its importance as a biomarker or therapeutic target in Fanconi anemia, cancer, or other human disease.

More information: Kerstin Knies et al, Biallelic mutations in the ubiquitin ligase *RFWD3* cause Fanconi anemia, *Journal of Clinical Investigation* (2017). DOI: 10.1172/JCI92069

Laura Feeney et al, RPA-Mediated Recruitment of the E3 Ligase *RFWD3* Is Vital for Interstrand Crosslink Repair and Human Health, *Molecular Cell* (2017). [DOI: 10.1016/j.molcel.2017.04.021](https://doi.org/10.1016/j.molcel.2017.04.021)

Shojiro Inano et al. RFWD3-Mediated Ubiquitination Promotes Timely Removal of Both RPA and RAD51 from DNA Damage Sites to Facilitate Homologous Recombination, *Molecular Cell* (2017). [DOI: 10.1016/j.molcel.2017.04.022](https://doi.org/10.1016/j.molcel.2017.04.022)

Provided by JCI

Citation: Study identifies new gene mutation associated with defective DNA repair and Fanconi anemia (2017, July 10) retrieved 4 May 2024 from <https://medicalxpress.com/news/2017-07-gene-mutation-defective-dna-fanconi.html>

<p>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.</p>
--