Media Information

TECHNISCHE UNIVERSITÄT DARMSTADT

How breaks in DNA are repaired

New insight is important for cancer research and gene therapy

Darmstadt, February 2nd, 2017. The results are significant for gene therapy procedures and for our understanding of cell transformation. A team of researchers from the biology department at TU Darmstadt has discovered that the processes for repairing DNA damage are far more complex than previously assumed. The ends of breaks in the double helix are not just joined, they are first changed in a meticulously choreographed process so that the original genetic information can be restored. The results have now been published in the research journal *Molecular Cell*.

Kommunikation und Medien
Corporate Communications

Karolinenplatz 5
64289 Darmstadt

Contact:
Jörg Feuck
Tel. 06151 16 - 20018
Fax 06151 16 - 23750
feuck@pvw.tu-darmstadt.de

www.tu-darmstadt.de/presse
presse@tu-darmstadt.de

DNA, the carrier of our genetic information, is exposed to continual damage. In the most serious damage of all, the DNA double-strand break, both strands of the double helix are broken and the helix is divided in two. If breaks like this are not efficiently repaired by the cell, important genetic information is lost. This is often accompanied by the death of the cell, or leads to permanent genetic changes and cell transformation. Over the course of evolution, ways to repair this DNA damage have developed, in which many enzymes work together to restore the genetic information with the maximum possible precision.

As it stands today, there are two main ways of repairing DNA double-strand breaks, which differ greatly in terms of their precision and complexity. The apparently simpler method, so-called non-homologous end joining, joins together the break ends as quickly as possible, without placing particular importance on accurately restoring the damaged genetic information. The second method of repair, homologous recombination, on the other hand, uses the exactly identical information present on a sister copy to repair the damaged DNA with great precision. However, such sister copies are only present in dividing cells, as the genetic information has to be duplicated before the cells divide. But most cells in the human body do not undergo division, which therefore assigns them to the apparently more inaccurate method of end joining.

Complex repair of DNA double-strand breaks

“This is where our research begins,” explains TU Professor Markus Löbrich, who, along with his working group and colleagues from the University of Sussex in England has already dedicated many years to studying the repair of DNA double-strand breaks. “We found it difficult to understand how it was that important genetic information could get lost during the non-

homologous end joining repair process." As a result, the research teams examined the enzymatic processes occurring at the breaks before they join together – with surprising results. In contrast to previous schools of thought, the break ends are not simply joining together, but are being changed by specific enzymes, so that the information that was lost as a result of the break could be identically repaired with the aid of a copy.

Also important for cancer research

These changes at the break ends – called "resection" in the lingo – are highly reminiscent of the homologous recombination process, where a sister copy acts as a matrix for precise repair. It is just that in non-dividing cells, there is no sister copy of the DNA, so at present it is still unclear where the copy of the genetic information necessary for precise repair could actually come from. However, the new findings provide clear evidence that cells that do not divide also use copies of genetic information to repair DNA double-strand breaks. This finding also allows advances to be made in gene therapy procedures, when in the case of existing hereditary diseases, genetic errors are, so to speak, repaired by means of copies that have been introduced.

Study

Ronja Biehs, Monika Steinlage, Olivia Barton, Szilvia Juhász, Julia Künzel, Julian Spies, Atsushi Shibata, Penny A. Jeggo and Markus Löbrich: „DNA double-strand break resection occurs during non-homologous end-joining in G1 but is distinct from resection during homologous recombination", in: Molecular Cell
http://dx.doi.org/10.1016/j.molcel.2016.12.016

Contact:

Department of Biology
Prof. Dr. Markus Löbrich
Tel.: +49 6151/16-24620
E-Mail: lobrich@bio.tu-darmstadt.de

MI-Nr. 08e/2017, Löbrich/feu