New understanding of DNA repair

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A mechanism by which genes are repaired has been described in detail for the first time. This new understanding may, in the long term, provide the scientific foundation upon which therapies to treat genetic diseases or cancers can be built.

DNA must be constantly repaired to ensure that genetic information is not corrupted or lost. For example, DNA can become damaged by excessive exposure to sunlight, which is why sunbathing carries a risk of skin cancer.

The results of this study by scientists from the Biochemistry Department at Bristol University, who are part of an international team, are published in the prestigious journal 'Cell'.

To understand the importance of this work, consider the genome of a cell as a railway network and DNA to be the rails along which trains (enzymes called polymerases) travel. If a train hits the damaged rails the first job will be to move the derailed train out of the way so that the repair crew can access the damaged rail and repair it. The derailed polymerase acts as a marker to tell the repair crew where the damaged DNA is located.

The body has breakdown trucks (proteins) called 'transcription-repair coupling factors' which use a tiny molecular motor to push the polymerase out of the way, rather like a bulldozer shifting a derailed train. They also act as transport which brings the molecular repair crew to the site of the incident.

Dr Nigel Savery and his colleagues have, for the first time, shown the complete molecular structure of one of these coupling factors. Dr Savery said: “It means that we can see the details of the motor, the parts of the protein that grab hold of the polymerase in order to move it, and the parts that the repair proteins hold on to as they're being brought to the place that they're needed.

“The structure shows us that the protein must change shape dramatically as it carries out the various parts of its job, and it will allow our future experiments to be more directed and more informative. It's a really exciting and important step forward.”

Like many proteins these repair-coupling factors are made up of ‘modules’ that are found in many other proteins. The type of molecular motor seen in this work, for example, is also found in many other molecular machines that use, repair or copy the genome.

These types of proteins are central to the function of a healthy cell and the highly detailed understanding of the individual modules as revealed by Savery and colleagues will allow them to better understand what has gone wrong in diseases where these enzymes do not work properly, and perhaps ultimately to devise treatments.

Source: University of Bristol