# DNA 'molecular scissors' discovered

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(PhysOrg.com) -- Scientists at the University of Dundee have discovered a protein that acts as a 'molecular scissors' to repair damaged DNA in our cells, a finding which could have major implications for cancer treatments.

Dr John Rouse and colleagues in the Medical Research Council (MRC) Protein Phosphorylation Unit, which is based in the College of Life Sciences at Dundee, discovered a protein, known as FAN1, which is present in each cell and plays a vital role in maintaining healthy DNA and thus prevents mutations which can lead to cancers.

'The DNA in our cells is like an instruction manual for the proper working of each cell,' said Dr Rouse, a Programme Leader in the Medical Research Council Protein Phosphorylation Unit in the College of Life Sciences.

'A major problem is that DNA becomes damaged regularly. If DNA damage is not fixed quickly then these instructions are changed and the result is mutations - undesirable changes in DNA - that can cause the cell to become abnormal. This is essentially what causes cancer.

'However, cells are very good at recognising when DNA has become damaged and they are good at finding DNA damage and repairing it. For example, cells can quickly detect breakages in DNA and quickly fix these breaks. Many different factors help this process but we still haven't identified all of them or exactly how this process works.

'With our findings we have unlocked a major part of the puzzle. We discovered a new protein, FAN1, which is essential for the repair of DNA breaks and other types of DNA damage.

'During repair of DNA damage, DNA 'flaps' are produced that must be trimmed for repair to be completed. These leftover pieces of DNA get in the way during DNA repair and that is why they have to be removed. FAN1 carries out this task, and in this sense it acts like a 'molecular scissors'.

'Our study shows that superfluous pieces of DNA are cut by FAN1. Cells that do not have FAN1 are unable to repair DNA breaks and their DNA becomes irreversibly damaged and cells die. This underlines the fundamental importance of FAN1.

'Now that we have identified FAN1 and the role it plays in repairing DNA we can start to develop drugs that inhibit it. This may have a significant effect in cancer, primarily in helping to greatly enhance the efficacy of drugs used in chemotherapy treatments.

'It is pure coincidence that last year we discovered a separate group of proteins called the SLX4 complex that acts as a 'molecular toolkit' for DNA repair and that are also required for trimming DNA during DNA repair! The SLX4 complex is another promising drug target.

Most of the work on FAN1 was done by Craig MacKay, a PhD student in Dr Rouse's team, with help from Anne-Cécile Déclais in the laboratory of Professor David Lilley, also based in the College of Life Sciences at Dundee.

Professor Lilley is a world-renowned expert on proteins that can cut DNA.

The research is published in the latest edition of the journal *Cell*.

Provided by University of Dundee