Medical Xpress

Study reveals how ionising radiation damages DNA and causes cancer

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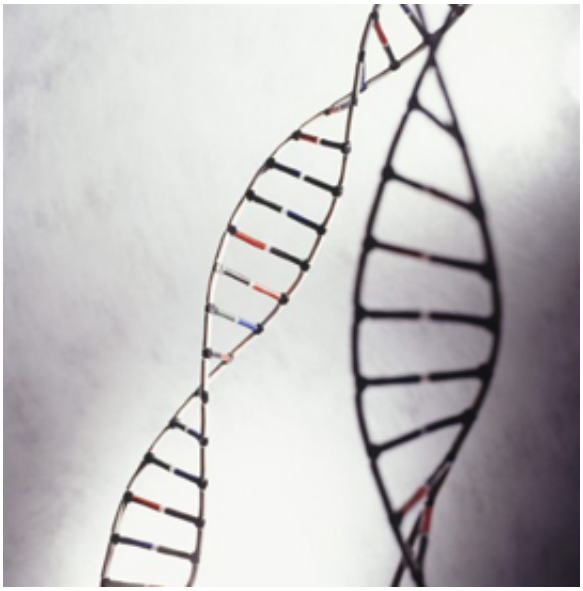

Credit: NIH

For the first time, researchers from the Wellcome Trust Sanger Institute and their collaborators have been able to identify in human cancers two characteristic patterns of DNA damage caused by ionising radiation. These fingerprint patterns may now enable doctors to identify which tumours have been caused by radiation, and investigate if they should be treated differently.

Published in *Nature Communications* today, the results will also help to explain how radiation can cause cancer.

Ionising radiation, such as gamma rays, X-rays and radioactive particles can cause cancer by damaging DNA. However, how this happens, or how many tumours are caused by radiation damage has not been known.

Previous work on cancer had revealed that DNA damage often leaves a molecular fingerprint, known as a mutational signature, on the genome of a cancer cell. The researchers looked for mutational signatures in 12 patients with secondary radiation-associated tumours, comparing these with 319 that had not been exposed to radiation.

Dr Peter Campbell from the Wellcome Trust Sanger Institute who led the study, said: "To find out how radiation could cause cancer, we studied the genomes of cancers caused by radiation in comparison to tumours that arose spontaneously. By comparing the DNA sequences we found two mutational signatures for radiation damage that were independent of cancer type. We then checked the findings with prostate cancers that had or had not been exposed to radiation, and found the same two signatures again. These mutational signatures help us explain how high-energy radiation damages DNA."

One mutational signature is a deletion where small numbers of DNA bases are cut out. The second is called a balanced inversion, where the DNA is cut in two places, the middle piece spins round, and is joined back again in the opposite orientation. Balanced inversions don't happen naturally in the body, but high-energy radiation could provide enough DNA breaks at the same time to make this possible.

Dr Sam Behjati, clinician researcher at the Sanger Institute and the Department of Paediatrics, University of Cambridge, said: "Ionising radiation probably causes all types of mutational damage, but here we can see two specific types of damage and get a sense of what is happening to the DNA. Showers of radiation chop up the genome causing lots of damage simultaneously. This seems to overwhelm the

DNA repair mechanism in the cell, leading to the DNA damage we see."

Professor Adrienne Flanagan, a collaborating cancer researcher from University College London and Royal National Orthopaedic hospital, said: "This is the first time that scientists have been able to define the damage caused to DNA by ionising radiation. These mutational signatures could be a diagnosis tool for both individual cases, and for groups of cancers, and could help us find out which cancers are caused by radiation. Once we have better understanding of this, we can study whether they should be treated the same or differently to other cancers."

More information: S. Behjati and G. Gundem et al. (2016) Mutational signatures of ionizing radiation in second malignancies. *Nature Communications*, DOI: 10.1038/ncomms12605

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