MedicalXpress

New research provides breakthrough in understanding common cancer

June 9 2011

Researchers from the University of Sheffield have discovered valuable insight into how people develop B-cell lymphoma, one of the most common cancers in the UK.

The team, from the University's Institute for Cancer Studies and funded by Leukaemia and Lymphoma Research, Biotechnology and Biological Sciences Research Council (BBSRC) and Yorkshire Cancer Research, found that a mechanism different to that previously thought to be the cause of lymphoma may be responsible for the development of the disease.

Lymphoma is a type of cancer that affects the blood, originating in the lymph glands. B-cells are the immune cells in the human body that are responsible for producing antibodies to fight infections and provide long-term immunity. B-cell lymphomas include both Hodgkin's lymphomas and most non-Hodgkin's lymphomas.

Prior to this research, the main theory to explain the origins of lymphoma was the malfunction of a mechanism (somatic hypermutation) used by B-cells to modify the genes coding for antibodies. This mechanism is required to produce highly specific antibodies, but it also accidentally alters other genes, leading to lymphoma.

However, the team from the University knew that this theory only accounted for affecting a handful of genes, and the model could only

explain certain types of lymphoma.

Led by Dr Thierry Nouspikel, the researchers discovered another mechanism, which potentially affects many more genes and can account for a wider palette of lymphomas. The research found that B-cells actually do not repair the bulk of their DNA and only take care of the few genes they are using. When the B-cells are inert in the blood flow, this is not a problem. However, when they receive a stimulation (e.g. an infection) they start to proliferate and then produce antibodies.

To proliferate they must replicate their DNA, and replication of damaged DNA results in the introduction of mutations, the accumulation of which can lead to lymphoma. Dr Nouspikel's team have designed a novel method to specifically detect such mutations, and have proved that they do occur in genes that have been implicated in lymphoma.

The researchers demonstrated that B-cells are deficient in one of the main DNA repair pathways, known as Nucleotide Excision Repair. This pathway repairs a lot of different DNA lesions, including UV-induced damage and chemical adducts (e.g. from air pollution and cigarette smoke). Their model therefore explains why strong UV exposure (e.g. unprotected sun bathing) is the number one environmental risk factor for lymphoma and also supports the evidence that exposure to air pollution and smoking are also risk factors.

Dr Nouspikel said: "Lymphoma is one of the ten most frequent cancers in adults in the UK, and the third among children. If we want to come up with efficient strategies for prevention and therapy, it is crucial to understand what causes it. The novel mechanism we have discovered potentially accounts for the development of many different types of lymphoma. It may also explain why strong exposure to sunlight is the main environmental risk factor for this cancer."

More information: The research is due for publication in *Blood* on 9 June 2011 and will also be published in Cell Cycle on 15 July 2011. To view the full research paper online, visit: bloodjournal.hematologylibrary … -2010-12-326637.long

Provided by University of Sheffield