Scientists discover how common treatment-related cancer develops

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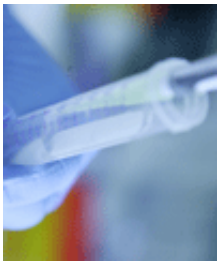

(Medical Xpress) -- Scientists in a team at Newcastle University have identified a mechanism by which treatment-related leukaemia develops, raising hopes that this side effect of toxic chemotherapy could be prevented.

Acute myeloid leukaemia (AML) is a blood cancer that can arise as a consequence of treatment for other cancers. AML is diagnosed in 2,200 adults each year and it is thought that up to 10% of these cases are treatment-related.

Leukaemia is often triggered by DNA mutations within white blood cells when part of one chromosome exchanges with part of another in a process called translocation. For these chromosome rearrangements to occur, their constituent DNA must be broken and then repaired incorrectly. These mutated cells then divide uncontrollably in the blood,

crowding out healthy blood cells.

Up to a third of treatment-related cases of AML can be attributed to chromosome rearrangements caused by the interaction between anti-cancer drugs and an enzyme called 'TOP2B'. This enzyme is critical in managing DNA movement within cells and many cancers including lymphoma, testicular, lung and prostate cancers are sensitive to drugs that block its activity.

In work funded by the charity Leukaemia & Lymphoma Research and published online in the journal *Proceedings of the National Academy of Sciences*, the Newcastle scientists showed that while drugs designed to inhibit TOP2 can be highly effective in preventing the rapid division of cancer cells, in some cases these drugs also cause key regions of important chromosomes to be held close together in a manner that increases the likelihood that the leukaemia inducing translocations occur.

Professor Caroline Austin, who led the team at the Institute for Cell and Molecular Biosciences at Newcastle University, said: "We are working to understand more about how these DNA breaks and rearrangements are made. The hope is that we will now be able to find ways of altering drug treatments to block this process, preventing secondary cancers from developing."

Professor Chris Bunce, Research Director at Leukaemia & Lymphoma Research, said: "Although thankfully relatively rare, diagnosis with a second cancer due to treatment is a devastating blow for patients. It is vital that we reform and improve standard chemotherapy drugs to not just make them more effective but also reduce side-effects. This study represents a huge breakthrough. It is the first time that scientists have looked into what is going on in the cell nucleus and explained exactly what happens when treatment-related DNA mutations occur."