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Genetic profiling tracks progression from manageable blood cancer into deadly disease

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Genetic profiling has painted the clearest picture yet of how a type of blood cancer – follicular lymphoma – develops and changes from a manageable disease into an aggressive cancer, offering new targets for treatment, according to research published in *Nature Genetics*.

Researchers from the Barts Cancer Institute at Queen Mary, University of London, and their collaborators sequenced the DNA of a patient's follicular lymphoma over the course of their cancer. The team used the

latest technology to catalogue the genetic changes in a patient's disease as it progressed and found a number of gene mutations responsible for the onset of the disease.

They also identified some of the key changes that drive the disease towards a more aggressive form. Crucially, these findings provide a number of new targets for treatment that may stop follicular lymphoma from developing resistance to therapy or becoming aggressive.

Follicular lymphoma is a common type of non-Hodgkin lymphoma – a group of blood cancers that affect the immune system. Nearly a third of all non-Hodgkin lymphomas are follicular lymphoma, with around 2,500 people diagnosed each year in the UK.

This type of blood cancer initially behaves like a chronic condition, which people live with for a number of years, with the majority of patients recovering and relapsing multiple times following treatment. Existing therapies are good at managing the disease but, in most cases, the cancer eventually develops resistance to treatment. In some patients, their cancer transforms into a more aggressive – and more deadly – form of the disease, called transformed follicular lymphoma.

The research was funded by Cancer Research UK through the Catalyst Club – a pioneering venture to raise £10 million for various research projects aimed at realising the benefits of personalised medicine for people with cancer – along with Leukaemia & Lymphoma Research and the Kay Kendall Leukaemia Fund.

Professor Jude Fitzgibbon, lead researcher, said: "Resistance to treatment is a major problem for follicular lymphoma patients, as they often respond well to treatment and later relapse. This can be both physically and emotionally draining. And it gives the cancer multiple opportunities to evolve into a more aggressive – and more difficult to

treat – form of the disease.

"We've been able to chronicle the chain of genetic events that leads to aggressive forms of the disease. If we can develop treatments to prevent some of these changes from taking place, we should be able to stop the cancer in its tracks."

Nell Barrie, senior science information manager at Cancer Research UK, said: "This study has uncovered some of the key molecular changes taking place and offers new targets for treating the disease. Research into the genetics that underpin cancer is helping us to better know the enemy and find new ways in which we might beat it.

"The most common symptoms for follicular and other non-Hodgkin lymphomas are painless swellings in the lymph nodes – typically in the neck, armpit or groin. If you notice these, or any other unusual or persistent symptoms, then it's important to get them checked out by your doctor as soon as possible.

More information: Okosun, J. E., et al. Integrated genomic analysis identifies recurrent mutations and evolution patterns driving the initiation and progression of follicular lymphoma. *Nature Genetics*, 2013. DOI: 10.1038/ng.285

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