

Scientists map the genetic evolution of childhood leukaemia

5 April 2018, by Henry Winter

The key genetic events responsible for initiating the early stages of a type of childhood leukaemia have been identified by scientists at The Institute of Cancer Research, London. Insights into the 'founder' genetic mutation for this type of leukaemia, present in all the cancer cells, could be used in the development of new targeted drugs. The research, which was funded by the blood cancer research charity Bloodwise, is published in the journal *Leukemia*.

Leukaemia develops when DNA faults – or mutations – occur in maturing blood cells, triggering further genetic mutations that cause the cells to grow out of control.

Genetic faults in childhood [leukaemia](#) cells evolve in a 'Darwinian' fashion – mutations that make certain [cancer cells](#) most resistant to treatment or multiply quickest are more likely to survive and drive the cancer forward. Cancer cells are constantly evolving genetically, explaining why cancer can sometimes return in a more aggressive form after treatment.

The Institute of Cancer Research (ICR) team used DNA analysis techniques to examine individual leukaemia cells from 19 different children and [young adults](#) with STIL-TAL1-positive T-cell [acute lymphoblastic leukaemia](#) (T-ALL), in order to determine the sequence in which these faults develop.

The researchers found that certain genetic alterations – the gene fusion STIL-TAL1, as well as inactivation of the CDKN2A gene—occurred very early in leukaemia development.

The fusion between the STIL and TAL1 genes was likely to be a 'founder event' for this type of leukaemia, present in all the cancer cells, meaning that targeting signalling pathways that are affected by this gene fusion could offer an effective way to treat the disease.

The PTEN gene, which is known to play an active role in suppressing cancer, was also deactivated in many individual leukaemia cells. Half of the patients examined had errors affecting the PTEN gene in their cancer cells. This suggests that, while they occur later than the STIL-TAL1 [gene fusion](#), PTEN gene alterations are key to maintaining leukaemia growth and survival.

Dr. Caroline Furness, who undertook the research in the laboratory of Prof Mel Greaves at The Institute of Cancer Research, London, said: "We need to understand how cancers evolve and unpick which mutations are key to triggering [cancer](#) development, and which are important for driving its growth and spread.

"Our study uncovered these crucial mutations in a type of leukaemia that accounts for around a quarter of cases of T-cell leukaemia in children and young adults. This will help us to develop more effective treatments, especially in those children who relapse, and kinder treatments that won't cause life-long side effects."

Dr. Alasdair Rankin, Director of Research at Bloodwise, said: "Survival rates for [childhood leukaemia](#) have improved significantly and eight in 10 children will now survive in the long-term. Treatments are still highly toxic and can have devastating side effects and there is a need to improve survival further.

"Every child's leukaemia is complex and genetically different, which can cause obstacles to the development of targeted treatments. Although this is early work, this study has identified common faults that play a role in driving the disease in the majority of children with this subtype of leukaemia, paving the way for future treatments."

T-ALL makes up around one in five cases of leukaemia in children and young adults.

More information: The subclonal complexity of
STIL-TAL1+ T-cell acute lymphoblastic leukaemia
Leukemia (2018) [DOI: 10.1038/s41375-018-0046-8](https://doi.org/10.1038/s41375-018-0046-8)

Provided by Bloodwise

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