

Unravelling the causes of an aggressive childhood cancer

January 13 2016, by Henry Winter

The origins of a type of aggressive childhood lymphoma have been found, giving hope that new drugs could be designed to prevent the disease coming back after treatment.

Researchers at the University of Cambridge studied the progression of anaplastic large cell lymphoma (ALCL) in mice for the first time. ALCL is an aggressive blood cancer that typically appears as tumours in the [lymph nodes](#), skin, lungs, liver and soft tissue and mostly affects children and [young adults](#).

Current treatment for ALCL consists of [intensive chemotherapy](#), which can have devastating long term side-effects including [heart disease](#), infertility and secondary cancers. Up to 40% of children with ALCL relapse, requiring extra chemotherapy.

The origins of ALCL were traced to a gene fault in developing blood-producing stem cells found in the thymus. The scientists believe that while current drugs can kill cancer cells that spread into the rest of the body, they may not always be effective at killing these original 'cancer stem cells'. This allows them to sow the seeds for future relapse after apparently successful treatment has finished.

The research, which was funded by the blood cancer charity Bloodwise, is published online in the journal *Nature Communications*.

The researchers also found that the spread of lymphoma around the body

requires the corruption of a vital element of the immune system specifically, the T-cell receptor (TCR). TCRs are molecules on the surface of T-cells - a type of white blood cell that looks out for viruses and harmful cells in the body. In mice where the ALCL had spread, the TCR molecule was needed initially, but was subsequently lost from the surface of the cancer cells, meaning that the molecule was having a suppressive effect on lymphoma development.

Dr Suzanne Turner, a Bloodwise Senior Lecturer at the Department of Pathology at the University of Cambridge, said: "We now have a fuller understanding of the origins of this type of lymphoma and the pivotal role that corruption of the immune system plays in its spread to different sites around the body. By targeting the cancer genes key to the lymphoma's development, we can design treatments that give a better chance of a long-term cure."

Dr Matt Kaiser, Head of Research at Bloodwise, said: "The chemotherapy currently in use is particularly gruelling for children and teenagers, particularly if relapse occurs and more treatment is needed. Greater understanding of this [lymphoma](#) will enable the development of more effective and less toxic drugs that allow every child to live a normal life after treatment."

More information: Tim I. M. Malcolm et al. Anaplastic large cell lymphoma arises in thymocytes and requires transient TCR expression for thymic egress, *Nature Communications* (2016). [DOI: 10.1038/ncomms10087](#)

Provided by University of Cambridge

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