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Study could boost effectiveness of chemotherapy in the treatment of lymphoma

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A study by scientists at the University of Glasgow, which reveals the critical role a common cancer-associated gene plays in lymphoma development, could lead to improved treatments for a range of cancers.

The RUNX1 gene helps maintain healthy blood cell formation by regulating the level of activity of other genes. It is frequently overactive, or 'over expressed', in many types of cancer - a key factor in the uncontrolled growth of tumour cells. Researchers funded by Bloodwise and Cancer Research UK have found that some cancers that were not previously linked to changes affecting RUNX1 still heavily rely on the gene to survive - even when it is functioning normally.

The study, published in the journal *Oncotarget*, showed that 'switching off' the RUNX1 gene made lymphoma cells more susceptible to chemotherapy. The team, led by Professors James Neil and Ewan Cameron, studied mice with a type of Burkitt lymphoma primarily associated with faults in the 'MYC' gene, in order to establish what role RUNX1 plays in cancer growth. The MYC gene governs healthy cell division and cell death and is over expressed in Burkitt lymphoma, a cancer of the immune system that affects around 200 people every year in the UK, including 60 children.

When the RUNX1 gene was deleted in lymphoma cell lines using modern molecular techniques, growth was significantly reduced and the cells were far more sensitive to chemotherapy than lymphoma cells with an intact RUNX1 gene. Furthermore, the lymphoma cells were far more

resistant to the deletion of RUNX1 than normal white blood cells were, suggesting that the lymphoma depends on this gene for its growth and survival.

The University of Glasgow researchers are now collaborating with scientists in the US who have developed a drug that specifically blocks the RUNX1 gene, which is showing promise in the laboratory at selectively killing cancer cells.

James Neil, Professor of Molecular and Cellular Oncology at the Institute of Infection, Immunity and Inflammation, said: "Many genes are altered or damaged when a healthy cell progresses towards cancer, leading to uncontrolled growth and the ability to survive when normal cells would die. Understanding how these faulty cancer genes collaborate with each other to alter the cell's behaviour helps us find the cancer's 'Achilles' heel'. We found that blocking the RUNX1 gene has a knock-on effect on the ability of many other cancer genes to drive this type of lymphoma forward."

RUNX1 and MYC gene faults also play a role in cervical, breast, stomach, lung and colon cancers, leading to the possibility that a wide range of cancers could potentially benefit from the findings.

Dr Alasdair Rankin, Director of Research at Bloodwise, said: "While this concept for treating lymphoma is still in the early stages, it is certainly very promising. The next step will be for further lab studies to understand the effects of blocking RUNX1 and then to see how effective and safe a drug is at treating patients in clinical trials. Precision treatments that target specific characteristics of cancer cells have the potential to be far more effective than traditional chemotherapy alone, reducing life-threatening side effects and the chance of relapse."

Dr James O'Malley, Cancer Research UK's research information

manager, said: "Studies like this, helping us understand exactly how the RUNX1 'molecular switch' works, form the foundations of future research to develop better, more effective treatments for people with cancer. RUNX1 turns on and off certain genes inside cells, and other research has already shown that this switch is faulty in a number of different types of cancer."

More information: Addiction to Runx1 is partially attenuated by loss of p53 in the Eμ-Myc lymphoma model. DOI: 10.18632/oncotarget.8554

Provided by University of Glasgow