# Scientists find genetic key to why some cancer patients don't respond to treatment

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(Medical Xpress) -- Researchers from Newcastle University have identified a gene variation carried by 20% of the population which can significantly affect how patients with a rare type of blood cancer will respond to treatment.

The researchers believe that possessing an abnormal version of the CD95 gene, one of the genes involved in controlling cell death in the body, may also dictate survival rates for other types of cancer, including lymphoma, breast cancer and prostate cancer.

The scientists, who were funded by the charity Leukaemia & Lymphoma Research, studied data from 231 people diagnosed with acute promyelocytic leukaemia (APL). APL is diagnosed in around 200 people in the UK each year, with young adults disproportionately affected by the disease. Unlike most other types of leukaemia, survival rates are high and the majority of APL patients can go on to be completely cured.

However the new research, which is published in the leukaemia journal *Blood* today (5th Jan), showed that those patients with an abnormal variant of the CD95 gene have a significantly lower chance of survival. Only 64% of APL patients in the study with the variant survived long-term, compared to 79% of patients with a normal version of the gene.

Those patients with a risk version of the gene often did not respond to treatment from the start, dying from infection within weeks of diagnosis. Infections often develop in leukaemia patients who do not respond to

chemotherapy, and predicting which patients are at high risk of developing this life-threatening complication is difficult. However, the Newcastle researchers found that APL patients with the risk gene were five times more likely to die from infection compared to patients with the more common version of the gene.

Dr. James Allan, of the Newcastle University team, said: “While further research is needed, these findings are very important. By testing for the risk variant of the CD95 gene, we should now be able to help doctors identify those vulnerable patients at high risk of either not responding to chemotherapy or developing potentially fatal side effects from their treatment. These patients can then be treated differently to minimise the risk of a poor response."

Treatment for APL has been revolutionised in recent years by the use of a combination of chemotherapy and a vitamin A-based drug known as ATRA. Importantly the Newcastle researchers found that patients with the risk version of the CD95 gene had a better chance of survival if they were given an increased dose of ATRA alongside their chemotherapy.

The protein produced by the CD95 gene plays several key roles in the life cycle of cells, explaining why mistakes within these 'genetic instructions' have such a serious effect on the ability of patients to fight the leukaemia. The CD95 gene dictates the sending out of 'death signals' to malignant cells, so when these signals are reduced, leukaemia cells do not die and continue to multiply in the blood. Crucially, ATRA is designed to restore this 'death signalling' process, making it the ideal drug for patients with the abnormal version of the CD95 gene. Findings from the new study will help doctors to develop new and better ways to use ATRA for the treatment of APL.

Dr. David Grant, Scientific Director at Leukaemia & Lymphoma Research, said: “Acute promyelocytic leukaemia is a very aggressive

blood cancer but treatment has improved dramatically in recent years. This exciting research is another step towards 'individualised' treatment, based on the specific genetic characteristics of each patient, which will push up survival rates even further."

Provided by Newcastle University