New research points to which leukaemia patients will need intensive treatment

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Researchers have identified a genetic fault in some leukaemia patients that could be responsible for halving survival times after diagnosis compared to patients without the fault – an average reduction from 16 years to seven years. The findings, from a study of over 800 patients with chronic lymphocytic leukaemia (CLL), could help doctors tailor treatment for this group.

Researchers at the University of Southampton, who were funded by blood cancer charity Bloodwise, announce the results at the Annual Meeting of the American Society of Hematology on Sunday 6 December.

CLL is the most common form of leukaemia in the western world and is diagnosed in around 4,000 people each year in the UK. The average age at diagnosis is 71 and it only progresses to the point of requiring treatment in around half of patients. If no symptoms are displayed, treatment will not start and doctors take an approach called 'watch and wait'. In some cases the cancer is very aggressive and requires intensive treatment, but it is currently difficult for doctors to accurately identify these patients in advance.

The scientists used sophisticated DNA screening techniques to analyse cancer cell samples from patients going through treatment and on 'watch and wait'. Around 7% of patients undergoing treatment were found to carry damage to the SETD2 gene, which plays a role in coordinating the repair of DNA in cells. These faults were found to have a serious impact

on patients' lifespans, with deletions to the gene particularly high in patients categorised as 'ultra high risk'.

Errors in SETD2 occurred in patients' lifetimes and were not inherited. The researchers believe these errors lead to faulty DNA repair signals, which could then be a significant trigger for further genetic damage that drives the progression of CLL. Patients with DNA deletions in the SETD2 genes tended to also have severe disruption to the TP53 gene, which is responsible for regulating healthy cell division and preventing uncontrolled cell growth. Large-scale rearrangement of chromosomes – the tiny packets of DNA in our cells – were also common forms of genetic damage in cancer cells in these patients.

While CLL patients in the study with normal SETD2 gene function survived an average of 16 years and seven months, those patients with DNA deletions to the SETD2 gene survived for an average of just seven years and one month after diagnosis. Before needing any treatment patients with normal SETD2 lived for eight years and nine months after diagnosis, compared with those with reduced SETD2 function who typically needed to start treatment much earlier – after three years and eight months on average.

Professor Jon Strefford, from the University of Southampton, said: "There are many DNA defects in leukaemia cells. The important part is identifying which ones are key to driving the cancer forward and responsible for the patient's prognosis. This study shows that malfunctioning of the SETD2 gene could be an important early stage in the progression of CLL into an aggressive disease. By recognising the DNA red flags in individual patients' leukaemia cells earlier, we can tailor treatment for these patients."

Dr Matt Kaiser, Head of Research at Bloodwise, said: "Survival times for this type of leukaemia are highly variable. Many patients will never

need treatment and will die with their leukaemia rather than from it, whilst others will have more aggressive disease and need treatment. Currently it is difficult to provide meaningful information on how individual patients will develop and respond to treatment, which can lead to significant uncertainty for patients. It's early days, but this research could help find ways of reassuring those patients who may never need treatment, and guide doctors more actively monitor those patients at higher risk."

More information: The findings will be presented to the American Society of Hematology's Annual Meeting on Sunday 6 December 2015, 5:30 PM (US Time) under the title 'Genomic disruption of the histone methyltransferase SETD2 in chronic lymphocytic leukemia'.
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