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Stem cell treatment to prevent leukemia returning is a step closer, say scientists

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Researchers at King's College London have identified a way of eliminating leukaemic stem cells, which could lead to new treatments that may enable complete remission for leukaemia patients. An early study in mice has shown that leukaemic stem cells can be abolished by suppressing two proteins found in the body.

Leukaemic stem cells sustain the disease and are likely to be responsible for relapse, so elimination of these cells is believed to be key for achieving complete remission. These encouraging findings highlight the two proteins as potential therapeutic targets to prevent the most aggressive forms of leukaemia returning. The study, funded by Cancer Research UK and Leukaemia Lymphoma Research, is to be published in the journal *Cell Stem Cell*.

King's scientists looked at leukaemic stem cells found in a type of leukaemia that involves mutations of the MLL gene. This accounts for around 70 per cent of infant leukaemias and 10 per cent of adult acute leukaemias. The prognosis for MLL in children is not good – only 50 per cent survive past two years after receiving standard treatment.

The protein Bmi1 was already known to play a key role in the survival and proliferation of various cancer stem cells. But this study has for the first time shown that, although the protein is needed for survival of various Acute Myeloid Leukaemia (AML) cells, in MLL leukaemia the cancer stem cells actually survive independently of Bmi1. This shows that for these MLL patients, targeting Bmi1 alone would not have a

major impact on eradicating leukaemic stem cells, as was previously thought.

However, the team also found high levels of another protein called Hoxa9 in the MLL mice and human patients. Similar to Bmi1, a major role of this protein is to ensure leukaemia cells divide and grow by allowing their escape from the inherent surveillance system, which will otherwise cause cell death. They found that in mice with MLL leukaemic stem cells (that can proliferate without Bmi1), suppression of both Bmi1 and Hoxa9 completely abolishes the ability of MLL mutation to induce leukaemia.

These findings provide evidence for the different pathways involved in the development of different types of leukaemic stem cells, and highlight the importance of targeting Bmi1 and Hoxa9 together to abolish MLL leukaemic stem cells in particular.

Professor Eric So, Head of the Leukaemia and Stem Cell Biology group at King's, said: 'These findings take us a step forward in our understanding of how this devastating disease can return in patients after they have received the standard treatment.

'Now we know that leukaemic stem cells in certain types of leukaemia, such as MLL, can survive and proliferate independently of the Bmi1 protein, we need to consider more carefully the future of stem cell therapy to treat the disease. It's not as easy as people originally thought it might be.

'But these findings provide us with vital information that will help us look at alternative ways of combating different forms of the disease, which will ultimately allow patients to achieve long-term complete remission.

'What we need to do now is to find out exactly how Bmi1 and Hoxa9 proteins sustains the growth of cancer cells in order to develop an effective treatment to stop the disease returning.'

Professor Peter Johnson, Cancer Research UK's chief clinician, said: 'This study builds on previous Cancer Research UK-funded work trying to pinpoint the molecules responsible for driving the development of MLL-related leukaemia stem cells.

'Cancer stem cells appear to be more resistant to radiotherapy and chemotherapy than the other leukaemia cells, so understanding how they originate – and how we can kill them – will be a major step in being able to help even more people survive leukaemia in future.'

Provided by King's College London