New insight into why leukaemia drug is successful

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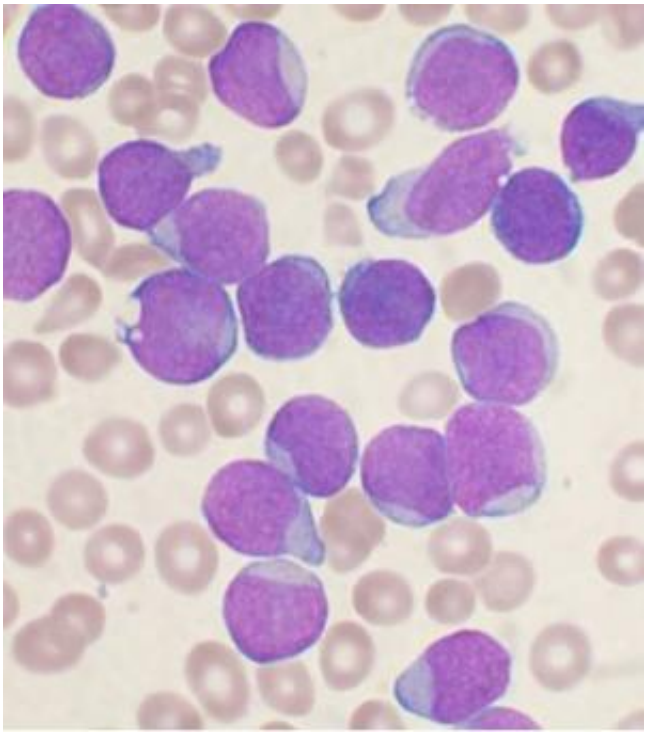

A Wright's stained bone marrow aspirate smear of patient with precursor B-cell acute lymphoblastic leukemia. Credit: VashiDonsk/Wikipedia

Researchers at the University of Southampton have shed new light on why and how a new class of drug is effective at fighting off leukaemia.

Chronic lymphocytic leukaemia (CLL) is the most common form of leukaemia, with over 4,000 cases in the UK every year. At the moment

CLL is incurable, but in recent years, new drugs called B-cell receptor (BCR) inhibitors, have revolutionised treatment.

However, it is not entirely clear how they work and why they are so effective. In addition, some patients can become resistant to these types of drugs..

A new study, led by Professor Mark Cragg at the University of Southampton and funded by The Kay Kendall Leukaemia Fund and Bloodwise, has characterised the molecular mechanisms responsible for how one of these drugs (idelalisib) work.

Published in the journal *Leukemia*, the study treated blood cells from CLL patients in the laboratory with idelalisib and found it disrupts important survival signals from within the tumour and prevents communication from surrounding cells that help the tumour survive; causing the tumour cells to die..

The response to idelalisib was linked to an increased production of a protein called Bim, which is responsible for the tumour cell death. Their results also showed idelalisib-like drugs can be successfully combined with antibody treatments to more effectively eradicate the cancer and give longer lasting protection and that this combination effect is also dependent on Bim.

Professor Cragg said: "These results are very interesting and positive. We now know how the drug is able to attack and slow the growth of the tumours, but not get rid of it completely. We also know that Bim is required for the death and for the combination effects with antibody treatments. With this knowledge we can design better, more effective combination treatments. In the future, we could even be looking at combinations that will give us a cure for some blood cancers where we don't currently have that possibility."

Dr Alasdair Rankin, Director of Research at Bloodwise, said: "Idelalisib and other BCR inhibitors have transformed the outlook for patients with CLL, but we are still not entirely clear how they work and why they are so effective. We now have a rising number of treatments available to people with CLL. A deeper understanding of how these drugs work is needed to guide treatment decisions and identify combinations that deliver the best benefits for patients."

More information: M J Carter et al. PI3Kδ inhibition elicits anti-leukemic effects through Bim-dependent apoptosis, *Leukemia* (2016). DOI: 10.1038/leu.2016.333

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