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New insight into why leukaemia drug is successful

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, a process called immunochemotherapy. This combination effect is also dependent on Bimk, the researchers found.

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.”

It is this detailed research to better understand new drugs and combinations with immunotherapy that will be taking place in the University of Southampton’s new Centre for Cancer Immunology, which is due to open in 2017.

The centre, which is being built on the Southampton General Hospital, will be the first of its kind in the UK to focus on immunotherapy, a revolutionary new treatment that supercharges the body’s natural defences to find and destroy cancer. The Centre will bring together world-leading specialists and aim is to accelerate research progress and conduct more clinical trials.

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.”

ENDS

Notes to editors

1. Paper details: *PI3Kδ inhibition elicits anti-leukemic effects through Bim-dependent apoptosis*
   doi: 10.1038/leu.2016.333

2. The University of Southampton is a leading UK teaching and research institution with a global reputation for leading-edge research and scholarship across a wide range of subjects in engineering, science, social sciences, health and humanities.

   With over 24,000 students, over 6000 staff, and an annual turnover in excess of £500 million, the University of Southampton is acknowledged as one of the country's top institutions for engineering, computer science and medicine. We combine academic excellence with an innovative and entrepreneurial approach to research, supporting a culture that engages and challenges students and staff in their pursuit of learning.

   The University is also home to a number of world-leading research centres including the Institute of Sound and Vibration Research, the Optoelectronics Research Centre, the Institute for Life Sciences, the Web Science Trust and Doctoral training Centre, the Centre for the Developmental Origins of Health and Disease, the Southampton Statistical Sciences Research Institute and is a partner of the National Oceanography Centre at the Southampton waterfront campus. www.southampton.ac.uk

3. The Kay Kendall Leukaemia Fund was established in 1984 under the Will of the late James Sainsbury CBE. It awards grants for research on aspects of leukaemia and for relevant studies on related haematological malignancies. Grants are awarded for first class research on innovative proposals, particularly those close to the care of leukaemia patients or the prevention of leukaemia or related diseases. Project grants are awarded twice yearly, and Intermediate, and Junior Fellowships of 3 – 4 years are awarded annually. The Fund also considers support for capital projects that will have direct benefit to leukaemia patient care. For more information please contact the Kay Kendall Leukaemia Fund: Tel: 020 7410 0330, email: info@kklf.org.uk website www.kklf.org.uk

4. Bloodwise is the UK's biggest blood cancer charity dedicated to improving the lives of patients. The charity, which was formed in 1960, changed its name from Leukaemia & Lymphoma Research in September 2015. The charity's research is targeted at understanding more about blood cancer, finding causes, improving diagnosis and treatments, and running groundbreaking clinical trials for patients. The charity champions patients' needs by influencing relevant decision makers and influencers, and seeking to raise awareness of the issues faced by patients. Their patient services provide information, support and assistance to patients at every stage of their journey. Around 38,000 people of all ages, from children to adults, are diagnosed with blood cancers and related disorders every year in the UK. It is a complex disease area made up of 137 individual diseases. Some affect thousands of people, such as common forms of leukaemia, lymphoma and myeloma. Others affect only a handful. But together, blood cancers are the fifth most common form of cancer. For more information visit www.bloodwise.org.uk.

5. Building on its cancer immunology research expertise and recent successes in immunotherapy trials, the University of Southampton has launched a major fundraising campaign to raise £25m to open the UK's first dedicated Centre for Cancer Immunology at Southampton General Hospital in 2017. The Centre will be the first of its kind in the UK and will bring together world-leading specialists in a unique state-of-the art centre. The aim of the new Centre is to accelerate research progress, conduct more clinical trials and save more lives from cancer. Find out more about it at www.southampton.ac.uk/youreit

For more information

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