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Unique approach to treatment of rare and aggressive blood cancers

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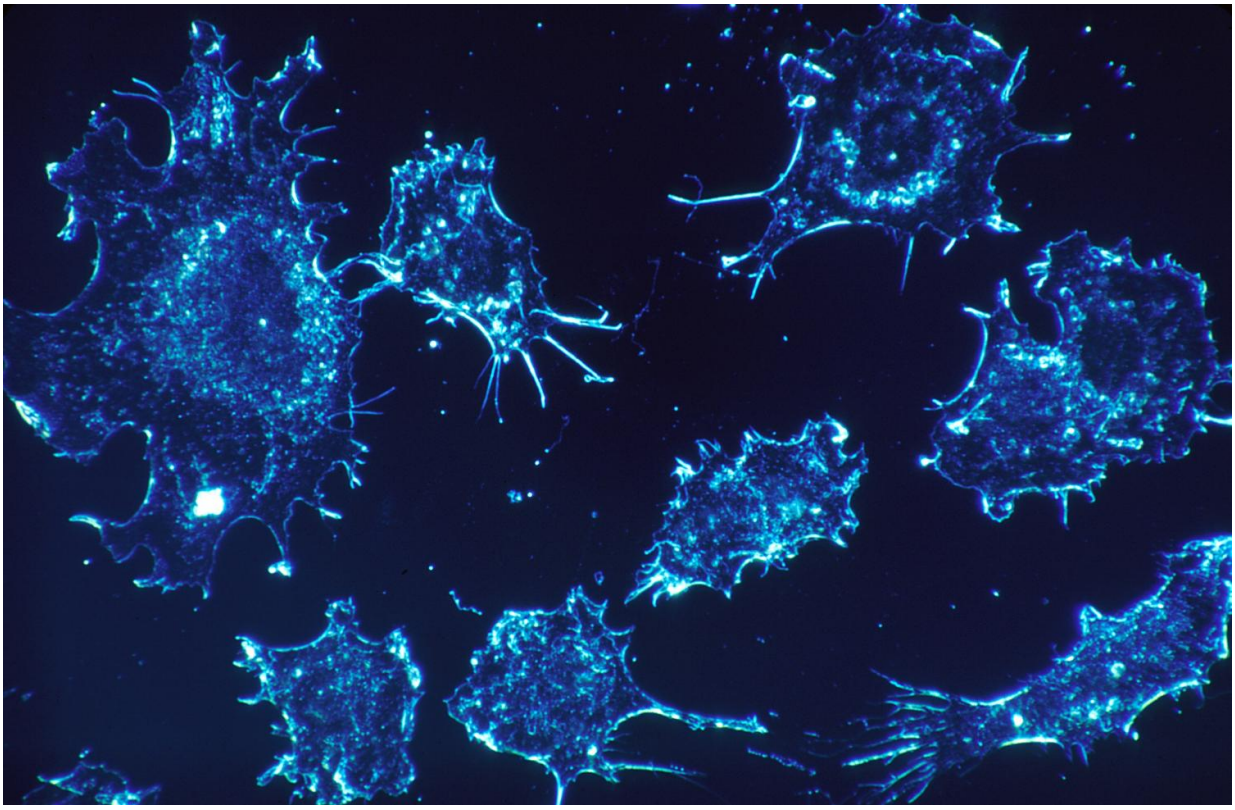

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A unique approach to targeting the abnormal T-cells that cause T-cell lymphomas could offer hope to patients with the aggressive and difficult-to-treat family of cancers, finds a study involving researchers from Cardiff University.

The team of researchers, working with biopharmaceutical company Autolus Ltd, have discovered a method of targeting the cancer without destroying healthy T-cells, essential to the immune system.

Lymphomas arise when immune cells, called lymphocytes, that protect us against germs, become cancerous. There are two types of lymphocytes: B-cells and T-cells. Recent developments, including immunotherapies, have transformed the once fatal diagnosis of B-cell lymphoma into a curable condition but there remains a critical need for new therapeutic approaches to the rarer, but often more aggressive, T-cell lymphoma.

A key challenge of treating these cancers has been to identify a way of eliminating the abnormal T-cells whilst sparing the healthy ones that play an essential role in providing protection against infections.

T-cells recognize and remove germs using a molecule on their surface called the T-cell receptor. This receptor is made using one of two duplicated copies of the T-cell receptor gene, called C1 or C2, at random. As a result, the T-cells we use to fight off viruses and other germs are a near equal mixture of cells using either the C1 or C2 genes. When a T-cell becomes cancerous all the cancer arises from a single cell so that the cancer is either all C1 or C2.

The research team have engineered a way to eliminate T-cells based on whether they use the C1 or C2 gene. The team demonstrate that targeting of C1 T-cells can kill C1 cancers while leaving all normal C2 T-cells unharmed so that they can take care of infections.

Professor Andrew Sewell from Cardiff University's School of Medicine said: "We wouldn't last a week without the essential job our T-cells perform by protecting us from infection. The devastating effects of low numbers of just one type of T-cell are all too evident in HIV/AIDS.

"T-cell lymphomas are particularly difficult to treat without damaging essential, healthy T-cells that are vital to the immune system. The new and innovative approach that Autolus have developed now allows potential for removal of all cancer cells without causing any damage to half of our T-cells. Since T-cells select use of the C1 or C2 gene at random, this remaining half of T-cells are capable of providing immunity to the pathogens we encounter every day."

Dr Justine Alford from Cancer Research UK, said: "This study has demonstrated it's possible to kill cancerous T-cells but importantly spare some healthy ones, opening up exciting new treatment possibilities. T cells are a vital part of our immune system and our survival; that's why when a patient has a cancer in these cells, it would cause serious harm to use a therapy that targets both healthy T cells and cancerous ones.

"This research is still in the experimental phase though, so researchers will need to do further studies to prove the method is safe and effective before starting clinical trials in people."

The full manuscript, "Targeting T-cell receptor β-constant for immunotherapy of T-cell malignancies," can be found in *Nature Medicine*.

More information: Paul M Maciocia et al. Targeting the T cell receptor β-chain constant region for immunotherapy of T cell malignancies, *Nature Medicine* (2017). DOI: 10.1038/nm.4444

Provided by Cardiff University

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