Drug mechanism opens door for new anti-cancer immunotherapies

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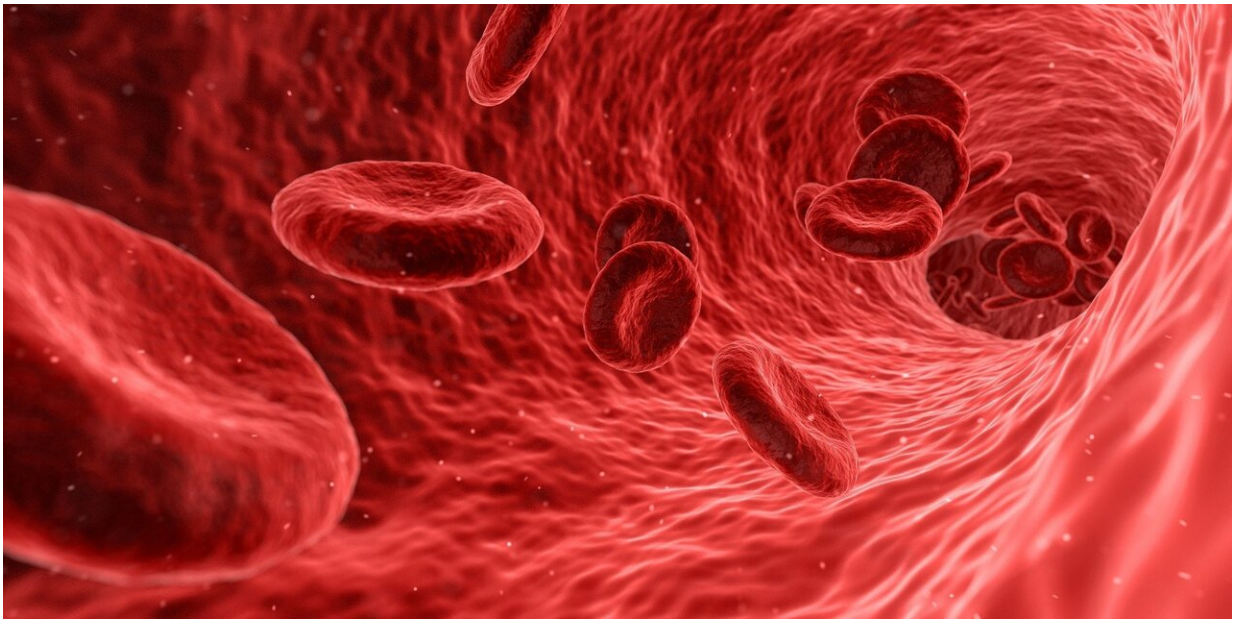

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Researchers have revealed a new mechanism of targeted drug treatment used against chronic lymphocytic leukemia, through the promotion of immune cell function, that could be exploited using new anti-cancer immunotherapies.

New research has revealed how a class of new medicines used to treat the blood cancer chronic lymphocytic leukemia (CLL) promotes

immune cell function to target cancer cells.

The study, led by Dr. Alan Ramsay, analyzed samples from patients with CLL from a seminal phase 3 clinical trial with the Mayo Clinic, U.S.. It compared the impact of recently developed Bruton's tyrosine kinase inhibitors (BTKi) against traditional chemotherapy-based therapy.

BTKis are a targeted therapy that have already begun to usher in a paradigm shift in how we treat Chronic lymphocytic leukemia (CLL)—a type of blood cancer (non-Hodgkin lymphoma) that affects white blood cells—by targeting chemical signaling within tumor cells to prevent their survival and growth.

However, researchers do not yet understand how BTKi therapies affect T cells—the immune cells that support targeted, direct attack against cancerous or pathogenic cells. Understanding this process could be important for exploiting new immunotherapies against cancer.

The results, published in *Blood Journal*, were able to identify a significant correlation between an increase in T-cells and favorable progression-free survival rates in patients who received BTKi-based therapy.

"This correlative science study provides valuable insight into how tumor-targeted therapy modulates immune T cell function in patients and has the potential to impact future combination immunotherapy research in the field," says Ramsay.

When further tests were conducted, the authors identified an enhanced anti-cancer killing function in T cells from samples undergoing BTKi-based therapy. Specifically, the type of T cell changed from samples dominated by T-helper to samples with a greater concentration of cytotoxic T cells in a "killing state."

Together, these insights help demonstrate the mechanisms behind BTKi-based therapies and how they can be used to increase the proportion of cytotoxic T cells, rejuvenating the body's immune response in its fight against cancerous cells.

Further experiments found that BTKi therapy also promoted the effectiveness of a novel type of immunotherapy—a "T cell bispecific antibody" called glofitamab. This suggests that BTKis can be exploited in new combination immunotherapy treatment approaches, which should be investigated further.

"This study underscores the importance of trial-associated science to understand how targeted therapy modulates immune and T cell function in patients, supporting the development of future immunotherapy-based therapeutic options for such cancers," says Ramsay.

More information: Despoina Papazoglou et al, Ibrutinib-based therapy reinvigorates CD8 T cells compared to chemoimmunotherapy: immune-monitoring from the E1912 trial, *Blood Journal* (2023). DOI: 10.1182/blood.2023020554

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