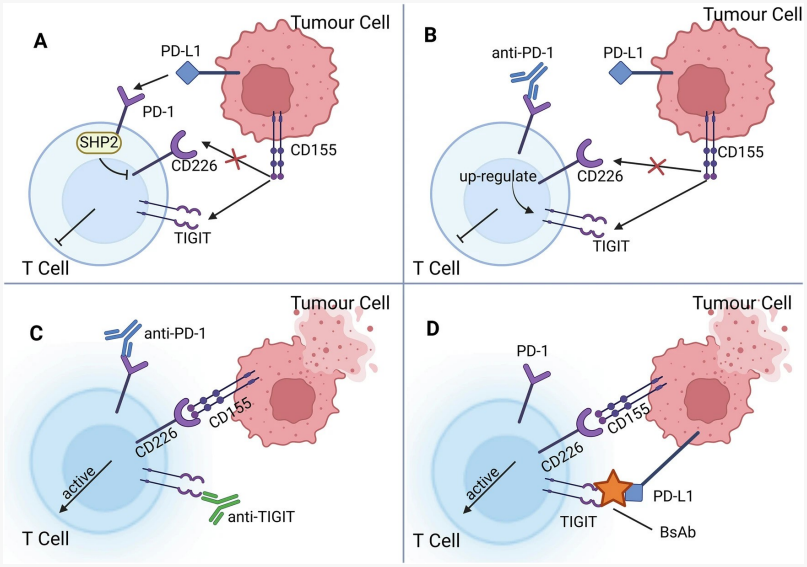
Medical breakthrough could help immune system target cancer cells

Scientists present a new approach that could empower the immune system to combat cancer cells and pave the way for new treatments for this deadly disease.



Synergistic effects of TIGIT and PD-1 immune checkpoints and co-inhibition therapy. Credit: Cell Death & Disease (2025). DOI: https://doi.org/10.1038/s41419-025-07984-4

SHARJAH, EMIRATE OF SHARJAH, UNITED ARAB EMIRATES, December 23, 2025 /EINPresswire.com/ -- Researchers at the University of Sharjah are exploring a promising approach that could enhance the immune system's ability to fight cancer, potentially paving the way for new treatments.

In a recent article published in the journal Cell Death & Disease, the team reviewed existing work on a protein called TIGIT, which prevents the immune system from effectively targeting and attacking cancer cells. (Original Source URL: https://doi.org/10.1038/s41419-025-07984-4)

TIGIT, an immune checkpoint protein, acts as a "double brake" on the immune system, stopping it from engaging cancerous cells. It suppresses immune cells directly and competes with an activating signal known as CD226.

Following intensive research and in vitro tests, scientists succeeded in releasing the brake with a single drug in laboratory trials, but clinical trials have been less successful.

The laboratory experiments the scientists successfully carried out "did not work well for most patients in real-world clinical trials," according to Mawieh Hamad, Professor of Molecular Immunology at the University of Sharjah's College of Health Sciences.

The authors write, "Recently, unsatisfactory results from several phase III clinical trials have

hampered the clinical translation of TIGIT as a target, with giants such as Roche and BeiGene announcing their withdrawal from their development programs for TIGIT mAbs."

The article addresses the mechanisms underlying TIGIT-mediated immune suppression, noting that "although treatment with ICIs has yielded some promising results in preclinical and clinical testing, a significant percentage (>50%) of the patients still respond poorly to ICIs or do not respond at all."

In their review, the researchers present strategies to enhance the engagement of the immune system with cancer cells.

"We highlighted the fact that although TIGIT doesn't work alone, when combined with another well-known brake called PD-1, it proved to be a game-changer. This one-two punch was found to be more effective in restoring the immune system's ability to recognize and destroy cancer cells," explained Prof. Hamad.

PD-1, or Programmed Death-1, is a crucial immune checkpoint protein, and together with TIGIT, they both can work to suppress immunity. "Blocking both is much more effective than blocking either one alone," noted Prof. Hamad.

The researchers claim that with the new approach, the field of immune checkpoint inhibitor-based immunotherapy has moved beyond traditional antibodies.

"The focus now is on developing innovative next-generation strategies, including bispecific antibodies that target both TIGIT and PD-1 at once, small molecule drugs that could be more effective, and engineered cell therapies (CAR-T cells) designed to be resistant to TIGIT's braking effect," continued Prof. Hamad.

Currently, researchers are developing innovative approaches, such as bispecific antibodies, small-molecule drugs, and genetically engineered CAR-T cells, to target TIGIT more effectively and with fewer side effects.

"Immune checkpoint (IC) receptors negatively regulate immune responses and play crucial roles in maintaining self-tolerance and preventing autoimmunity," said Prof. Eyad Elkord from the Biomedical Research Center, School of Science, Engineering and Environment, University of Salford, Manchester.

"However, tumor cells can exploit these pathways to evade immune recognition and destruction. TIGIT has emerged as a key immune checkpoint receptor, which exerts immunosuppressive effects through direct and indirect mechanisms."

Prof. Elkord, the research's corresponding author, said while preclinical studies with TIGIT-blocking monoclonal antibodies demonstrated encouraging antitumor activity, clinical trials of

anti-TIGIT monotherapy showed disappointing outcomes, shifting attention toward alternative strategies.

“Our research focuses on the discovery and validation of peptide-based inhibitors against TIGIT, which have the potential to improve tissue penetration, reduce immunogenicity, and exert an improved safety profile.”

Although published only three months ago, the review has already attracted significant attention. The authors hope it will generate interest from big pharma and the oncology research community alike.

Moreover, it includes an exhaustive list of the clinical trials (Phase I-III) by major pharmaceutical companies involving anti-TIGIT drugs, demonstrating substantial investment and engagement from industry actors.

The authors emphasize the practical implications of their study for cancer treatment, saying that developing TIGIT/PD-1 combination therapies is expected to improve outcomes for cancer patients, especially those resistant to current immunotherapies.

In the meantime, they hope that the pharmaceutical industry will utilize the new findings to create new types of drugs like bispecific antibodies and small-molecule inhibitors that could be more effective and easier to administer than traditional antibodies.

“Engineering CAR-T cells (a type of cell therapy) to be resistant to TIGIT braking, making them more potent against solid tumors,” said Prof. Hamad.
However, he emphasized that major challenges lie ahead, particularly “identifying which patients will benefit, as current trials lack reliable biomarkers to predict success.”

He mentioned that several knowledge gaps remain to be addressed, such as finding reliable biomarkers to select patients most likely to respond to anti-TIGIT therapy. “Scientists need to further develop and clinically test bispecific antibodies, small molecule inhibitors, and peptide-based drugs, and engineer antibodies with specific Fc regions, or Fragment crystallizable regions, to selectively deplete regulatory T cells in the tumor without harming effector immune cells.”

Other challenges, Prof. Hamad said, were related to combining TIGIT blockade with other therapies like cancer vaccines or drugs targeting other immune checkpoints like LAG-3 to treat "cold" tumors.

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