Better tools, better cancer immunotherapy

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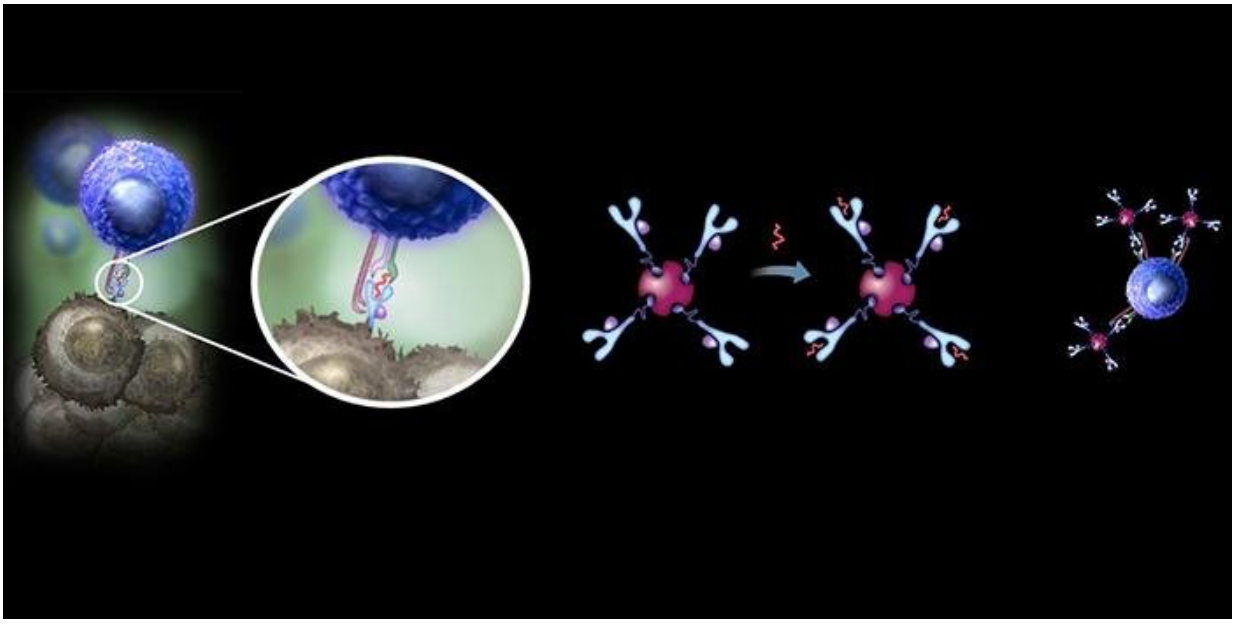

A new super-stable form of the MHC tetramer reagents, developed by Danish and German researchers, opens a range of new possibilities for improved monitoring and tracking disease relevant T cells in development of personalized cancer immunotherapies. Credit: DTU

In the journal *Science Immunology*, researchers from DTU Health Technology and Jacobs University in Bremen have just published their cutting-edge research demonstrating advancement in detection of a certain type of immune cells, called T cells. Improved detection of T cells have several therapeutic implications. For example, in cancer immunotherapy (a therapeutic approach that engages patients own

immune cells) characterization of T cells that recognize cancer cells is crucial for tailoring personalized treatment strategies.

T cells are white blood cells of the immune system that have amazing properties: they can detect cancer cells and virus-infected cells in the body, and they even attack and eliminate these. This is why T cells constitute an essential part of the immune response, which patients mount, against tumors and viruses.

When applying immunotherapy, an immune response against a tumor takes place, and the tumor-fighting T cells in the blood of the patient multiply. To find out how well the immunotherapy is working, scientists and doctors want to check how many tumor-specific T cells a patient has mounted. The tumor-specific T cells are identified by their specific T cell receptor using a colored reagent called an MHC tetramer. Using this reagent, the tumor-specific T cells become visible and can be counted under the microscope or in a high-throughput machine called a flow cytometer.

Super-stable molecule

The MHC proteins of the MHC tetramer reagent were previously difficult to produce due to the inherent instability of the MHC protein, and that used to be a bottleneck in research and diagnosis.

"Whenever a researcher needed MHC tetramers, they had to ask a company to make them, and the process took four to six weeks", explains Prof. Sebastian Springer, Jacobs University Bremen.

"Of course, that created big problems if they had a sick patient they wanted to diagnose, or if they were pursuing a really urgent scientific project. The problem was that every MHC protein contains a little piece of a tumor or virus called a peptide, which varies from one patient to the

other, and without the peptide, the MHC protein was unstable and perished quickly, even if it was kept in the fridge, thereby destroying the MHC tetramer."

The development and use of a super-stable form of MHC tetramer reagents is the subject of research professor Sine Reker Hadrup, DTU Health Technology, and her collaborators at the Jacobs University Bremen in Germany, led by Prof. Sebastian Springer has published in *Science Immunology*.

With the new invention, MHC molecules can be loaded with peptides instantly, on demand.

"The technology opens a range of new possibilities for tracking disease relevant T cells in patients and to manipulate T cells to specifically fight e.g. cancer" says Sine Reker Hadrup.

Cause for a company

Hadrup and Springer have now co-founded a company named Tetramer Shop to produce and sell this innovative MHC tetramer reagent. The company has already seen significant interest in its MHC tetramer reagents, from academia and pharma working on T cell immunotherapy as well as from various diagnostic platform companies.

Furthermore, Hadrup and Springer believe that the stabilized form of the MHC protein holds great promise within a new field of personalized T cell therapy, termed 'precision activated cell therapy,' where patients own tumor-specific T cells, in a personalized protocol, are isolated and activated before being used as the therapeutic product. This use could potentially give rise to yet another company.

More information: Sunil Kumar Saini et al, Empty peptide-receptive