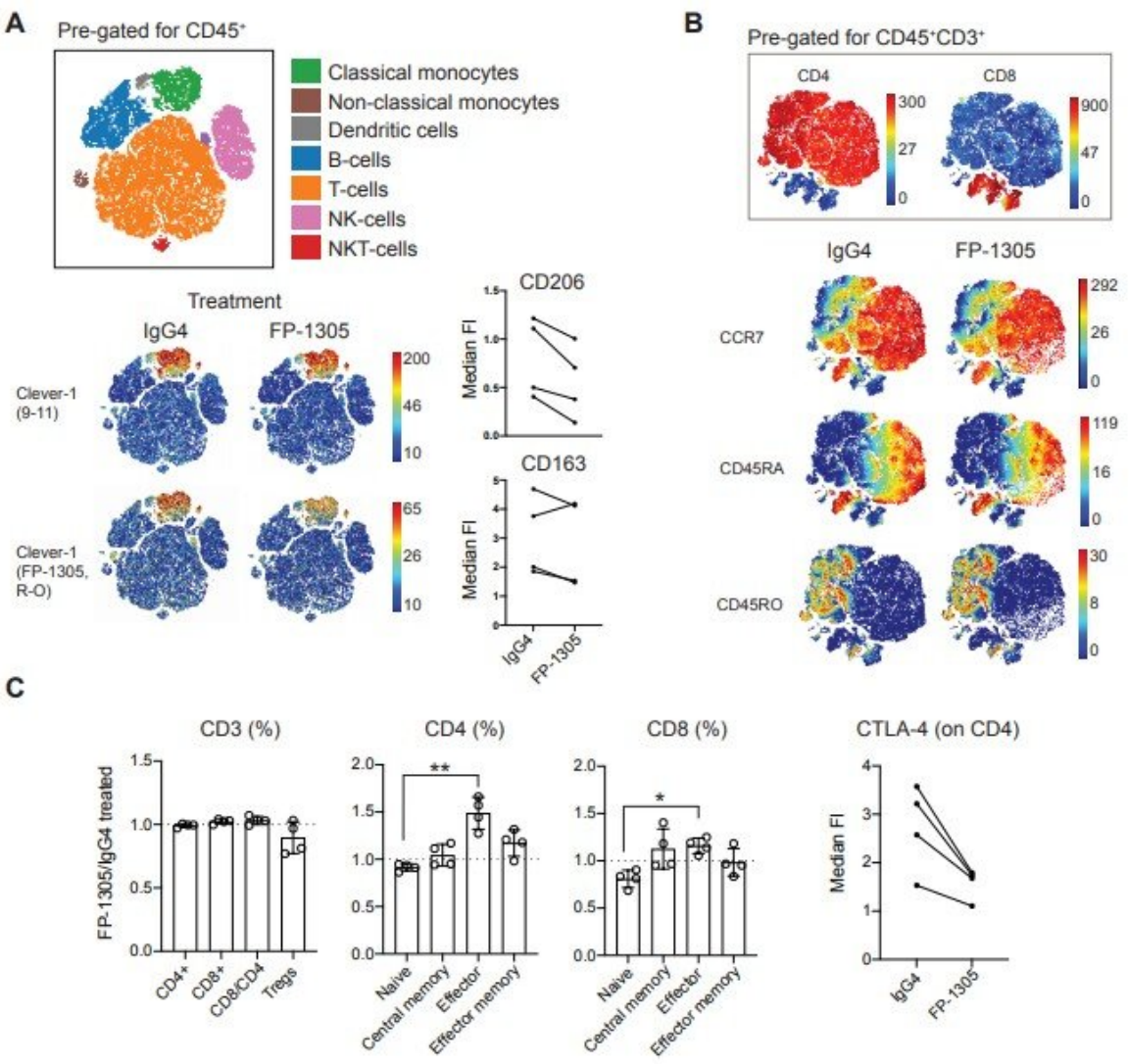
Novel antibody drug wakes up the body's defense system in advanced-stage cancer

June 3 2021



Supplementary Fig. 3. Whole blood from 4 healthy donors was incubated with FP-1305 or relevant isotype control (IgG4) for 24 h at a dose representing 1 mg/kg in a 65 kg weighing person (concentration in blood 13.3 µg/mL). Cellular and molecular changes were measured in PBMCs by mass cytometry. **A**, tSNE plots of the identified cell populations and heatmaps of Clever-1 expression detected by 9-11 (non-competing) or FP-1305 (competing, receptor occupancy (R-O)) antibodies. The graphs show CD206 and CD163 expression after IgG4 and FP-1305 treatment in CD14+ classical monocytes. **B**, tSNE plots of CD4+ and CD8+ T-cell populations showing naïve (CCR7+CD45RA+) and memory (CD45RO+) subsets. **C**, Quantification of T-cell population changes after FP-1305 treatment relative to isotype control and median expression of CTLA-4 on CD4+ effector T-cells. Friedman test with Dunn's multiple comparison. *P* *< 0.05, **< 0.01.

Credit: *Clinical Cancer Research* (2021). DOI: 10.1158/1078-0432.CCR-20-4862

Researchers at the University of Turku, Finland, showed that the antibody treatment reactivates the immune defense in patients with advanced-stage cancer. The treatment alters the function of the body's phagocytes and facilitates extensive activation of the immune system.

The immune defense is the body's own defense system equipped to combat cancer. However, cancer learns to hide from immune attacks and harnesses this system to promote its own growth. Therefore, it would be beneficial to be able to return the immune defense back to restricting the advancement of cancer.

Macrophages, a type of white blood cell, are central in the fight against cancer. Cancer educates macrophages to subdue the defense system and renders many treatments targeting the immune system ineffective.

Academy Research Fellow Maija Hollmén's research group has searched for means of altering the activity of macrophages in order to direct the immune defense to attack cancer. The antibody bexmarilimab, developed based on this research and in collaboration with Faron Pharmaceuticals, is currently undergoing clinical trials in patients. Hollmén's group has studied the changes occurring in the defense systems of patients with cancer following antibody treatment.

"In the majority of patients, the antibody treatment activated killer T cells, which are the body's strike force against cancer. Additionally, the antibody treatment successfully lowered the suppressive potential of macrophage precursors traveling in the blood circulation. The patients also showed increases in certain mediators of inflammation and types of white blood cell in the blood," says Hollmén.

"The activation of the killer T cells is a very promising demonstration of the antibody's capability to boost the defense system against cancer. The treated patients had very advanced and poorly treatable cancers, which

highlights the significance of the results," says Doctoral Candidate Jenna Rannikko.

Bexmarilimab May Benefit Patients for Whom Current Treatment Options Are Ineffective

The research also yielded new information on the mode of action of bexmarilimab. The antibody binds the molecule Clever-1 present on macrophages and alters its function.

Clever-1 transports material needless to the body inside macrophages to be degraded. Objects disposed in this manner are swept under the rug, in a manner of speaking. This kind of concealment is beneficial for the body's natural balance and helps to avoid stirring the immune defense unnecessarily.

"However, cells originating from cancer should be detected. When the antibody is used to block Clever-1 from performing its cleaning job, it facilitates the activation of cells of the immune defense. This in part leads to the waking up of the T cells in patients," says Doctoral Candidate Miro Viitala.

There is demand for treatments that boost the activity of the immune defense since the current options on the market only help some patients.

"Bexmarilimab's mode of action is different from the drug treatments against cancer currently on the market. Therefore, it can be beneficial for patients for whom current treatment options are ineffective," says Postdoctoral Researcher Reetta Virtakoivu.

The research article has been published in *Clinical Cancer Research*.

More information: Reetta Virtakoivu et al, Systemic blockade of

Clever-1 elicits lymphocyte activation alongside checkpoint molecule downregulation in patients with solid tumors: Results from a phase I/II clinical trial, *Clinical Cancer Research* (2021). DOI: 10.1158/1078-0432.CCR-20-4862