New methods for understanding human regulatory T cell functions

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研究の概要

We have developed a new method using mass cytometry (CyTOF) to study how regulatory T cells (Tregs) - crucial controllers of our immune system - function. The research, introduces “single cell suppression profiling of human Tregs” (scSPOT) , providing unprecedented detail about how these important immune cells work. The study reveals that Tregs primarily target specific immune cells called CD8-Eeffector memory T cells and identifies how two FDA-approved drugs affect different types of Tregs. Importantly, they discovered a specific pattern in Treg cells that could serve as a biomarker for severe viral infections, building on their previous COVID-19 research. This comprehensive approach could accelerate the development of new treatments for various diseases.

研究の背景と結果

Regulatory T cells (Tregs) are essential peacekeepers of the immune system, preventing it from attacking the body's own tissues while allowing it to fight off infections and cancer. Since their discovery in 1995 by recent Nobel prize winner Professor Shimon Sakaguchi, who is also a co-author of this study, scientists have recognized their crucial role in various diseases, including autoimmune conditions, cancer, and organ transplantation.

Traditional methods for studying Tregs have been limited to observing interactions with just one or two cell types at a time. The importance of Tregs has grown with the development of immunotherapies, particularly in cancer treatment, but understanding how drugs affect Tregs and their role in viral infections has remained challenging.

We developed scSPOT to observe 52 different markers on immune cells simultaneously, discovering that Tregs most strongly affect effector memory CD8 T cells through multiple mechanisms. They found that the cancer drug Ipilimumab primarily affects Tregs themselves, while Tazemetostat prevents the conversion of naive Tregs into effector Tregs.

Furthermore, they identified distinct Treg subtypes, including a pattern mirroring what they previously observed in severe COVID-19 patients, suggesting a potential biomarker for severe viral infections.

研究の意義と将来展望

The new scSPOT method provides scientists with a valuable tool to study immune regulation, potentially speeding up the development of treatments for both cancer and autoimmune conditions. The discovery of a potential biomarker for severe viral infections could help healthcare providers identify high-risk patients earlier, enabling more timely interventions during outbreaks or pandemics. Additionally, the insights into how existing drugs work could lead to more effective treatment strategies, helping doctors better predict which patients will respond to treatment. Together, these advances could lead to more personalized medical treatments, improving patient outcomes across multiple diseases. We have already used these methods to help us understand the function of new types of Tregs such as the precursor T follicular regulatory cells that we recently discovered.

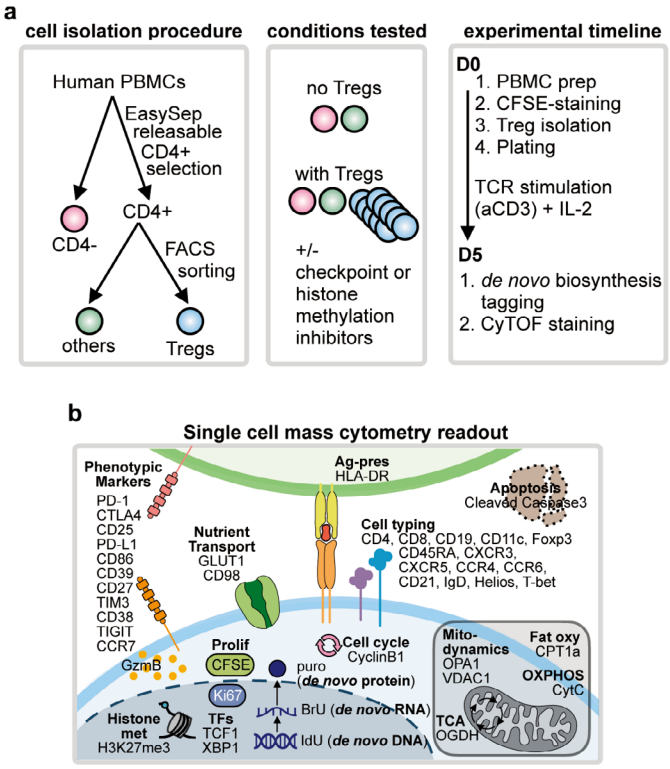

Fig 1. **Methods.** (a) Regulatory T-cells (Tregs) are removed from human peripheral blood mononuclear cells by FACS sorting and then re-added at set ratios to test their function. (b) A Mass cytometry (CyTOF) panel was used to assess the type of immune cells that become more activated in the absence of Tregs.

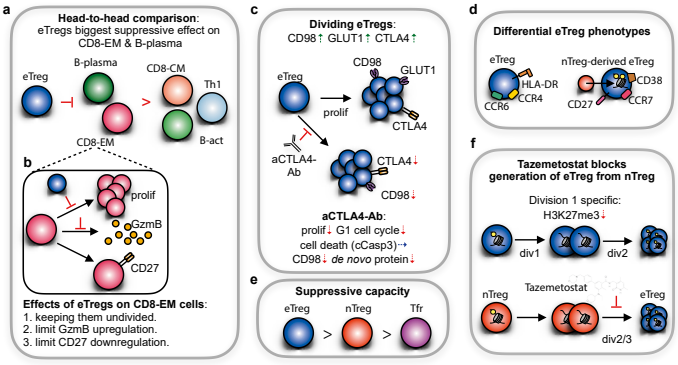

Fig.2 **Main findings.** (a-b) Effector Tregs (eTregs) most strongly affect CD8-EM cells and B-plasma cells. (c) Dividing eTregs increase CD98 and CTLA4 proteins, an anti-CTLA4 antibody affects this process. (d) Two distinct types of eTregs: one expressing HLA-DR and another expressing CD38 - a biomarker seen in severe viral infections. (e) Ranks different Treg types by their suppressive ability. (f) The drug Tazemetostat blocks naive Tregs from becoming eTregs.

特　　許	
論　　文	Søndergaard, Jonas Nørskov; Tulyeu, Janyerkye; Wing, James Badger et al. Single cell suppression profiling of human regulatory T cells. Nature communications. 2025, 16(1), 1-16. doi: 10.1038/s41467-024-55746-1 Søndergaard, Jonas Nørskov; Tulyeu, Janyerkye; Wing, James Badger et al. Assessing human Treg suppression at single-cell resolution using mass cytometry. Bio-Protocols. 2025, 15(16), e5424. doi: 10.21769/BioProtoc.5424 Tulyeu, Janyerkye; Søndergaard, Jonas Nørskov; Wing, James Badger et al. Human precursor T follicular regulatory cells are primed for differentiation into mature Tfr and disrupted during severe infections. Science Advances. 2025, 11(39), eadv6939. doi: 10.1126/sciadv.adv6939
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