Regulatory T Cell for Immunotherapy

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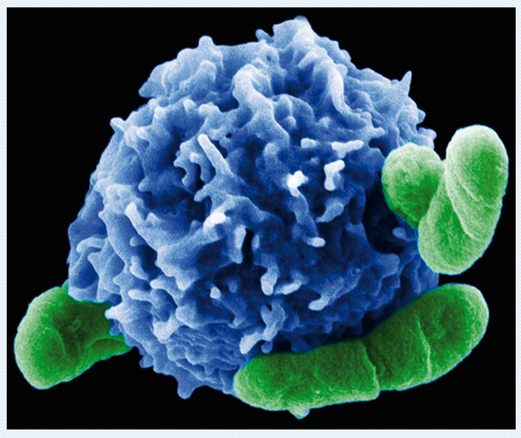
Introduction

Regulatory T cells (Tregs) are Tcells which have regulatory functions. Nowadays, they are considered as a target of cancer therapy.CTLA-4 antibody was approved as the treatment for melanoma in USA in 2011. Tregs concern with it. However, this therapy can cause serious side effects.
The aim of this paper
→1, improve the understanding of Tregs
2, think about new therapeutic ways to reduce side effects.



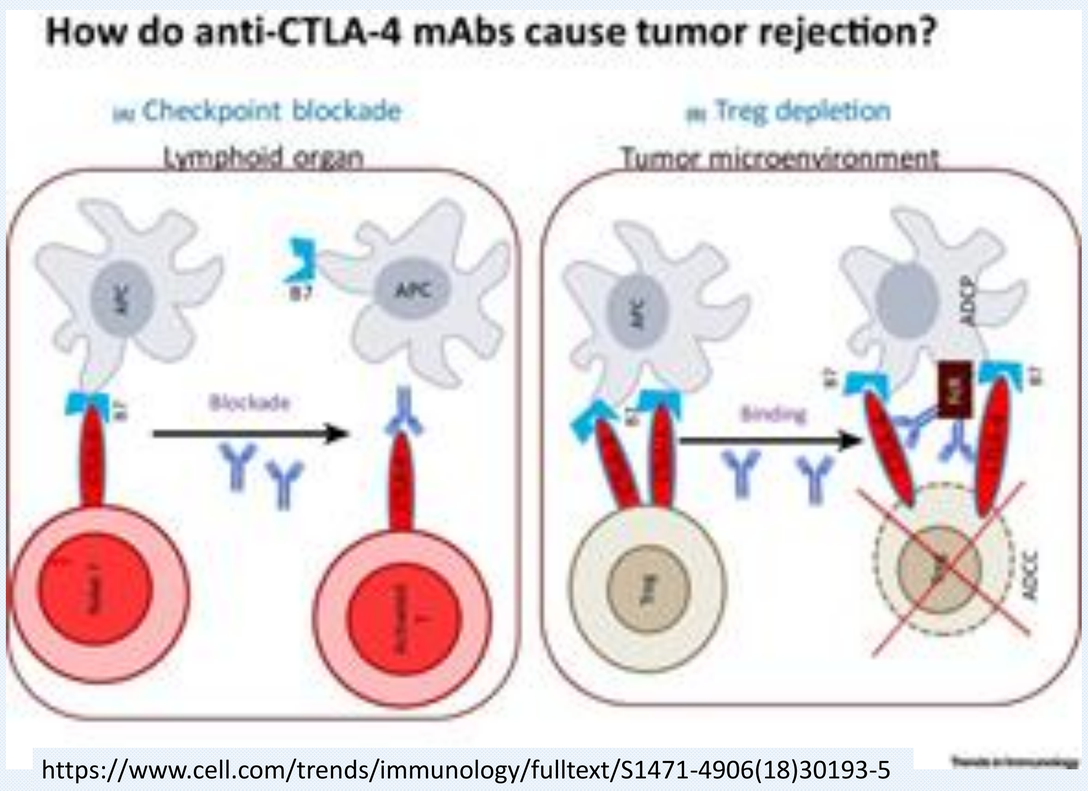
A regulatory T cell (blue) interacting with bacteria (green)↑
https://www.labroots.com/trending/immunology/2324/protective-autophagy-in-regulatory-t-cells

Fundamental

Regulatory T Cell

Tregs are often expressed as CD4+CD25+FoxP3+T cells. There are a lot of kinds of pathways of regulation.

CTLA-4 Antibody



https://www.cell.com/trends/immunology/fulltext/S1471-4906(18)30193-5

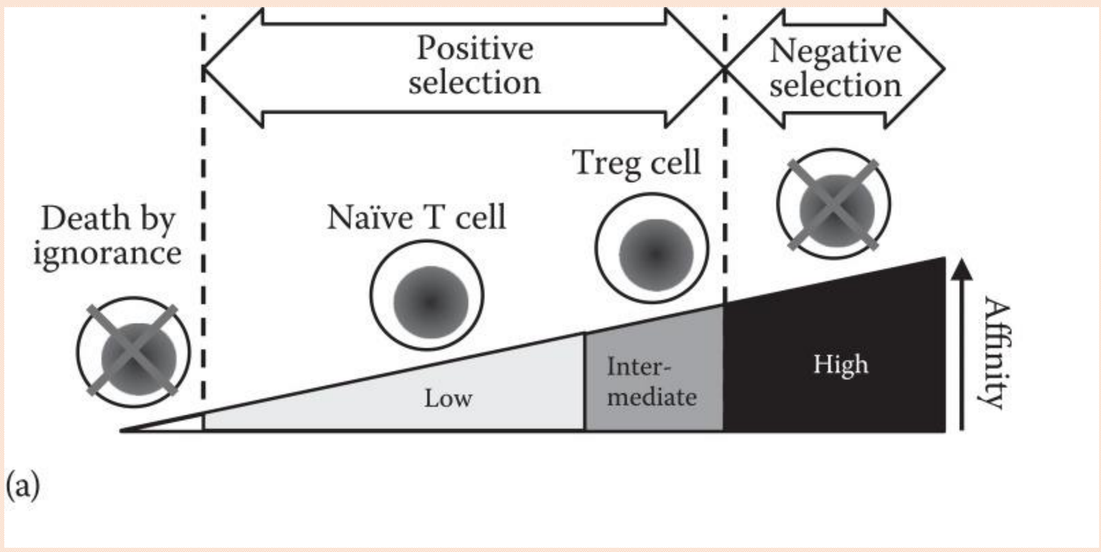
CTLA-4 expressed on Tregs. Combination between CD28(on T cells) and CD80/86 (on antigen presenting cells)→ Necessary for T cell activation. However, CTLA-4 combine with CD80/86 priority.→Inhibit activation. Besides, activated T cells start to express CTLA-4, and regulated through CTLA-4 when they encounter CD80/86 again. CTLA-4 antibody activate immune by inhibiting these two.

Methodology

I did an interview to Dr Nick Holmes(Division of Immunology, Department of pathology, University of Cambridge), he studies about how lymphocytes can regulate their activation at Department of Pathology.
I asked these questions.
Q1:What is the way to reduce side effect of immunotherapy especially anti CTLA-4 antibody?
Q2: What point Tregs start to be activated ?
Q3:What is the reason that T cells which have high affinity to self antigen become Treg cells?

Result

Dr Nick answered the questions.
A1: Difficult to avoid side effects. It improves the effect of treatment which using both CTLA-4 antibody and PD-1 antibody (another type of immunotherapy) and reduce side effects ,but it's not perfect.
A2: Stimulation of cytokines produced by antigen presenting cells.
→Necessary for T cells differentiation.
The presence of antigen→For activation.
After differentiation, T cells increase by feedback.
A3: Not all the high affinity (to self antigen) T cells differentiate Tregs. However, Treg cells tend to have high affinity . The reason is only a guess, but Tregs can control attack to self antigen easily.



T cell differentiation. ↑
https://www.ncbi.nlm.nih.gov/books/NBK532318/ figure 1

Discussion

- The way to control side effects of immune check point treatment completely isn't founded yet.
- Tregs' differentiation, activation, and increasing are leaded by different ways.
  → There are some more possibilities to use Tregs for medication.
- Tregs have high affinity to self antigen. However, the reason is not revealed. If that reason is founded, and used, it may be able to control the number of Tregs artificially.

Conclusion

- Immune system is very complex. It is difficult to make a way of immunotherapy which influence is controlled.
- I couldn't get exact answer whether there is a mechanism which works to decrease Tregs or not.
- By developing research which uses Treg's differentiation, activation, or inactivation, it may be real that safer immunotherapy in the future.

Acknowledgements

I am deeply grateful to Dr Nick Holmes who answered my questions, and gave me helpful comments. Also, I'd like to thank Ms. Keiko Kurokawa, Ms. Misaki Nakamura, Mr. Hidehiro Narita, Mr. Masato Suzuki, and Mr. Akihiro Yasuhara. Their advice helped me a lot. Without them I couldn't conduct this research.

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