

Continuous Turnover of Regulatory T Cells Enables Rapid Immune Morphogenesis

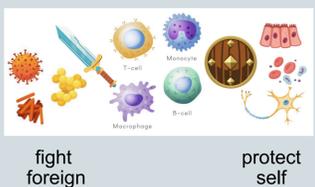
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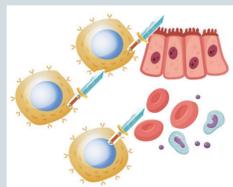
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Background

The immune system must distinguish between self and foreign.



Self-reactive T cells cause autoimmunity.

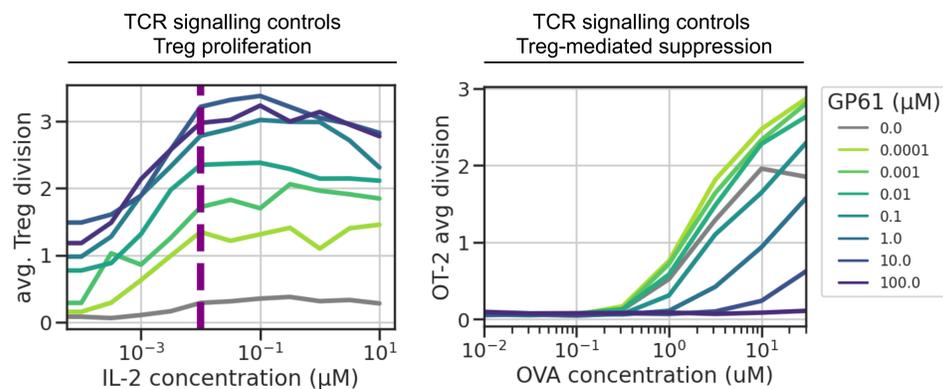


Regulatory T cells (Tregs) suppress self-reactive T cells.



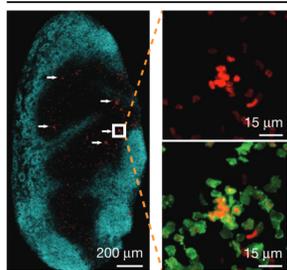
Illustrations from iStock

TCR signalling drives Treg proliferation and suppression of Tconvs

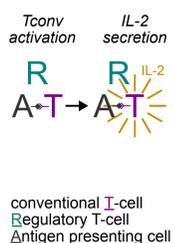


Regulatory niches suppress self-reactive T cells during priming

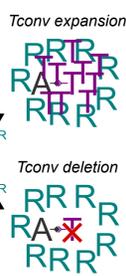
Regulatory niches form around self-reactive Tconv in lymph nodes



IL-2 secretion by Tconv induces local Treg proliferation

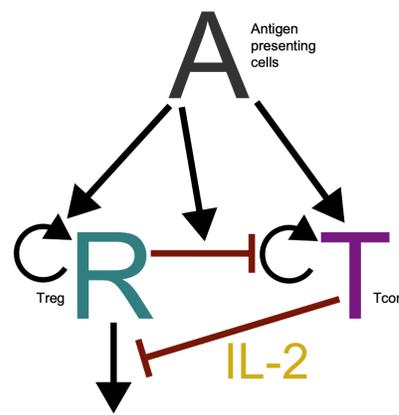


Tregs limit Tconv expansion



Oyler-Yaniv et al. 2018, Wong et al. 2021

A new model for Treg dynamics and function



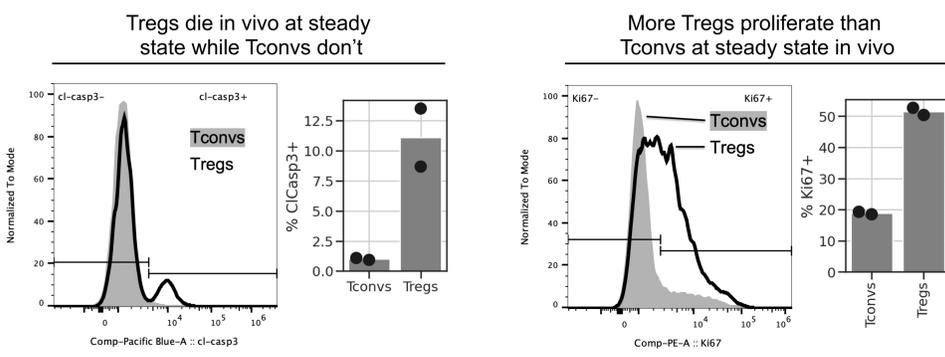
Prediction:

If IL-2 induces Treg expansion in vivo, Tregs need to continuously proliferate (via self-antigens) and die to maintain a stable population

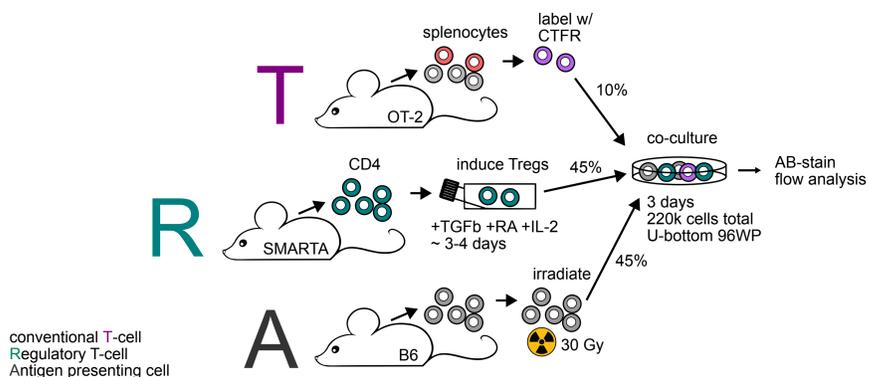
Questions

How do TCR- and IL-2-signalling control Treg dynamics?
How do regulatory niches form rapidly enough to control an ongoing T cell response?

Tregs continuously turn over in vivo

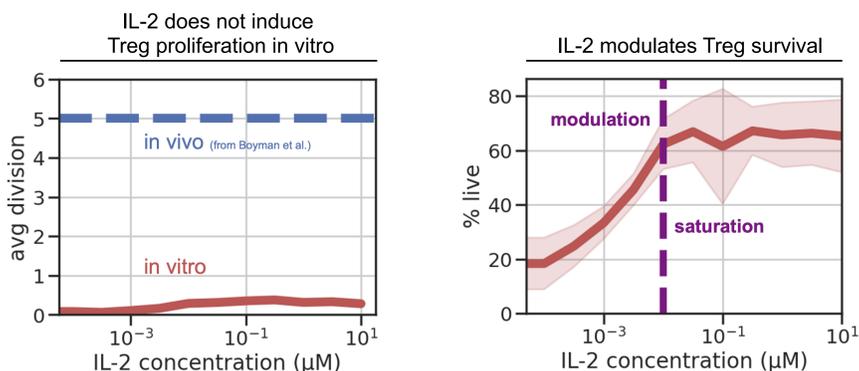


An in vitro setup to investigate Treg dynamics

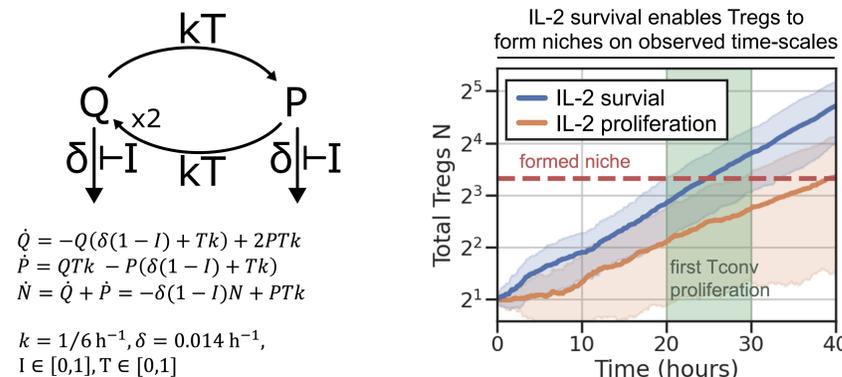


conventional T-cell
Regulatory T-cell
Antigen presenting cell

IL-2 does not impact Treg proliferation, but is essential for survival



Parameterized model predicts rapid regulatory niche formation via Treg turnover



Summary

- TCR signalling drives Treg proliferation and suppression, IL-2 is a survival signal
- Self-antigen abundance drives continuous Treg turnover in vivo
- Local IL-2 release by activated Tconvs instantly rescues dying Tregs, enabling rapid niche formation without cell division.