Resistance of T Follicular Helper Cells to Depletion by Anti-Thymocyte Globulin

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Background

T follicular helper (Tfh) cells are a subset of CD4+ T cells that specialize in providing help for germinal center (GC) reactions where B cells are activated, differentiate and produce high-affinity antibodies.

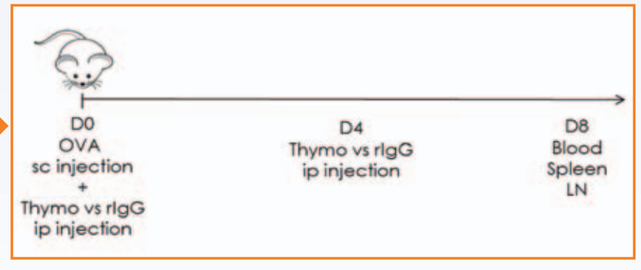
In addition to those residing in lymph nodes (rTfh), a small percentage of Tfh cells called circulating Tfh (cTfh) can be found in peripheral blood. In the setting of kidney transplantation, higher percentages of cTfh have been associated with **donor-specific-antibodies and chronic antibody-mediated rejection.**

Anti-thymocyte globulin (ATG) is a widely used potent depleting induction therapy. However, little is known about its effect on Tfh population. We aimed to analyze the effect of mouse ATG (mATG) on both secondary lymphoid-resident and circulating Tfh.

Methods

We generated mATG by **immunizing rabbits** with splenocytes retrieved from three different mouse strains (DBA/B, C3H and SJL) followed by **purification**.

Materials:
Mice B6-GFP-FoxP3
NP-OVA (100mcg) + CFA (1:1)
mATG 500 mcg (per shot)
Rabbit IgG 500 mcg (per shot)

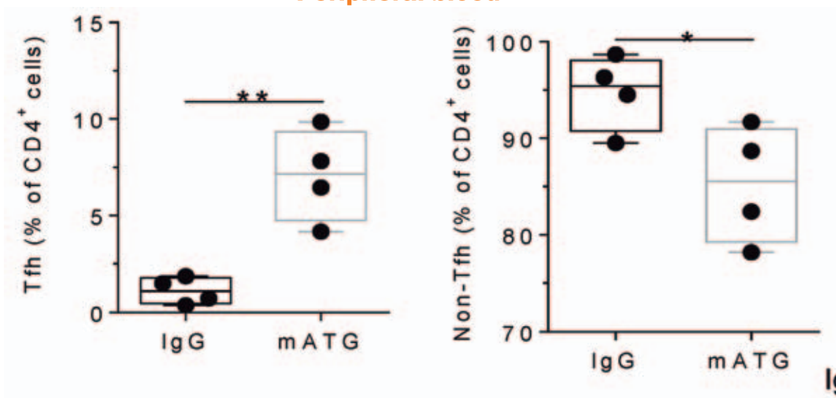


Draining lymph nodes (dLNs) and blood were harvested and Tfh population (**CD4+CXCR5+PD1+**) was examined on day 8.

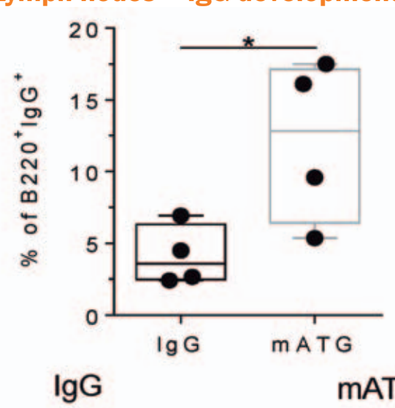
Authors have no commercial interests to disclosure

Results

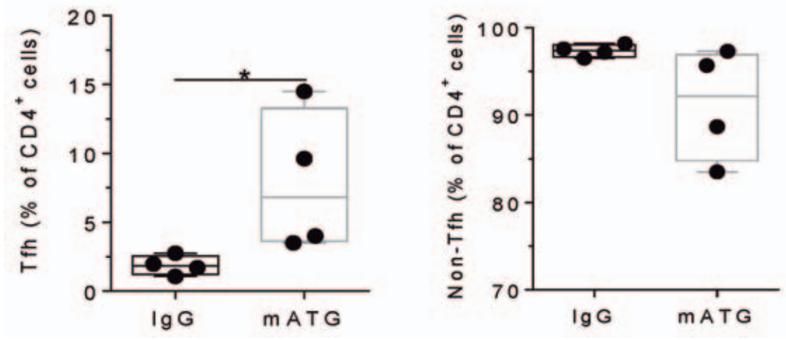
Peripheral blood

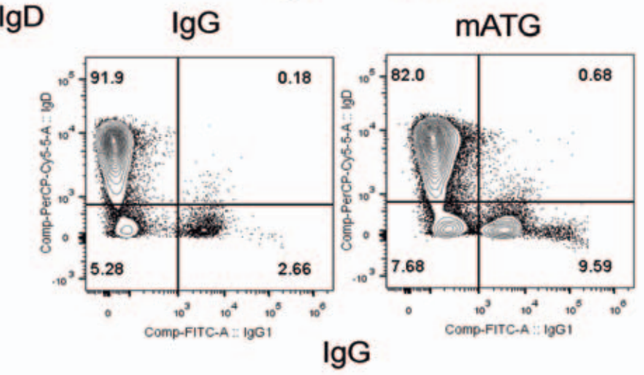


Lymph nodes – IgG development

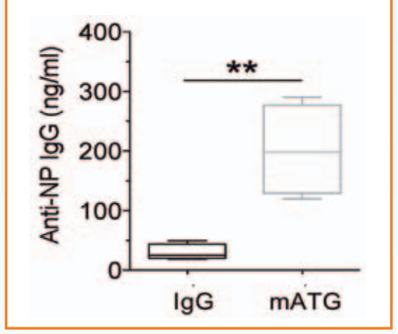


Lymph nodes





Serum



Conclusions

mATG is effective in depleting T cells both in peripheral blood and secondary lymphoid organs.

However, **Tfh are resistant** to its effect.

The mechanisms of that remain uncertain and require further investigation.

Since antibody-mediated rejection is a dominant cause of graft failure, investigating the **mechanism of this resistance** is crucial for the development of more effective therapies in restraining Tfh cells.