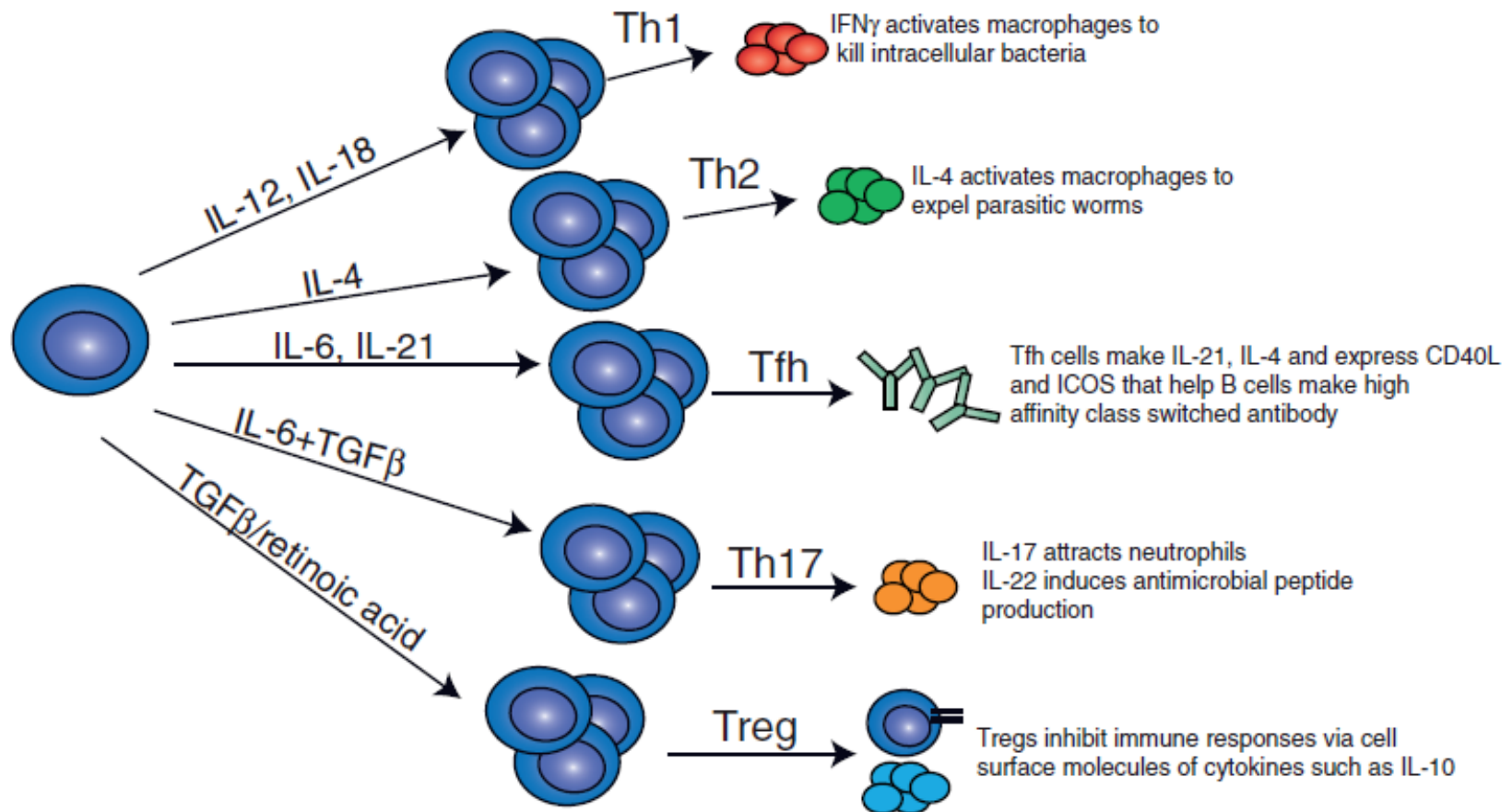


**Batf is essential for IL-4 expression in
T follicular helper cells.**

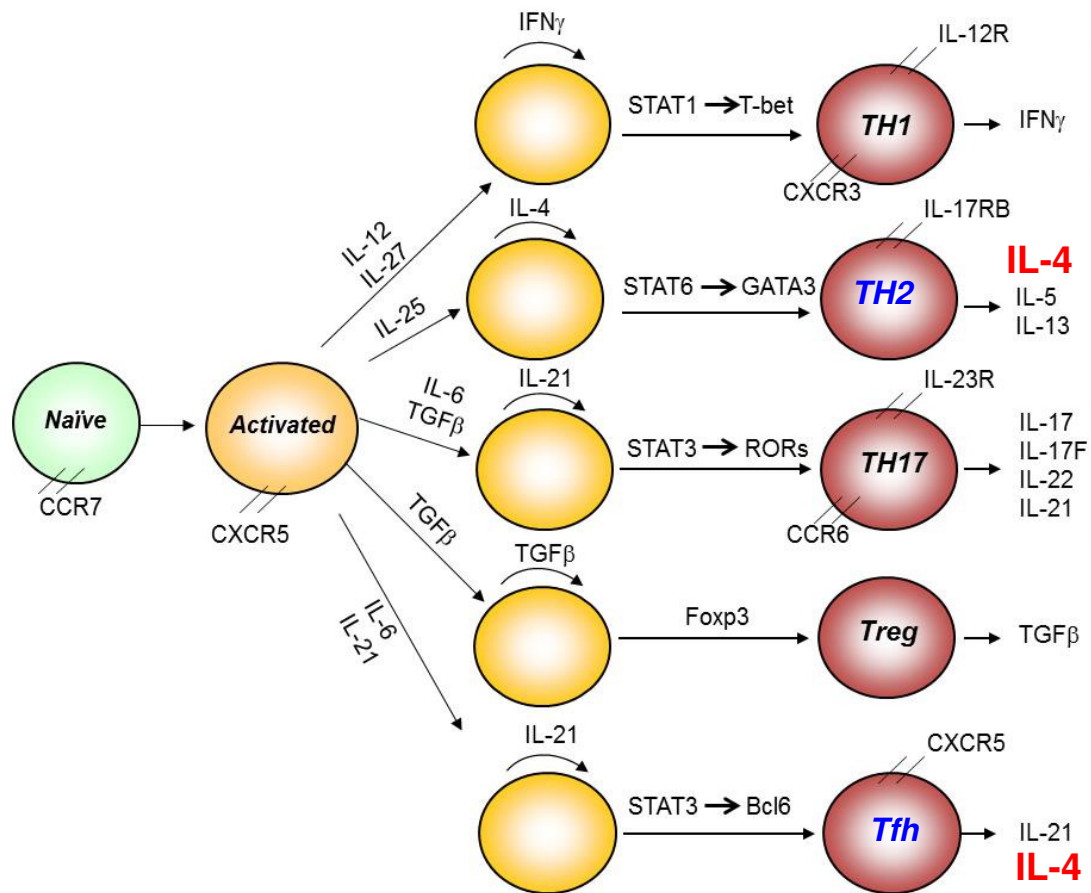
Roza Nurieva

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MD Anderson Cancer Center.
Houston, TX. USA

T helper subsets: differentiation and function

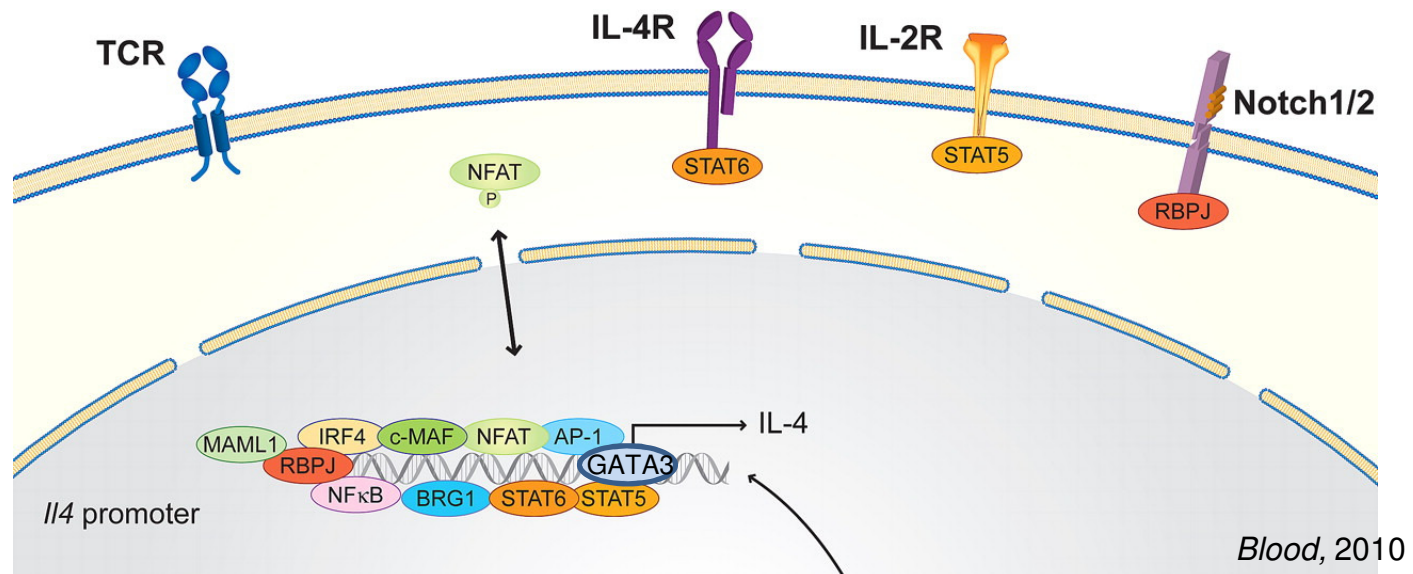


Transcriptional control of T helper subsets



Il-4 transcription in Th2 and Tfh cells

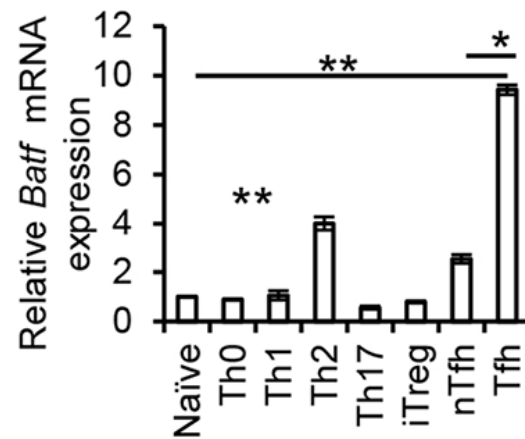
- In Th2 cells: Various Cis-Regulatory Elements including Il4 Promoter and TFS



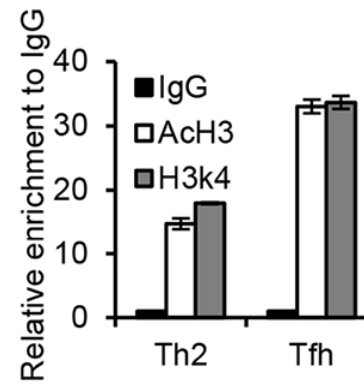
- In Tfh cells: CNS2 element of the IL-4 locus and TFs?
 - The 3' enhancer CNS2 is a critical regulator of interleukin-4-mediated humoral immunity in follicular helper T cells. *Immunity, 2012.*

Batf is expressed in Th2 and Tfh cells

A.

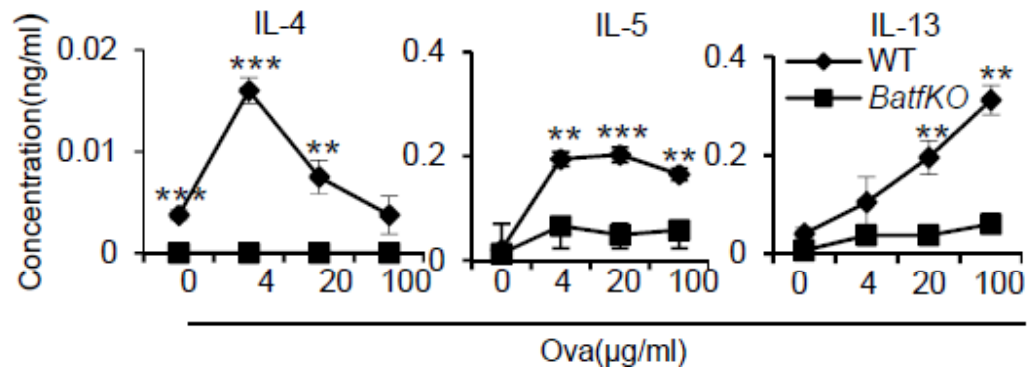


B.



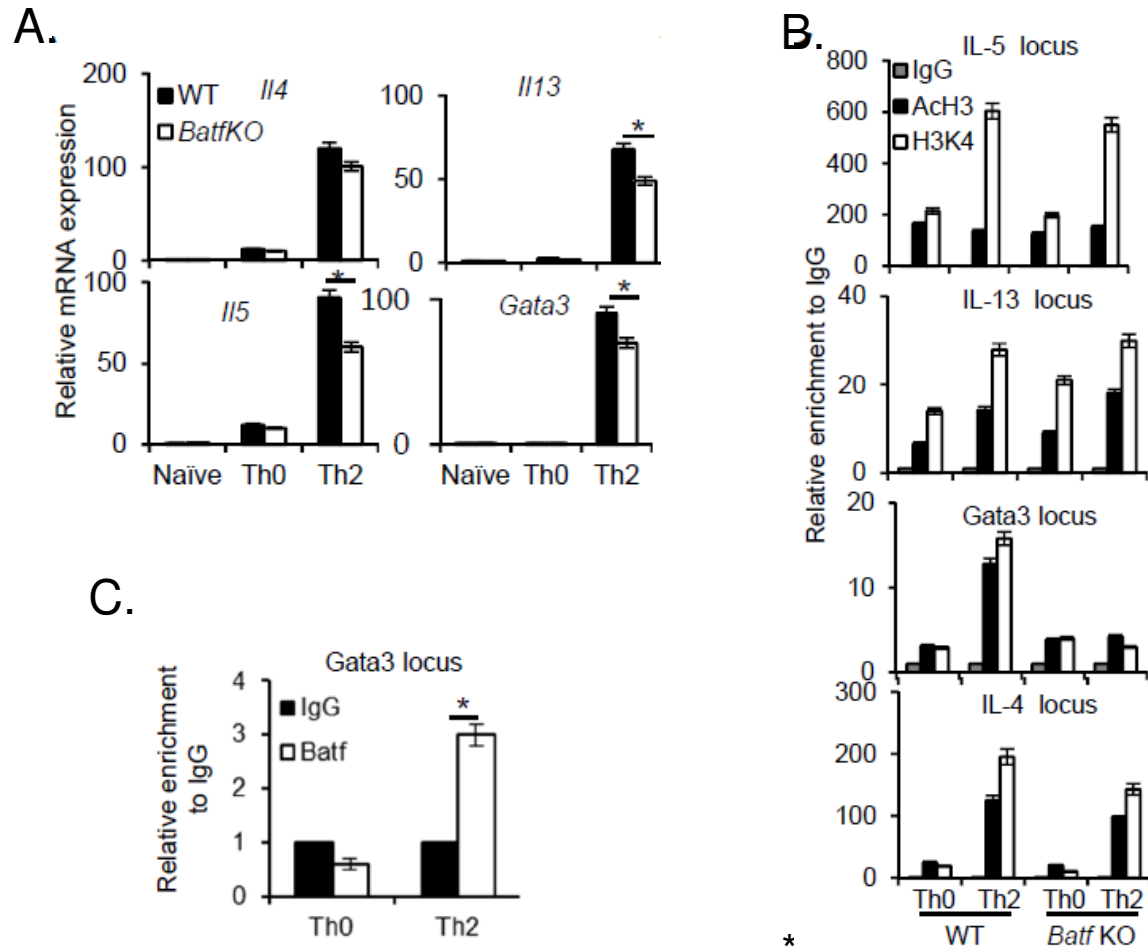
- CD4⁺CD44^{hi}CXCR5^{hi}PD1^{hi} (Tfh)
- CD4⁺CD44^{hi}CXCR5⁻ (nTfh)
- Active histone modifications (AcH3, H3k4)

Batf deficiency abrogates Th2 cytokines in vivo



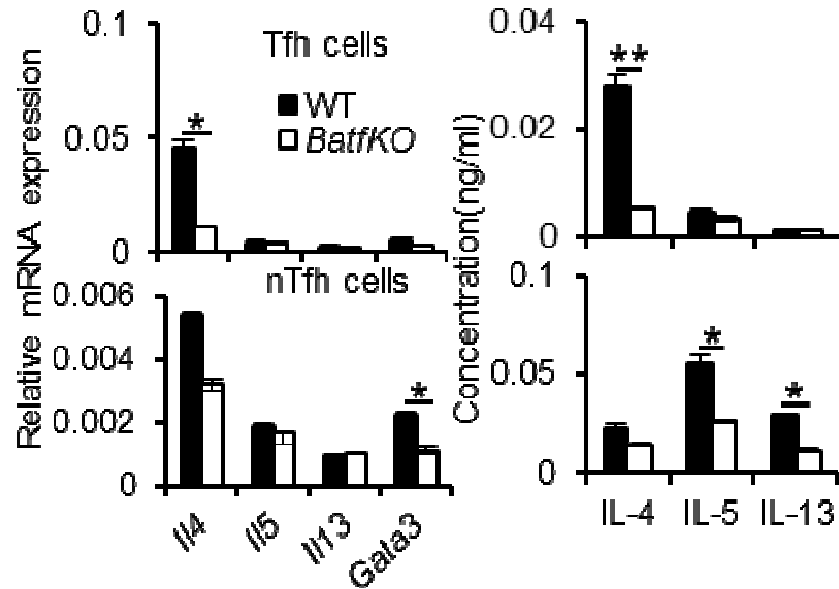
➤ WT and Batf deficient mice immunized with ovalbumin in alum.

Batf has partial control over Th2 genes in vitro

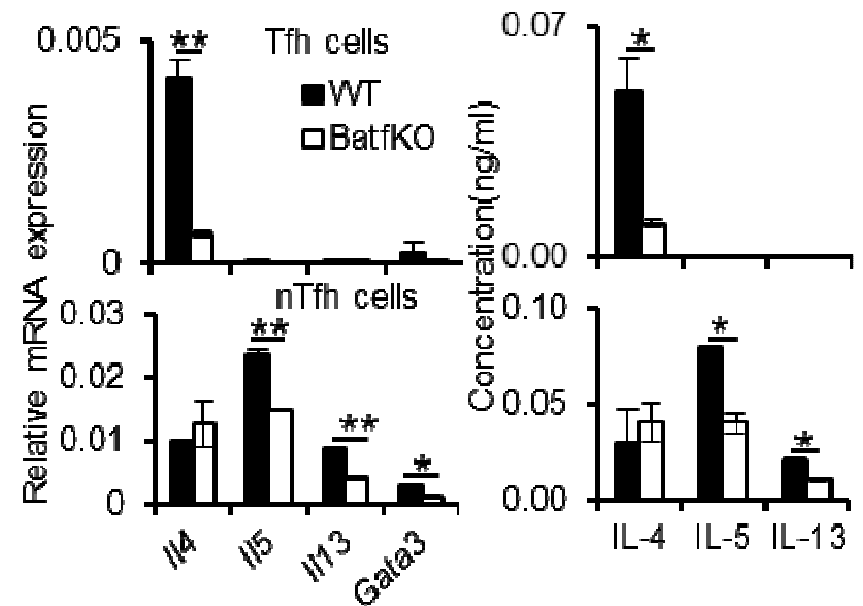


The IL-4 defect in Tfh cells upon Batf deficiency is T cell intrinsic

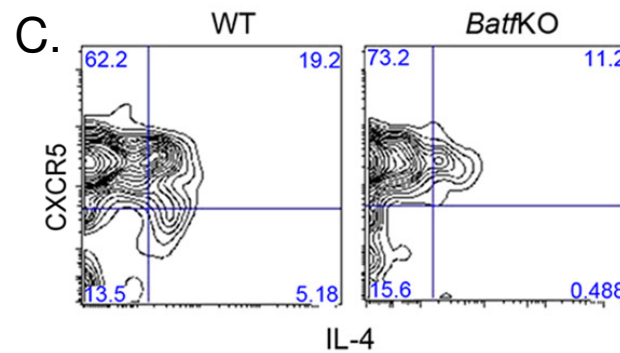
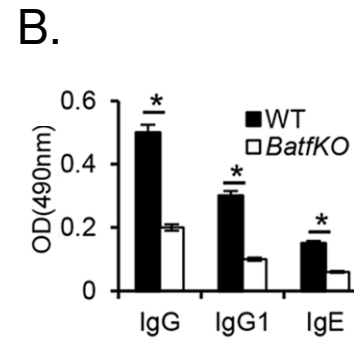
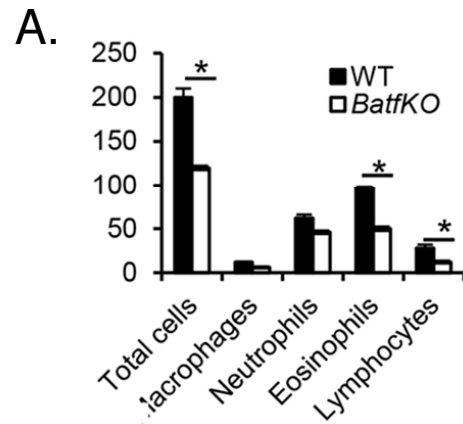
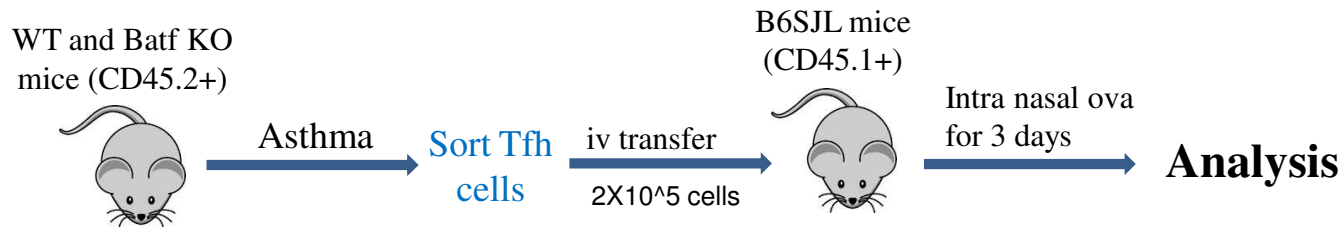
a



b

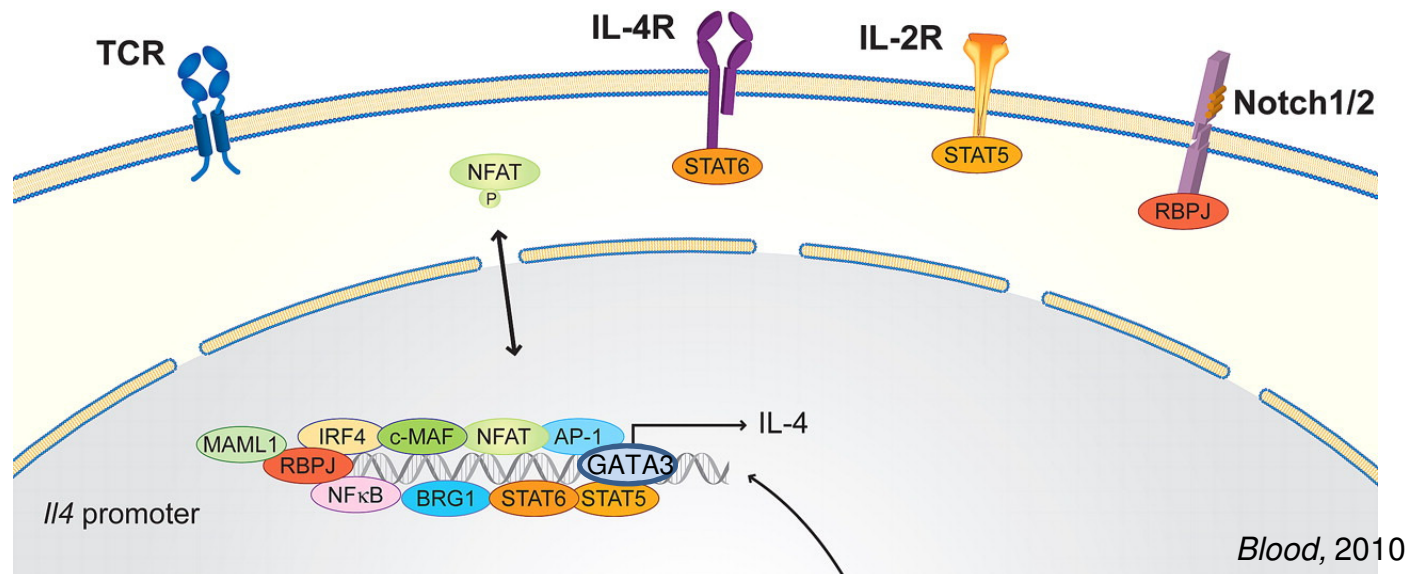


IL-4 producing Tfh cells can trigger asthmatic symptoms



Il-4 transcription in Th2 and Tfh cells

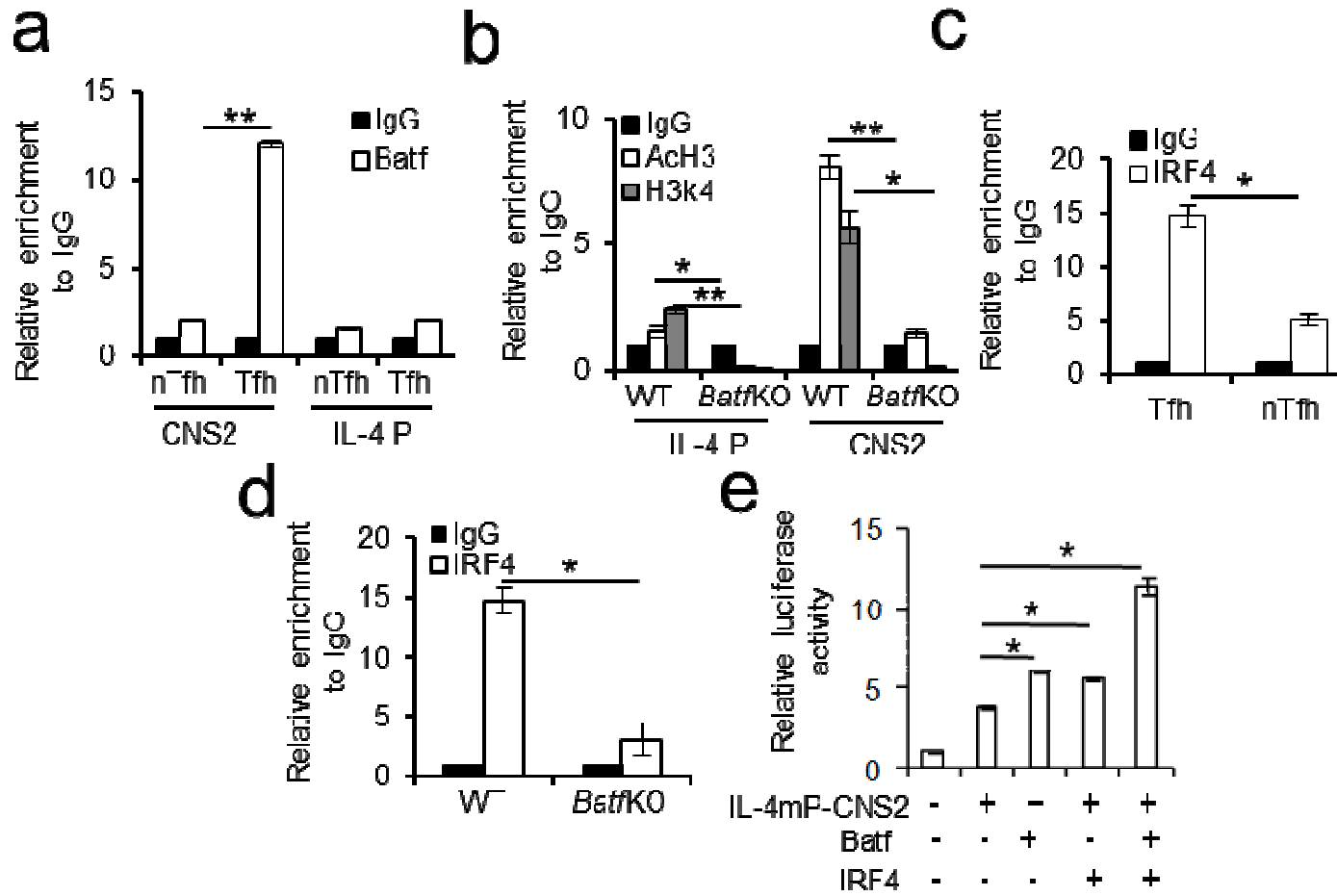
- In Th2 cells: Cis-Regulatory Elements including Il4 Promoter



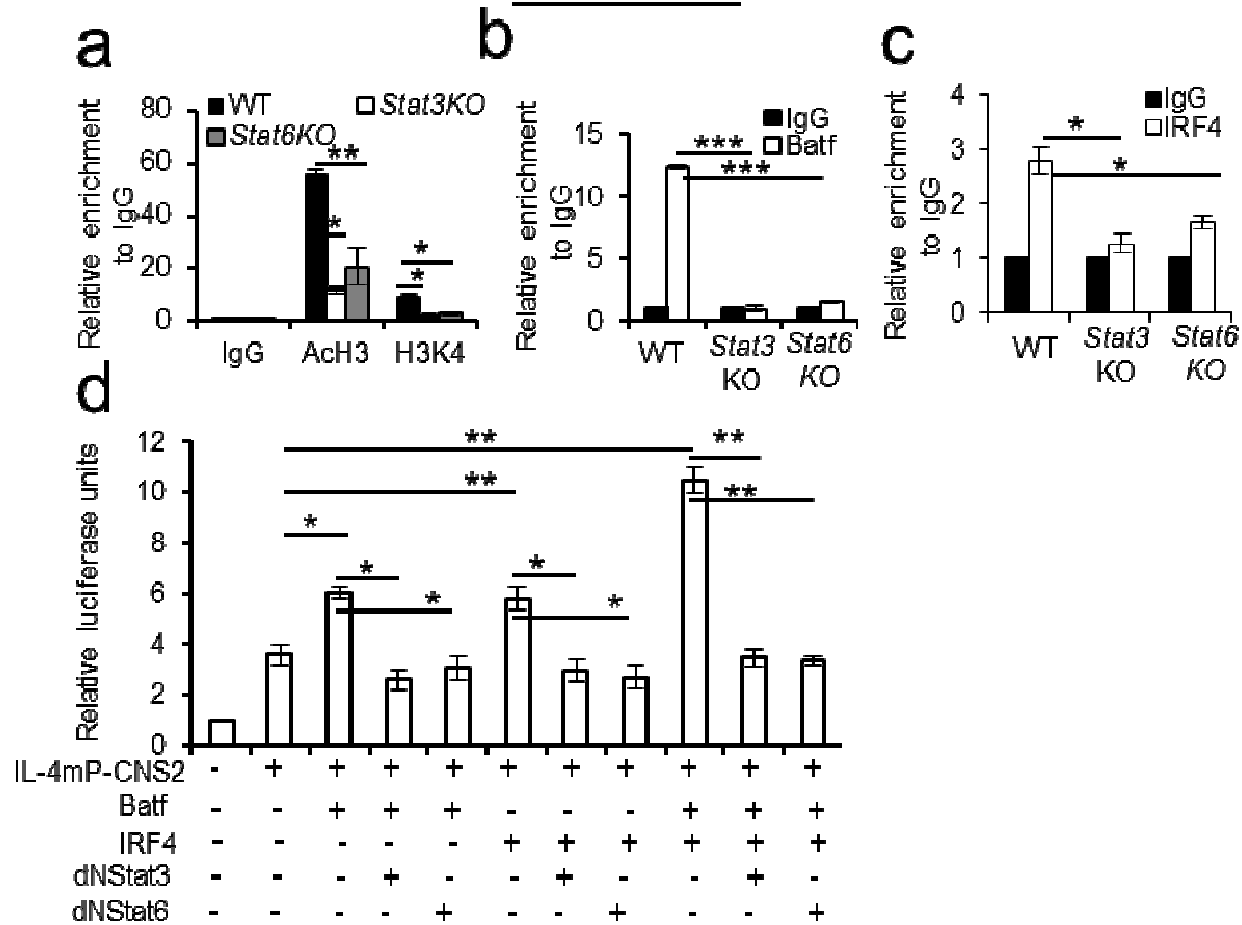
- In Tfh cells: CNS2 element of the IL-4 locus and TFs?

- The 3' enhancer CNS2 is a critical regulator of interleukin-4-mediated humoral immunity in follicular helper T cells. *Immunity*, 2012.

Batf in cooperation with IRF4 regulates IL-4 expression in Tfh cells
through the CNS2 locus



Batf/IRF4 along with Stat3 and Stat6 controls IL-4 production
in Tfh cells



Summary

- The transcription factor Batf, a member of the AP-1/Jun family, shows enhanced expression in both Th2 and Tfh cells.
- Functionally, Batf is required for IL-4 expression in Tfh cells and its deficiency leads to subsequent reduction in their pro-allergic function.
- Batf in cooperation with IRF4 and along with Stat3 and Stat6 controls IL-4 production in Tfh cells by directly binding to and activation of the CNS2 region of the IL-4 locus.

These results indicate a critical role of Batf in promoting the generation of pro-allergic IL-4 producing Tfh cells.

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