

FoxP3: More than just a marker of regulatory T cells

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Accumulating evidence suggests that defective regulation is an essential underlying cause of autoimmunity. In these settings, the most prominent regulation is determined by the balance of pathogenic T cells and a small subset of CD4+ T lymphocytes known as regulatory T cells (Tregs) that are critical to maintaining peripheral self tolerance. However, there is only a limited understanding of the basis for Treg development, stability and plasticity. We have developed a new Treg-specific, FoxP3-GFP-Cre BAC transgenic mouse strain. These mice can be used to study the stability of Tregs, the selective loss of individual Treg-specific gene expression and lineage tracking. In this presentation, I will present ongoing studies demonstrating that a fraction of Tregs are unstable as a significant percentage of thymically-derived Tregs down-regulate FoxP3, lose their characteristic Treg phenotype, exhibit an activated-memory phenotype and lose suppressive function. In addition, the talk will focus on understanding the critical roles of microRNAs and TGF β in the development and function of Tregs in controlling autoimmunity. Together, the data suggest that local inflammation influences the balance of immunity and regulation, which can be key determinants in the productivity of an immune response.

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References

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