Abstract

Abstract Title: Foxp3 expression in iT_{reg} cells is stabilized by C/EBP in inflammatory environments

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Abstract (not more than 300 words)

Proper control of immune responses by $Foxp3^+$ regulatory T cells at inflamed sites is crucial for the prevention of immunopathology. TGF-β-induced $Foxp3^+$ regulatory T (iT_{reg}) cells are generated in inflammatory environments as well as in steady state conditions. Inflammatory cytokines such as IFN-γ and IL-4 have an antagonistic effect on iT_{reg} cell conversion. However, it is not known how naive $CD4^+$ T cells overcome the inhibitory environment in inflamed sites to differentiate into iT_{reg} cells. Here, we show that CCAAT/Enhancer-binding protein (C/EBP) functions as a safeguard that enhances iT_{reg} generation by dampening the inhibitory effect of IFN-γ and IL-4 on Foxp3 expression. We found that C/EBPβ is induced by retinoic acid and binds to the methyl-CRE sequence in the *Foxp3* TSDR to sustain its expression. C/EBPβ-transduced iT_{reg} cells showed more potent suppressive activity in mouse disease models for experimental autoimmune encephalitis. We also found that C/EBPβ-transduced human iT_{reg} cells exhibited more enhanced suppressor function in *in vitro* suppression assay. These results establish C/EBP as a new molecular target for stabilizing iT_{reg} cells in inflammatory environments.

Keywords— *Tregs, inflammation, stability, C/EBPs*

Professional Biography (100-150 words)

Rho H. Seong has completed his PhD from Stanford University and postdoctoral studies from Stanford University School of Medicine. He is the director of Institute of Molecular Biology and Genetics, Seoul National University. He has published more than 90 papers in reputed journals and has served as an editor-in chief of *Molecules and Cells*.



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