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FOXP3 EXPRESSION IN ITREG CELLS IS STABILIZED BY C/EBP IN INFLAMMATORY ENVIRONMENTS

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

Biography

Rho H Seong has completed his PhD from Stanford University and Post-doctoral 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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