Role of Methylation in Trafficking of Stat6

Mandeep Ghuman, Weiguo Chen, Michael O. Daines, Gurjit Khurana Hershey
Division of Allergy and Immunology, Department of Pediatrics

Asthma is the most common chronic disease of childhood, and its incidence is on the rise. It is characterized by airway inflammation, bronchial hyperresponsiveness, and reversible obstruction. IL-4 and IL-13 have been shown to be critical for the development of BHR in human and animal studies. IL-4 and IL-13 signal through specific receptor complexes resulting in the activation of the JAK/Stat pathway, specifically (signal transducer and activator of transcription) Stat6. Activated Stat6 dimers translocate to the nucleus, bind specific DNA recognition sequences, and activate transcription of downstream genes. We have previously reported that the Stat6-dependent gene induction requires a constant cycle of activation, nuclear transport, deactivation, nuclear export, and reactivation of Stat6. The activity of Stat proteins is regulated by phosphorylation, however the regulation of Stat cycling is unknown. Recently, arginine methylation of Stat1 on a conserved arginine residue in the N-terminal domain, Arg37 was shown to modulate Stat1 activity. Herein, we examined whether Stat6 was methylated and the role of methylation on Stat6 cycling. The central hypothesis for these studies is that Stat6 is methylated on Arg27 and that cycling is modulated by methylation.