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Meeting abstract

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SUMOylation of the transcription factor NFATc1 leads to its subnuclear relocalization and IL2 repression by HDAC

A Nayak*[1], J Glöckner-Pagel[1], M Vaeth[1], M Buttmann[2], T Bopp[3], E Schmitt[3], E Serfling[1] and F Berberich-Siebelt[1]

Address: [1]Department of Molecular Pathology, Institute of Pathology, University of Würzburg, Würzburg, Germany, [2]Department of Neurology, University of Würzburg, Würzburg, Germany and [3]Institute of Immunology, University Mainz, Mainz, Germany

* Corresponding author

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The family of NFAT (Nuclear Factor of Activated T-cells) transcription factors plays an important role in cytokine gene regulation. In peripheral T-cells, NFATc1 and c2 are pre-dominantly expressed. Due to different promoter and polyA site usage as well as alternative splicing events, NFATc1 is synthesized in multiple isoforms. The highly inducible NF-ATc1/A contains a relatively short C-terminus whereas the longer, constitutively expressed isoform NFATc1/C spans an extra C-terminal peptide of 246 amino acids. Interestingly, this NFATc1/C-specific terminus can be highly sumoylated. Upon sumoylation, NFATc1/C – but not the unsumoylated NFATc1/A – translocates to Promyelocytic Leukemia-nuclear bodies (PML-nbs). This leads to interaction with HDACs followed by deacetylation of histones, which in turn induces transcriptionally inactive chromatin. As a consequence, expression of the NFATc1 target gene interleukin-2 is suppressed. These findings demonstrate that the modification by SUMO converts NFATc1 from an activator to a site-specific transcriptional repressor, revealing a novel regulatory mechanism for NFATc1 function.