

P037 Translational Control of Inducible Nitric Oxide Synthase by Arginine Availability and Arginase in vitro and in vivo
Ulrike Schleicher, Till König, and Christian Bogdan
Institute of Medical Microbiology and Hygiene, University of Freiburg, Germany

Inducible NO synthase (iNOS) and its generation of NO from L-arginine are subject to transcriptional as well as posttranscriptional control by cytokines. Using primary mouse peritoneal macrophages we investigated by which mechanism interleukin (IL)-13 affects the expression of iNOS protein. For induction of iNOS the macrophages were stimulated with interferon (IFN)- γ plus lipopolysaccharide (LPS). Pretreatment with IL-13 downregulated the expression of iNOS protein, whereas the level of iNOS mRNA remained unaltered. The expression of iNOS protein was completely restored by the addition of arginine during the stimulation phase or the presence of an arginase inhibitor during the pretreatment phase. Suppression of NO production and iNOS protein, but not of iNOS mRNA, was also seen, when IL-13 was replaced by purified arginase or when the macrophages were stimulated with IFN- γ /LPS in arginine-free medium. Arginine-deficiency specifically impaired the de novo synthesis of iNOS, but did not affect the production of other macrophage products or the overall protein synthesis. Taken together, these data suggest that the expression of iNOS is regulated translationally by arginine availability. Ongoing studies revealed that the translational control of iNOS protein by arginase also takes place in vivo.