

P061 The E3 ubiquitin ligase Ro52 inhibits IFN- β gene transcription by initiating proteasomal degradation of IRF3
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Induction of type I interferons is a critical cellular response to both viral and bacterial infection. The role of the transcription factor, interferon regulatory factor-3 (IRF3), is well established in this process. Following infection, IRF3 is phosphorylated and translocates to the nucleus to initiate IFN- β transcription, which promotes the subsequent secondary stage of type I interferon release. Ro52 is a RING-finger protein targeted by autoantibodies in both Sjögren's syndrome and systemic lupus erythematosus. We provide evidence that Ro52 targets IRF3 following LPS stimulation. The observed association between Ro52 and IRF3 results in the polyubiquitination of IRF3 and subsequent proteasomal degradation. In addition, we show that Ro52 inhibits IFN- β promoter activity, and that this effect is reversed in the presence of the proteasomal inhibitor MG132. Collectively, these results suggest a role for Ro52 in the negative regulation of type I interferon induction.