

P013 Inhibition of Neutrophil Apoptosis by Type 1 Interferon depends on cross-talk between PI-3-kinase, Protein Kinase C- δ and NF- κ B signaling pathways
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Neutrophils are abundant, short lived leukocytes that play a key role in the defense against rapidly dividing bacteria. However, their life span can be extended during inflammatory responses by a variety of pro-inflammatory cytokines. Inappropriate survival of neutrophils contributes to chronic inflammation and tissue damage associated with diseases such as Rheumatoid Arthritis (RA). IFN- β locally produced by hyperplastic fibroblasts within the pannus tissue of patients with RA contributes to the inappropriately extended lifespan of infiltrating T-cells. Type I Interferons are equally effective at delaying spontaneous apoptosis in human neutrophils. We have investigated the signaling pathways involved in mediating this effect. The anti-apoptotic actions of IFN- β were phosphatidylinositol 3 kinase (PI3K) dependent and analysis of signaling pathways downstream of PI3K revealed that the anti-apoptotic effect of type I Interferon required the activation of protein kinase C- δ and NF- κ B and was dependent on *de novo* protein synthesis. The activation of NF- κ B occurred downstream of PI3K and PKC- δ activation and supershift assays revealed that the p50/p65 and c-Rel isoforms of NF- κ B were specifically involved.