

Spatial and temporal control of early signalling events following Interferon alpha and T-cell Receptor ligation

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Abstract:

Interferons (IFNs) are pluripotent, antiviral cytokines that signal through ubiquitously expressed dimeric receptors. The JAK-STAT is the best characterised signalling pathway emanating from the interferon receptor, but it is now becoming increasingly clear that this cascade alone is not sufficient to generate all of the biological effects of interferons upon different cell types. For example, in recent years it has been illustrated that in Jurkat T-cell line, ligation of the interferon also activates the MAPK pathway. Furthermore, T-cell receptor associated proteins, including Lck, Zap-70 CD45, are all imperative for this MAPK phosphorylation.

In the present study, we showed that two additional T-cell receptor associated proteins become activated on IFN α R stimulation in the Jurkat T cell lines. Firstly, the 95kDa guanosine nucleotide exchange factor, Vav, is shown to be phosphorylated and its expression forms a pre-requisite for the IFN α -induced MAPK response. In addition, a novel role is ascribed to the 76kDa adaptor protein, Slp-76, at the IFNAR. Absence severely diminishes the IFN α -dependent MAPK response and involvement of Slp-76 in this pathway is also shown to be phosphorylation dependent.

From these, and previous studies, it is clear that the IFN α R utilises a growing number of adaptor and kinase proteins which also are recruited in TCR signalling. This raises the possibility that crosstalk occurs between the IFN α R and TCR. To demonstrate this we showed that the MAPK response observed post-IFN α R ligation, relies on an intact TCR being expressed at the cell surface. These results highlight for the first time an intimate connection between the TCR and IFN α R.