

NF- κ B Activation: Elucidating Upstream Events

Article Summary:

NF- κ B (Nuclear Factor-KappaB) is a heterodimeric protein composed of different combinations of members of the Rel family of transcription factors. The Rel/NF- κ B family of transcription factors are involved mainly in stress-induced, immune, and inflammatory responses.

The classical pathway for activation of NF- κ B, a key transcriptional regulator of the immune system, is controlled by the IKK complex. Activated IKK phosphorylates I κ B which is ubiquitinated and rapidly degraded, allowing NF- κ B to translocate from the cytoplasm to the nucleus where it activates gene transcription. However, the mechanisms regarding IKK activation have been elusive.

Now CARMA1, Bcl-10, and MALT1 are helping to fill in the blanks of IKK activation. These proteins are downstream of the T cell receptor (TCR) and upstream of the IKK complex (Fig. 1). Antigen-TCR signaling in the adaptive immune system leads to PKC- η activation and formation of an oligomerization-ubiquitination (Ub)-phosphorylation (P) pathway leading to activated IKK. Oligomerization-Ub-P pathways have also been found to mediate NF- κ B activation through TLR (Toll-like receptor) signaling; suggesting these emerging IKK activation pathways may play key roles in regulating both adaptive and innate immunity.

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About the Author

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