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Meeting abstract

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NF-κB activation by the viral oncoprotein StpC is enhanced by ERK-mediated p52 and RelB upregulation

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Induction of T-cell lymphomas and T-cell growth transformation by Herpesvirus saimiri strain C-488 depend on the saimiri transformation-associated protein of subgroup C (StpC). Previous studies identified the transcription factor NF-κB as the major cellular target of StpC. NF-κB activation relies on a TRAF binding motif in StpC and was enhanced by coexpression of constitutively active Ras or Raf. Concomitantly, StpC repressed Ras-mediated ERK and AP-1 activation. Nevertheless, we now found that specific inhibitors of MEK as well as ERK abrogated cooperative NF-κB activation. Triggering the ERK pathway by external stimuli, e.g. PMA, also enhanced StpC-induced NF-κB activity, however, with a significant delay relative to ERK1/2 phosphorylation. These observations suggested that ERK activity regulates the expression of proteins limiting StpC's capacity to induce NF-κB. Westernblot analyses of proteins representing the classical and alternative pathways of NF-κB activation revealed that StpC cooperates with Ras and even more with PMA to upregulate the expression and nuclear localization of RelB and NF-κB2/p52; furthermore, StpC coimmunoprecipitated TRAF2, but not TRAF6, Ras or Raf. In summary, these data suggest that ERK-inducing signaling pathways support NF-κB activation by StpC through an enhanced expression of NF-κB proteins utilized by the alternative pathway, which is triggered by StpC:TRAF2 complexes. Future studies will have to address the relevance of the enhancing effect for the proliferation of Herpesvirus saimiri-transformed human T lymphocytes.