Reviewer’s report

Title: Respiratory Syncytial Virus and TNFalpha Induce Chemokine Gene Expression Through Distinct NF-kappaB Pathways

Authors:

Laura R Carpenter (lcarpent@rush.edu)
James N Moy (jmoy@rush.edu)
Kenneth A Roebuck (kroebuck@rush.edu)

Version: 1 Date: 16 Sep 2001

Reviewer: Dr Zhu Guo

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Unable to decide on acceptance or rejection until I see revised version

This paper provides some insights on the chemokine induction by RSV. It clearly showed that RSV induced the expression of IL-8, MCP-1 and RANTES at the transcriptional level. However, the data cannot adequately support the conclusion that RSV induces chemokine expression through a distinct mechanism involving NFkB, which is different from that by TNF.

Major concerns:

1. The induction levels of chemokines by TNF in Figure 3 are much lower in comparison to those in Figure 2 (or the labels for TNF and RSV are switched). Further experiments are required to demonstrate the effect of NAC and DEX on optimally induced expression of chemokines by TNF and RSV.

2. Different NFkB complexes could bind to the promoters of MCP-1, IL-8 and RANTES. Therefore, the DNA fragments containing NFkB binding sites for each chemokine gene should be used in EMSA, instead of the consensus binding sequence. In addition, supershift analysis using antibodies against different NFkB subunits should be performed to identify different NFkB complex. Similar experiments should be applied to test the inhibition effect of NAC and DEX.

3. The induction of MCP-1 and IL-8 by RSV appears to precede the translocation of NFkB into the nucleus. It is possible that RSV induces the transcription of MCP-1 and IL-8 mainly through the activity of AP-1. Induction of mouse MCP-1 gene by PDGF has been shown to be accomplished through Sp1 alone. Additional experiments, such as transient-transfection reporter assay, should be performed to clarify if NFkB is involved in the RSV-mediated activation of above two chemokine genes.

In summary, several important points have to be confirmed by experiments and incorporated into the paper.

Competing interests:
None declared.