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View Abstract

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AUTHORS

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Study Group: (none)

ABSTRACT

TITLE: Modulation of inflammatory-related signalling by PERP-mediated apoptosis in uveal melanoma cells

ABSTRACT BODY:

Purpose: Downregulation of PERP (p53 apoptosis effector related to PMP22) is a determinant of impaired apoptosis in aggressive monosomy 3 Uveal Melanoma (UM). The functional importance of PERP downregulation in this scenario is further supported by the requirement of chromosome 3-localised p63 for PERP transcription. Given the role of p63-mediated signalling in inflammatory responses, we hypothesised that altered levels of PERP influence the major NFκB inflammatory signalling pathway.

Methods: The effect of increased PERP expression on NFκB-related proteins was investigated in the human UM cell line Mel202. Changes of specific NFκB proteins and gene expression were assessed in cells transiently transfected with GFP-tagged PERP for 24 hours using Proteome (R&D Systems) and TaqMan (ThermoFisher) NFκB Pathway Arrays. A total of 45 proteins including 4 serine or tyrosine phosphorylation sites and 92 genes, respectively, were analysed. Phosphorylated and non-phosphorylated I Kappa B Alpha (p-IκBα/IκBα) protein expression was determined by immunoblotting.

Results: Following increased PERP expression, protein levels of the transcription factors cRel, p65, p105/p50 and p100/p52 decreased compared to GFP-only control by 0.63-fold, 0.63-fold, 0.85-fold and 0.73-fold, respectively, 24 hours post-transfection (PT). Decreased protein levels mirrored gene expression changes of cRel, p65 and p105/p50, with the exception of p100/p52 which showed an increase by 4.4-fold. While the increase in PERP level did not lead to changes in non-phosphorylated IκBα protein expression at 24 or 48 hours PT, p-IκBα level showed a significant decrease by 0.61-fold (+/-0.042) followed by a significant increase by 1.4-fold (+/-0.019) after 48 hours (One-Way ANOVA +/-SEM, $p<0.05$, $n=3$).

Conclusions: The results support the hypothesis that increased PERP expression in UM cells affect gene/protein expression related to NFκB signalling pathway. The initial response is characterised by a decrease in transcription factors involved in the translocation and activation of NFκB, corroborated by a decrease in p-IκBα, therefore retaining NFκB in an inactive state, which is conceivably in line with the non-inflammatory characteristics of apoptosis. The subsequent increase of p-IκBα level suggests differences between an early and late response in relation to induction of apoptosis by PERP.

(No Image Selected)

DETAILS

PRESENTATION TYPE - PLEASE NOTE, IF YOU CHANGE YOUR PRESENTATION TYPE AFTER APPLYING FOR AN AWARD (BELOW), YOU MUST GO BACK AND RESELECT THE APPLY BUTTON.:
Poster Only : Travel Award Applicant

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CURRENT SECTION: Biochemistry/Molecular Biology

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