Investigating a role for MAP kinase phosphatase-2 in prostate cancer

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INTRODUCTION

An increase in the activity of the mitogen activated protein kinases has been correlated with a more malignant phenotype in several tumor models in *vitro* and in *vivo* (Arnoldussen and Saatcioglu, 2009). A key regulatory off switch for the MAPKs, extracellular signal-regulated kinase (ERK) and c-jun NH_2-terminal kinase (JNK), is the dual specificity phosphatase,DUSP-4 (McCubrey et al, 2007), also known as MAP kinase phosphatase-2 (MKP-2). This study was designed to examine the role of MKP-2 in cell proliferation *in vitro* and cancer development *in vivo.*

Methods

◆Two prostate cancer cells, LNCaP androgen sensitive(AS) and LNCaP androgen insensitive (AI), between p3 and p38,were used in this study.
◆ LNCaP AS and LNCaP AI, after reaching 50-60 % confluency, were infected with Adv. MKP-2 for 40 hrs prior to stimulation with EGF (20 $ngml^{-1}$) and UV (60j/m2).
◆mRNA and protein levels were analysed using PCR, immunofluorescence and western blotting.

Results

LNCaP AS and AI both express endogenous MKP-2 (see Figure 1). overexpression of Adv. MKP-2 was observed between 24hr-72hr in AS (Figure 2) and AI cells (data not shown). Figure 3 shows the nuclear localisation of Adv.MKP-2 in both LNCaP AS and AI.

Figure 1

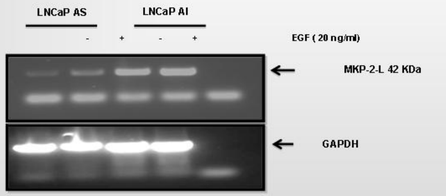


Figure 2

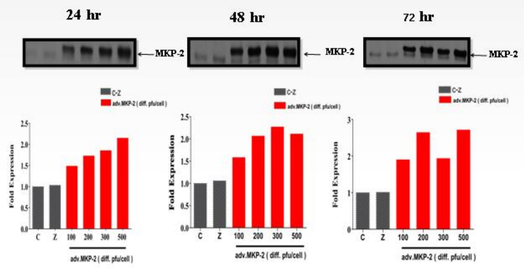
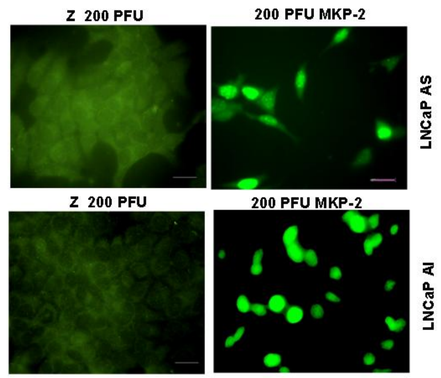


Figure 3



EGF(20 ng/ml) and UV(60 j/m2) stimulated a strong increase In ERK and JNK phosphorylation respectively in both LNCaP AS and AI.

Figure 4

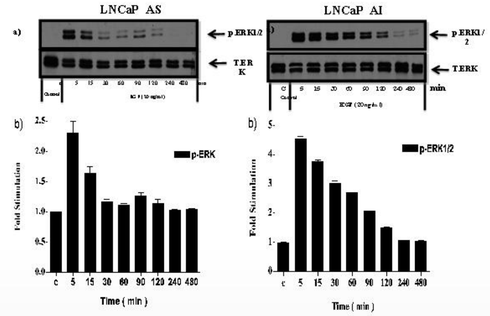
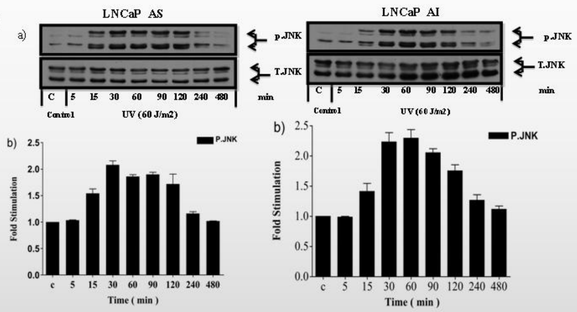


Figure 5



Overexpression of Adv.MKP-2 in both LNCaP AS and AI inhibited the phosphorylation of ERK in response to EGF.

Figure 6

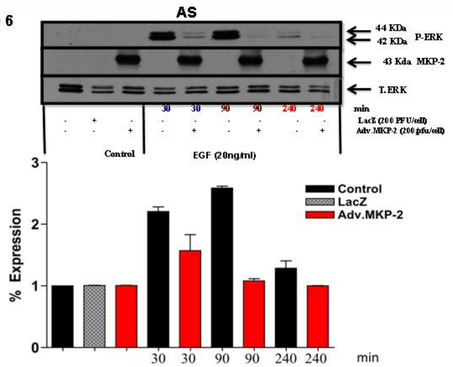
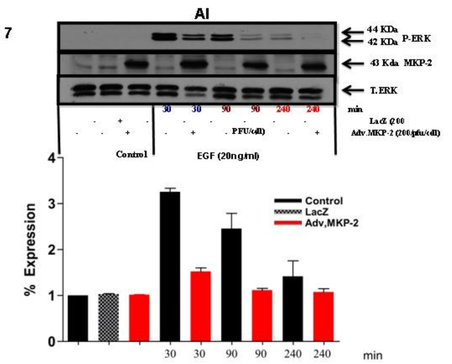


Figure 7



Overexpression of Adv.MKP-2 in both LNCaP AS and AI inhibited the phosphorylation of JNK in response to UV.

Figure 8

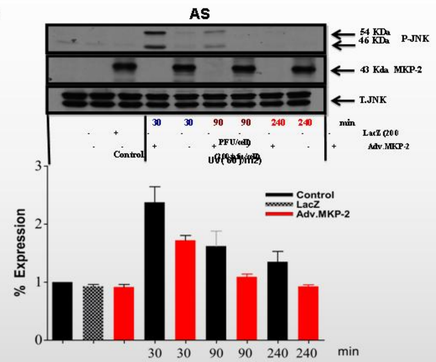
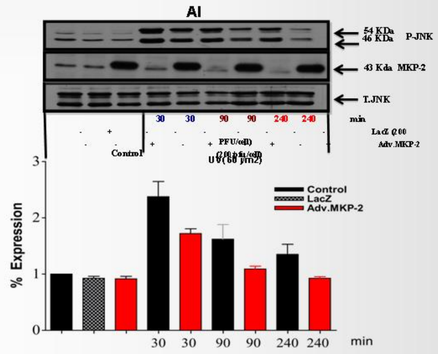


Figure 9



Conclusions

◆Infection of LNCaP AS and AI cells with Adv.MKP-2 significantly inhibited the phosphorylation of JNK and ERK.
◆Future work will examine the effect of overexpression of MKP-2 in both LNCaP AS and AI on cell cycle and *in vivo* xenograft.
◆Endogenous MKP-2 will be Knocked down by siRNA and similar parameters tested.

Acknowledgements

◆The work presented would not have been done without the support from Professor Robin Plevin, Dr. Andrew Paul and Dr.Marie Boyd.
◆I would like to thank all of my work colleagues for their continued support.
◆This work has been supported by Government of Saudi Arabia.

Refrenceces

◆ARNOLDUSSEN,. 2009.. *Mol Cell Endocrinol,* 309, 1-7.
◆MCCUBREY,. *Biochim Biophys Acta,* 1773, 1263-84.