way to characterize the biological significance of our findings. Our results contribute to better understand the pathological signalling of androgen-independent prostate cancer cells and to find novel treatment strategies.

Legal entity responsible for the study: MTA-SE Pathobiochemistry Research Group.

Funding: National Research, Development and Innovation Office - Hungary.

Disclosure: All authors have declared no conflicts of interest.

2012P Heat shock protein 90 chaperones and protein kinase D3 regulates androgen-independent prostate cancer development

A. Varga[1], B. Bátai[2], P. Gyulavári[1], M.T. Nguyen[3], C. Sőti[3], T. Vántus[3]

[1]MTA SE Pathobiochemistry Research Group, Semmelweis University, Budapest, Hungary, [2]MTA-SE Momentum Molecular Oncohematology Research Group, First Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, Hungary, [3]Department of Medical Chemistry, Molecular Biology and Pathobiochemistry, Semmelweis University, Budapest, Hungary

Background: Prostate cancer is the second leading cause of cancer related deaths in men worldwide. Heat Shock Protein 90 (Hsp90) is expressed in tumour cells at high levels – 3-5% of total proteins – and regulates the function of oncogenes and other tumour related proteins. Protein kinase D3 (PKD3) has a proven role in the progression of androgen-independent prostate cancer. In the present study we set out to explore the impact of Hsp90 and PKD3, respectively, on prostate cancer growth and their potential interaction.

Methods: We employed the DU145 and PC3 well-characterized androgen-independent prostate cancer cell lines. Cell viability was determined by Trypan Blue exclusion cell counting. Apoptosis analysis was performed by flow cytometry after AnnexinV and propidium-iodide co-staining. Protein levels were detected by western blot and protein-protein interactions were investigated by co-immunoprecipitation.

Results: We found that the clinically used Hsp90 inhibitor ganetespib induced apoptosis and significantly reduced the viability of the androgen-independent DU145 and PC3 cell lines. The pan-PKD inhibitor CRT0066101 also decreased cell viability of the prostate cancer cells in a dose-dependent manner. Further, we demonstrated that ganetespib reduced PKD3 protein level in a concentration-dependent manner and induced its proteasomal degradation. Finally, a co-immunoprecipitation study revealed a physical connection between PKD3 and Hsp90.

Conclusions: We identified and confirmed an Hsp90-PKD3 chaperone client interaction, which may be important in prostate cancer cell survival. Further studies are under