

P022 Functional studies of BASP1, a WT1 transcriptional co-suppressor

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The Wilms' tumour suppressor protein (WT1) regulates gene expression and plays a central role in the development of several organs, including the kidneys. Furthermore, WT1 is aberrantly expressed in Wilms' tumour (a paediatric malignancy of the kidneys) and many other cancers. Alternative splicing generates WT1 isoforms that function in either transcription or RNA processing. Transcriptionally competent WT1 appears to be particularly important for nephrogenesis. However, the function of WT1 as a transcription factor in this context is poorly understood. Recently, BASP1 was identified as a WT1 transcriptional co-suppressor, which is co-expressed with WT1 during mouse nephrogenesis and in adult kidney podocyte cells. The mechanisms by which BASP1 acts as a co-suppressor, and the physiological relevance of this to WT1 function, are unclear. BASP1 exists within high molecular weight complexes in cells. To examine the mechanism of action of this co-suppressor, studies are currently underway to purify BASP1-containing complexes, and identify their components by mass spectrometry. In addition, the physiological role of BASP1 in kidney development is under investigation using zebrafish. We find that WT1 and BASP1 are co-expressed during zebrafish development and in the adult kidney, and research is now focused towards elucidating the function of BASP1 in nephrogenesis using this model organism.