

P010 Co-operation between WT1 and BASP1 in podocyte differentiation

Hayley Campbell, Laura Green, Stefan Roberts

Faculty of Life Sciences, University of Manchester

The development of the kidney is a complex and highly controlled process orchestrated by a rigid transcriptional network. Tight regulation of this network is crucial and failure can result in aberrant kidney development or carcinogenesis. The Wilms' Tumour Suppressor protein (WT1) is a dichotomous transcription factor involved in regulating the mesenchyme to epithelial transition (MET) and mutation of WT1 can result in the formation of Wilms' Tumour, a paediatric nephroblastoma. Upon kidney maturation, WT1 is confined to the kidney podocyte cells along with a recently identified co-suppressor BASP1. We have been using a cell line model to study the role of WT1 and BASP1 in podocyte differentiation. Microarray analysis has identified a number of proposed WT1 target genes that are either upregulated or downregulated during podocyte differentiation. Using chromatin immunoprecipitation, we have also found that WT1 and BASP1 assemble at the promoters of several previously proposed WT1 target genes. Moreover, we find selective changes in the promoter occupancy of WT1/BASP1 during the transition to podocyte phenotype. Our results suggest a differentiation-dependent interplay of WT1 and BASP1 that regulates the transcription of target genes in podocytes.