

STEM CELLS

DECORIN HAS ROLE
IN DIFFERENTIATION

Nephron progenitor cell differentiation is negatively regulated by the extracellular matrix protein decorin, according to findings in mice just published by researchers at the Maine Medical Centre Research Institute, Scarborough, USA.

Transgenic mice with targeted deletion of forkhead box protein D1 (*Foxd1*^{-/-} mice) show accumulation of undifferentiated nephron progenitor cells, indicating a role for this transcription factor (which is expressed during kidney development and regulates many extracellular matrix proteins) in nephrogenesis. Intriguingly, forkhead box protein D1 is expressed not in nephron progenitor cells, but in adjacent interstitial cells, suggesting that the interstitial cells secrete factors that regulate nephron progenitor cell differentiation. To identify these factors, the researchers compared the transcriptional profiles of kidney cells from *Foxd1*^{-/-} mice with those of their wild-type littermates.

The most prominent differentially expressed gene was *Dcn*, which encodes decorin, a potent antagonist of TGF- β signalling implicated in renal fibrosis. Overexpression of forkhead box protein D1 repressed expression of *Dcn*; conversely, decorin accumulated around renal progenitor cells in *Foxd1*^{-/-} mice. Further, decorin antagonized the response of nephron progenitor cells to BMP-7, a protein previously demonstrated to be essential for nephron progenitor cell differentiation. When the investigators genetically inactivated *Dcn* in *Foxd1*^{-/-} mice, the failure of progenitor cell differentiation was partially ameliorated in the resulting dual-knockout mice. Overall, the findings suggest that decorin promotes retention of nephron progenitor cells in an undifferentiated state through inhibition of BMP-7 signalling.

The researchers also found that forkhead box protein D1 expression maintains interstitial cells in an undifferentiated progenitor-like cell state. "Cells of the *Foxd1* lineage expand in kidney fibrosis and understanding mechanisms regulating the differentiation state of this lineage could identify pathways of clinical importance in chronic kidney disease," states lead investigator Leif Oxburgh.

David Holmes

Original article Fetting, J. L. *et al.* FOXD1 promotes nephron progenitor differentiation by repressing decorin in the embryonic kidney. *Development* doi:10.1242/dev.089078