THE ROLE OF β-CATENIN/FOXO IN HUMAN KIDNEY BIOPSIES

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Aim: To visually examine the role of β-catenin/Foxo and β-catenin/TCF in kidney biopsies from patients with chronic kidney disease and transplant.

Background: β-catenin is the common transcription factor in TFG-β's profibrotic signalling pathways. β-catenin either binds to T-cell factor (TCF) or to forkhead box O (Foxo). β-catenin/TCF promotes cell proliferation and fibrosis while β-catenin/Foxo promotes cell survival. We propose that β-catenin/Foxo is negatively correlated with fibrosis.

Methods: Human kidney biopsies of CKD or a kidney transplant were assessed by Duolink - Proximity Ligation Assay (PLA). This PLA detects interaction of either β-catenin/Foxo or β-catenin/TCF and were examined by Deltavision microscope. Deconvolved images were used for analysis.

Results: The PLA study showed that β-catenin/TCF correlated positively with fibrosis ($r=0.763$ in transplant kidney biopsies, $r=0.948$ in diabetic nephropathy, $r=0.925$ in hypertensive nephropathy, $r=0.914$ in IgA nephropathy, $r=0.682$ in other kidney diseases and overall in CKD with a value of $r=0.806$, $P<0.001$) while β-catenin/Foxo1 correlated negatively with fibrosis ($r=-0.773$ in kidney transplants, $r=-0.834$ in diabetic nephropathy, $r=-0.795$ in hypertensive nephropathy, $r=-0.915$ in IgA nephropathy, $r=-0.739$ in other kidney diseases and overall with a value of $r=-0.740$, $P<0.001$). These PLA studies showed colocalization of β-catenin and Foxo1 in normal kidney biopsies (0-5% fibrosis score considered as normal) and colocalization of β-catenin and TCF1 in diseased biopsies by microscopy imaging.

Discussions: These visualised results identify that β-catenin/Foxo correlated negatively while β-catenin/TCF correlated positively with fibrosis. This may have broad therapeutic approach for fibrotic diseases.