Examining the molecular pathways of cellular senescence in human primary proximal tubular epithelial cells (PTEC) in chronic kidney disease (CKD)

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Results

• CKD is one of the most common chronic diseases in Australia.

• Its progression is critically dependent on the functioning of the specialised parenchymal cell, the PTEC.

• In response to pathobiological drivers of CKD (e.g. oxidative stress), PTEC can: (1) regenerate and repair the damage; (2) undergo cell death; and/or (3) initiate a process of cellular senescence, a program of permanent cell cycle arrest and resistance to cell death.

• In this study we explore the role of cellular senescence and associated molecular pathways in human primary PTEC isolated from histologically “normal” and “diseased” kidney cortical tissue.

Methodology

• Our data provide evidence of cellular senescence in diseased human primary PTEC.

• We hypothesise that cellular senescence blocks repair/regeneration of healthy PTEC = maladaptive response of CKD.

• We are now establishing in situ correlations in clinical kidney biopsies and urine samples to explore the therapeutic potential of targeting senescent PTEC in CKD using senolytic agents (e.g. quercetin, dasatinib).

Conclusion and Future Directions

• The authors gratefully acknowledge the funding provided by Pathology Queensland, the Kidney Research Foundation and National Health and Medical Research Council (NHMRC) Projects Grants (GNT1099222 and GNT1161319).

• We also wish to thank the tissue donors for provision of renal bio specimens.

• For further information, please contact A/Prof. Helen Healy: (Helen.Healy@health.qld.gov.au)

Acknowledgements