Reciprocal inductive interactions between the ureteric bud (UB) and cap mesenchyme (CM) initiate nephron development.

Podocyte-parietal epithelial cell (PEC) cross-talk maintains glomerular microarchitecture and glomerular barrier function.

Biopsy-derived selected renal cells (SRCs) express developing kidney (UB-CM) and podocyte markers.

In models of chronic kidney disease (CKD), administration of SRCs is associated with improvements in glomerular microarchitecture, glomerular barrier function and renal metabolic function.

The introduction set of directionally aligned podocyte AND PEC shared genes functions was queried as the hub node. SRCs, podocytes and PECs share podocyte activity is evidenced by HUVEC tube formation. SRCs represent a standalone cell-based platform with renal reparative and restorative potential.

A vegfa anchored podocyte-PEC transcriptome expressed by cellular components of SRCs may participate in recapitulating events associated with the developing nephron and mediate the improved glomerular microarchitecture and glomerular barrier function associated with its administration in CKD models.

SRCs represent a standalone cell-based platform with renal reparative and restorative potential.

SRC-secreted VEGFA may act as a potency marker for product (REACT®/rilparencel) release.

The SRC admixture is composed of 3 components of the nephron characterized by ureteric bud, cap mesenchyme and podocyte markers.

SRCs were isolated from human kidneys obtained from the National Disease Research Interchange (Philadelphia, PA; protocol ID R012 0100A) and characterized by vascular endothelial growth factor A (VEGFA) gene expression by qPCR.

The intersection set of directionally aligned podocyte AND PEC shared genes functions was identified by knowledgebase.

Angiogenic activity of VEGFA secreted by SRCs was evaluated using human umbilical vein endothelial cell (HUVEC) tube formation assay.

RESULTS CONTD.

RESULTS

• osr1, six2, lhx1, fgf8, fgf9, nphs1, nphs2, vegfa, cd44 and hes1 are expressed by SRCs, podocytes and PECs.

• These genes are associated with maintenance of undifferentiated nephron precursors, maturation of the glomerular barrier, formation of the glomerular capillary bed and nephron development.

• vegfa is a hub node within this network.

• SRCs express vegfa and secrete VEGFA whose angiogenic activity is evidenced by HUVEC tube formation.

RESULTS CONTD.

DISCUSSION

• A vegfa anchored podocyte-PEC transcriptome expressed by cellular components of SRCs may participate in recapitulating events associated with the developing nephron and mediate the improved glomerular microarchitecture and glomerular barrier function associated with its administration in CKD models.

• SRCs represent a standalone cell-based platform with renal reparative and restorative potential.

• SRC-secreted VEGFA may act as a potency marker for product (REACT®/rilparencel) release.

CLINICAL STATUS

• Preliminary data from patients with advanced CKD (Stage 3A-4) suggest that administration of SRCs (REACT®/rilparencel) is associated with preservation of kidney function.

• REACT®/rilparencel is currently being evaluated in a Phase 3 Global Registrational trial for treatment of CKD and has been awarded Regenerative Medicine Advanced Therapy Designation by Food and Drug Administration.

REFERENCES


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POSTER CONTACT

Prakash Narayan, PhD
VP - R&D
Prakash.Narayan@prokidney.com