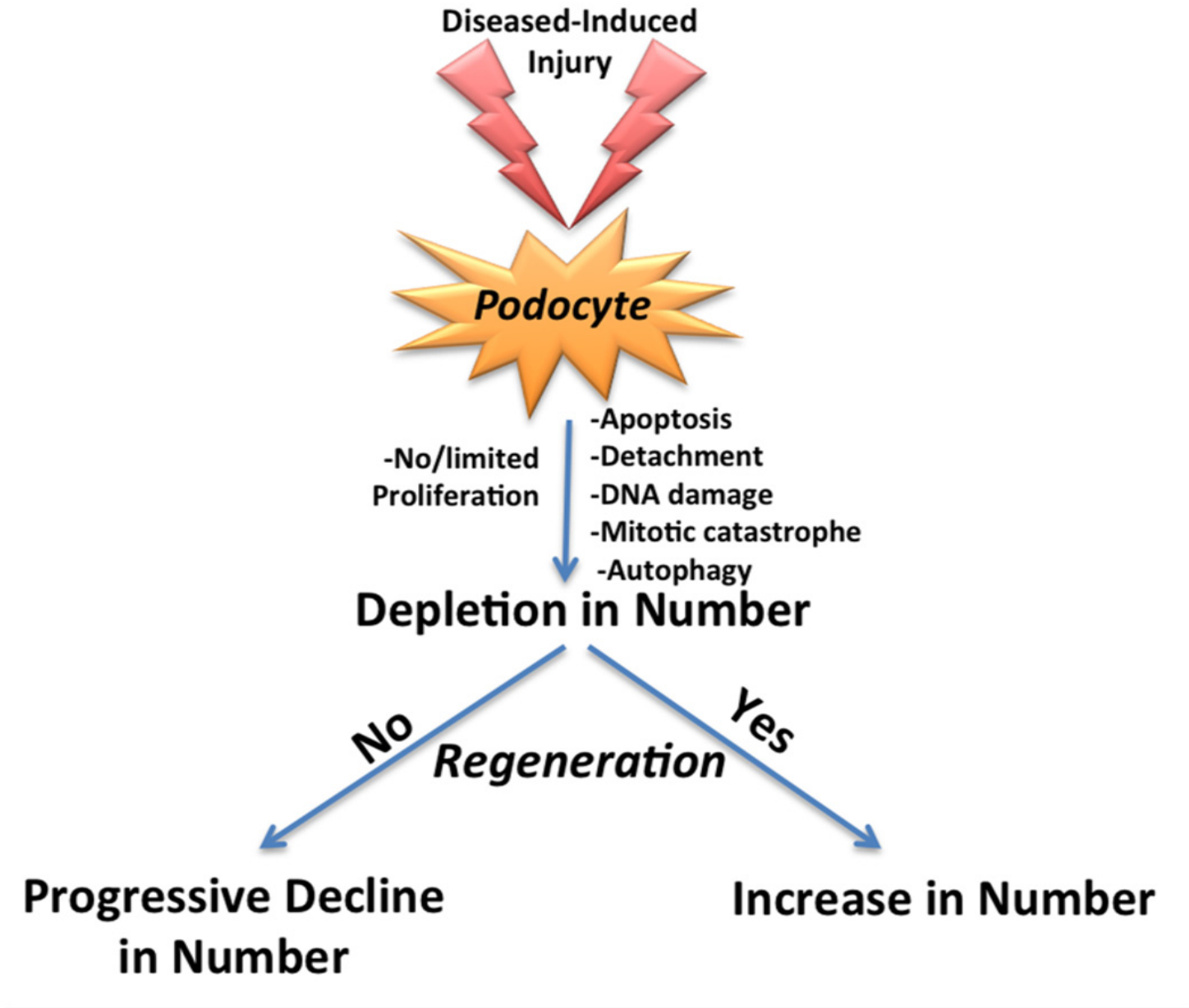
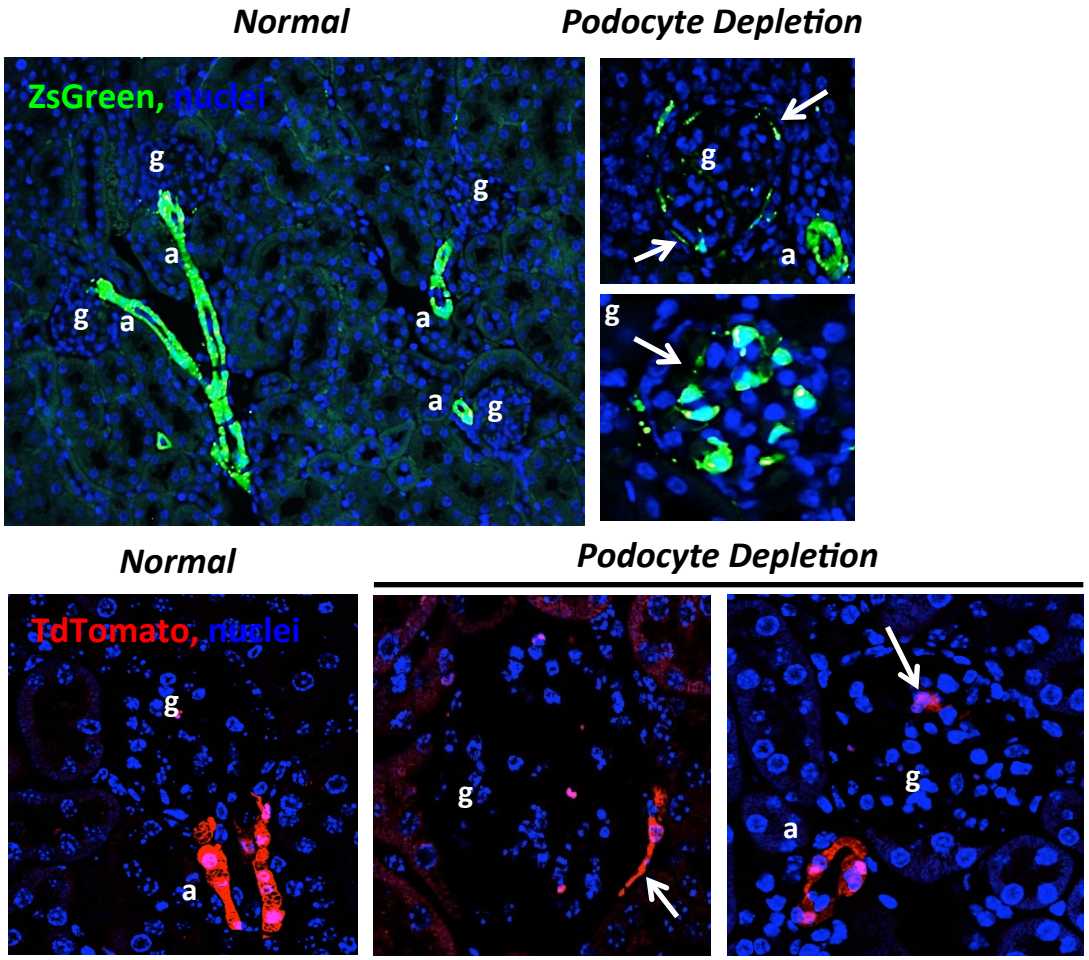
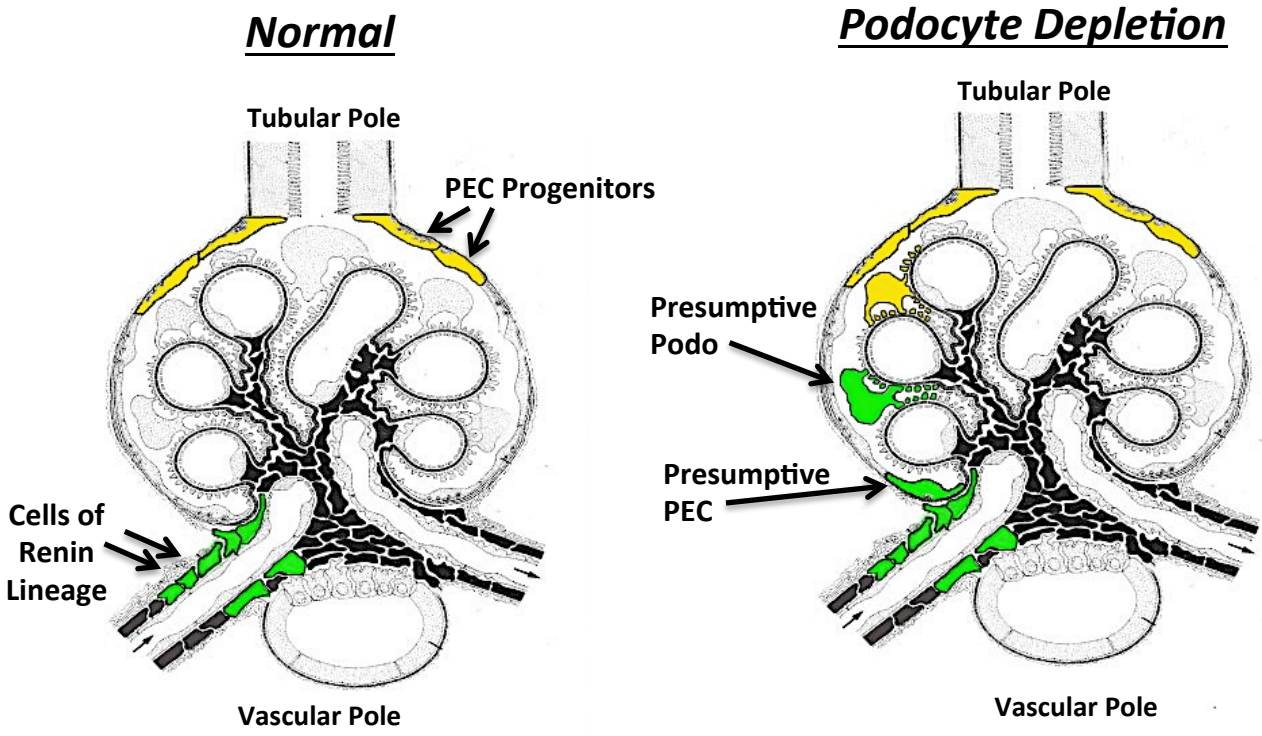

Diseased-Induced Injury
Podocyte
-No/limited Proliferation
-Apoptosis
-Detachment
-DNA damage
-Mitotic catastrophe
-Autophagy
Depletion in Number
No
Regeneration
Yes
Progressive Decline in Number
Increase in Number


Normal
Podocyte Depletion
ZsGreen, nuclei
g
a
Normal
Podocyte Depletion
TdTomato, nuclei
g
a


Normal
Tubular Pole
PEC Progenitors
Cells of Renin Lineage
Vascular Pole
Podocyte Depletion
Tubular Pole
Presumptive Podo
Presumptive PEC
Vascular Pole

# GLOMERULAR STEM / PROGENITOR CELLS

## *Identification that cells of renin lineage are novel adult progenitors*:

When podocyte number is depleted in glomerular diseases, they cannot self-renew because they cannot undergo adequate proliferation. The consequences of inadequate repair include proteinuria, and progressive glomerular scarring. Several labs are seeking to identify potential stem/progenitor cells that might augment podocyte regeneration in states of depletion. Cells of renin lineage are located in the juxta-glomerular compartment of the kidney, and are best known for being the sole source of the body's renin supply. In collaboration with Ken Gross, we showed that in several strains of renin reporter mice, the forced depletion of podocytes was accompanied by the migration of cells of renin lineage to the glomerulus (*a*). A subset of cells of renin lineage in the glomerulus begin to express four different podocyte specific proteins, and acquire characteristic ultrastructural features of podocytes such as foot processes and slit diaphragms.
Similarly, when podocyte number decreases in aging, cells of renin lineage migrate to the glomerulus, and also take on a podocyte phenotype (*b*). Noteworthy is that the reservoir of cells of renin lineage progenitors decreases significantly in aging, thus limiting the regenerative pool of progenitors. These studies provide novel opportunities to study a recently discovered adult podocyte progenitor source.

(a) Pippin JW, Sparks MA, Glenn ST, Buitrago S, Coffman TM, Duffield JS, Gross KW**,** **Shankland SJ**. Cells of renin lineage are progenitors of podocytes and parietal epithelial cells in experimental glomerular disease. Am J Pathol. 2013 Aug;183(2):542-57. *PMID: 23769837. PMCID: 3730767.*

(b) Pippin JW, Glenn ST, Krofft RD, Rusiniak ME, Alpers CE, Hudkins K, Duffield JS, Gross KW, **Shankland SJ**. Cells of renin lineage take on a podocyte phenotype in aging nephropathy. Am J Physiol Renal Physiol. 2014 May 15;306(10):F1198-209 *PMID: 24647714. PMCID: 4024732.*

## Schema showing proposed dual role for PECs and CoRL as adult podocyte progenitors in glomerular disease.

Images from normal adult kidney and following podocytes loss during kidney disease in RenCre;ZsGreen reporter mice. Note the vascular arteriolar wall is labeled due to Renin expression during development and the adjacent glomerulus is devoid of cells of renin lineage. Following podocyte loss cells can be seen along Bowman's capsule and in the glomerular tuft. Images from RenCreER;tdTomato reporter mice that received tamoxifen to induce recombination and activate tdTomato expression in renin producing cells at 6 weeks of age. Only cells in the JGA at the tip of the afferent arteriole are permanently labeled. Note that following podocytes loss during kidney disease, there is migration of renin labeled cells from the Bowman's capsule and the glomerular tuft. Schema shows the fate of juxtaglomerular cells of renin lineage and PEC progenitors at the tubular pole in the setting of kidney disease. Both of these cells from fate mapping experiments have the capacity to acquire podocyte qualities.