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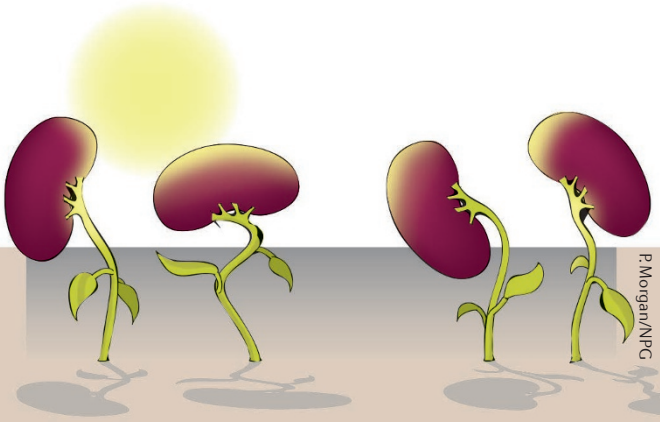

P. Morgan/NPG

REGENERATIVE MEDICINE

Isolation of nephron progenitors: a step towards growing kidneys?

A recent study has described the isolation of nephron progenitors, providing opportunities for further understanding of nephrogenesis and, perhaps, the potential to regenerate kidneys.

In humans, nephrogenesis occurs before weeks 34–36 of embryological development, when nephrogenic progenitor (NP) cells are fully depleted and nephrogenesis, therefore, stops. Previous studies have demonstrated that a small pool of cells that express *CITED1* and *SIX2*, the so-called master genes of renal development, exists in the cap mesenchyme, and are nephron-committed, multipotent, and capable of generating all the segments of the nephron. As they are depleted before birth, these NP cells are not well characterized in humans, and most studies have focussed on isolation of cells that are either *SIX2*$^+$ or *CITED1*$^+$ from murine kidneys, but not those positive for both genes. Now, for the first time, cells expressing both *SIX2* and *CITED1* have been isolated from human fetal kidney (hFK).

Da Sacco and colleagues used hFK tissue of 17 weeks gestational age for their studies. Using Smartflare fluorescent-tagged RNA probes designed to recognize *SIX2* and *CITED1* mRNA in live cells, they confirmed the presence of *SIX2*$^+$*CITED1*$^+$ NPs within the cap mesenchyme. By using both Smartflare and antibody staining, they were also able to identify both *SIX2*$^+$*CITED1*$^+$ (uninduced) and *SIX2*$^+$*CITED1*$^-$ (induced) NPs. After creating a single-cell suspension of hFK cells, FACS analysis showed that 0.16% of cells were positive for both *SIX2* and *CITED1*. In accordance with previous studies, cultured NPs lost expression of *SIX2* and *CITED1* with increased passaging, suggesting differentiation. Loss of *CITED1* was induced by exposure to BMP-7 and Wnt9b, which are known to induce differentiation into epithelial renal cells. Confocal microscopy also confirmed that *SIX2*$^+$*CITED1*$^+$ cells localized into recognizable developing renal structures, forming tubular structures and suggesting nephrogenic potential.

> “*SIX2*$^+$*CITED1*$^+$ cells localized into recognizable developing renal structures...”

The authors hope that their novel *in vitro* system will both facilitate studies of human renal development and provide a tool for renal regeneration.

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ORIGINAL ARTICLE Da Sacco, S. *et al.* Direct isolation and characterization of human nephron progenitors. *Stem Cells Transl. Med.* http://dx.doi.org/10.5966/sctm.2015-0429 (2016)