Response to ‘Could tubular interstitium be a source of adult epithelial stem cells?’


Cappello and Zummo suggest that interstitial cells could be a source of stem cells that are 'epithelial oriented'. This is not a new concept. Although interstitial cells can derive from bone marrow, contrary to their interpretation of our studies, our work indicates that few if any epithelial cells derive from bone marrow, and only a minority of endothelial cells derive from bone marrow cells after injury. It is possible that a sub-population of surviving intratubular cells possess multi-potentiality and selectively proliferate after damage to neighboring cells. To date, however, studies have not unequivocally identified cells expressing 'stem cell' markers in the tubule. Our studies have supported a model whereby many surviving renal epithelial cells after injury become dedifferentiated, take on mesenchymal characteristics, proliferate, and subsequently redifferentiate into functional epithelial cells restoring the integrity of the epithelium.

Populations of cells have been isolated from the human and rodent kidney that express stem cell antigens in vitro and under certain conditions express epithelial markers. Oliver et al. reported a stem cell niche in the papillary interstitium based on 5-bromo-2’-deoxyuridine retention, although thymidine analogs may not be ideal for tracking cell fate due to potential leakage from the cells and uptake by others. If interstitial cells are precursors to epithelial cells in the adult mammalian kidney, they would have to cross the basement membrane. Interstitial multipotent mesenchymal cells have been demonstrated to generate new tubules in adult fish following partial nephrectomy; however, unlike fish, mammalian kidneys do not regenerate new nephrons.

Interstitial cells with mesenchymal stem cell characteristics can also have a significant role in repair through processes that do not involve differentiation into epithelial cells. We and others have shown that systemic infusion of bone marrow-derived mesenchymal cells can result in functional improvement in the kidney after an ischemic insult. This effect may be due to paracrine effect on the repair process due to potentiation of proliferation of surviving renal epithelial cells. In addition, the interstitial cells may decrease inflammation, which is an important contributor to the pathophysiology of many forms of renal injury. Another possibility is that the interstitial cells may play a trophic role in mesenchymal to epithelial conversion and differentiation of cells into endothelial structures.
Thus, renal interstitial cells may play an important role in recovery of the kidney epithelium after injury but not necessarily by being ‘epithelial oriented’.

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