Stem Cells in the Adult Kidney

Juan Oliver and **Qais Al-Awqati**

Columbia University College of Physicians and Surgeons, New York, NY

Although cell division is infrequent in the adult kidney, this organ has a remarkable capacity to repair and regenerate, as illustrated by the cellular proliferation and functional recovery after ischemic tubular necrosis. The origin of newly generated renal cells is largely undefined, but some cells appear to originate from division of fully differentiated cells, and recent work has shown that other cells might derive from the bone marrow. In addition, by analogy with other organs, it is likely that new cells also derive from organ-specific pluripotent cells (i.e., adult renal stem cells). Organ-specific stem cells were initially recognized in self-renewing organs such as the hematopoietic system, skin, and intestinal epithelia, but they are also present in organs that do not have rapid rates of cell turnover such as the nervous system, prostate, liver, etc. While the number of organs harboring adult stem cells continues to grow, it remains unknown whether the adult kidneys possesses stem cells among its many cell types.

In an attempt to search for stem cells in the adult kidney, we have used a two-pronged strategy. First, we reasoned that if renal stem cells exist in the adult kidney, they are likely present in embryonic life and that embryonic and adult renal stem cells may share molecular characteristics. At the beginning of its development, the embryonic kidney contains two cell types, metanephric mesenchyme and ureteric bud, and the simplicity of this system made it attractive to examine for the presence of stem cells. Indeed, we found that the metanephric mesenchymal cells are able to differentiate into epithelia, myofibroblasts, and smooth muscle and to self renew, suggesting that they are embryonic renal stem cells.

In the second strategy, we made use of the characteristically slow cycling time of organ-specific adult stem cells. Cells with slow cycling time can be distinguished by retention of a nucleotide label such as bromo-deoxyuridine (BrdU) which is incorporated into the DNA of the cells during its synthesis. If after administration of a "pulse" of BrdU the cells are observed for long periods of "chase", only the slow cycling cells retain a high enough concentration of label. Adult organ-specific stem cells are often termed "label-retaining cells." Accordingly, to identify adult kidney-specific stem cells, we administered BrdU to 3-day old rat and mice pups and analyzed their adult kidneys. We found that starting at 2 months of chase only the renal papilla contains an abundant population of cells that retain a strong BrdU signals and are thus slow cycling. These cells are likely involved in renal repair because while they remain in the papilla throughout the life of the animal, they disappear after the reparative phase of transient renal ischemia. Isolation of renal papillary cells showed that *in vitro* the cells are multi-potent and display other characteristics of adult stem cells. The results suggest that the renal papilla is the "niche" for adult kidney stem cells.