STEM CELLS AND ANIMAL MODELS OF KIDNEY DISEASE

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Adult stem cells have been characterized in several tissues as a subpopulation of cells capable to maintain, generate and replace terminally differentiated cells in response to physiological cell turnover or tissue injury. Little is known regarding the presence of stem cells in the adult kidney but it is documented that after an acute injury, the kidney can regenerate itself by increasing the proliferation of some resident cells. The origin of these cells is largely undefined, but some studies suggest the possibility that they derive from resident renal stem or progenitor cells. During kidney development, the metanephric mesenchymal cells give rise to all the epithelial cell types of the nephron other than those of the collecting ducts which derive from ureteric bud cells. Certainly, the characterization of the embryonic renal stem cells would provide clues to identify adult renal stem cells. The identification of the renal stem cell takes advantage of the slow dividing time typical of stem cells. In tubuli of normal rat kidneys, it has been demonstrated the existence of slow-cycling cells, defined as progenitor-like tubular cells -mainly adjacent to capillary endothelial cells- which underwent division during the recovery after ischemia/reperfusion injury and function as a source of regenerating cells. In mouse models and in humans, there is evidence that extrarenal stem cells of bone marrow origin take part to renal cell turnover and regeneration. This remarkable stem cell ability prompted us to investigate the reparative potential of mesenchymal stem cells to cure acute renal failure. We studied the model of acute renal injury induced in mice by the nephrotoxic agent cisplatin. Injection of mesenchymal stem cells isolated from male bone marrow remarkably protected cisplatin-treated syngeneic female mice from renal function impairment and severe tubular injury. Y-chromosome containing cells localized in the context of the tubular epithelial lining and displayed binding sites for *Lens culinaris* lectin, indicating that mesenchymal stem cells engraft the damaged kidney and can differentiate into tubular epithelial cells. Of note, mesenchymal stem cells also markedly accelerated tubular cell proliferation in response to cisplatin-induced damage, thereby restoring renal structure and function. In this experimental model, preliminary data indicate an important role of mesenchymal–derived growth factors in tubular cell regeneration. Recent experiments in NOD-SCID mice show a protective effect of human mesenchymal stem cells of bone marrow- and cord blood-origin on renal function impairment, renal injury and apoptosis.These results offer a strong case for exploring the possibility that mesenchymal stem cells by virtue of their renotropic property and tubular regenerative potential may have a role in the treatment of acute renal failure in humans.