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REVIEW ARTICLE

Urine-derived stem cells: A novel and versatile progenitor source for cell-based therapy and regenerative medicine

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Abstract Engineered functional organs or tissues, created with autologous somatic cells and seeded on biodegradable or hydrogel scaffolds, have been developed for use in individuals with tissue damage suffered from congenital disorders, infection, irradiation, or cancer. However, in those patients, abnormal cells obtained by biopsy from the compromised tissue could potentially contaminate the engineered tissues. Thus, an alternative cell source for construction of the neo-organ or functional recovery of the injured or diseased tissues would be useful. Recently, we have found stem cells existing in the urine. These cells are highly expandable, and have self-renewal capacity, paracrine properties, and multi-differentiation potential. As a novel cell source, urine-derived stem cells (USCs) provide advantages for cell therapy and tissue engineering applications in regeneration of various tissues, particularly in the genitourinary tract, because they originate from the urinary tract system. Importantly, USCs can be obtained via a non-invasive, simple, and low-cost approach and induced with high efficiency to differentiate into three dermal cell lineages.

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Introduction

Stem cells have shown potential as a therapeutic strategy for repair of various tissues, including genitourinary organs. Stem cell-based therapy for genitourinary tissue repair is most relevant to congenital conditions or disorders such as radiation damage, chronic inflammatory diseases, and tumors. Multiple types of stem cells have been used in preclinical animal models to repair or regenerate tissue, employing either trans-differentiation or paracrine effects to stimulate endogenous cells participating in tissue regeneration. These stem cells include pluripotent stem cells such as embryonic stem cells (ESCs); induced pluripotent stem cells (iPS),[1] multipotent mesenchymal stem cells (MSCs), including bone marrow-derived mesenchymal stromal cells (BMSC)[2–6]; adipose-derived stem cells (ASCs)[7]; hair follicle stem cells[8]; and amniotic fluid stem cells.[9]

We recently found that a subpopulation of cells isolated from urine possess biological characteristics with stem cell characteristics, i.e. clonogenicity, cell growth patterns, expansion capacity, cell surface marker expression profiles, multipotent differentiation, pro-angiogenic paracrine effects, immune-modulatory properties, and easily-induced pluripotent stem cells. Thus, we have termed these cells "urine-derived stem cells" or USCs.[10–12] These stem cells can be obtained from humans and different animal species, such as monkeys, pigs, and rabbits. Although stem cells make up a small proportion of the total cell population, they play an important role in replacing aged, injured, and diseased cells and promoting tissue regeneration from organs where they originate. USCs consistently expressed MSC/pericyte markers and some key cell surface markers, but not hematopoietic stem cell markers (except for MHC-1), endothelial cell markers (CD31), or human leukocyte antigen (locus) DR (HLA-DR). Compared to other MSCs, USCs have several advantages: i) they can be obtained regardless of a person's age, gender, or health condition (except in those urinary tract infection and anuria); ii) the cells can be collected using a simple, safe, low-cost and non-invasive procedure; iii) it is easier to isolate pure stem cells, which do not require an enzyme digestion process; iv) the cells display telomerase activity so that they are able to generate more cells, but not teratomas or tumors; and v) they differentiate into podocytes, smooth muscle, and endothelial and urothelial cells with higher efficiency.[10–12]

Origin of USCs

The source of endogenous stem cells in the kidney may be the renal tubules or the papilla. Glomerular parietal epithelial cells function as stem cells in the glomeruli (Fig. 1), displaying self-renewal properties and the potential to give rise to podocytes and proximal tubular cells.[13–28]

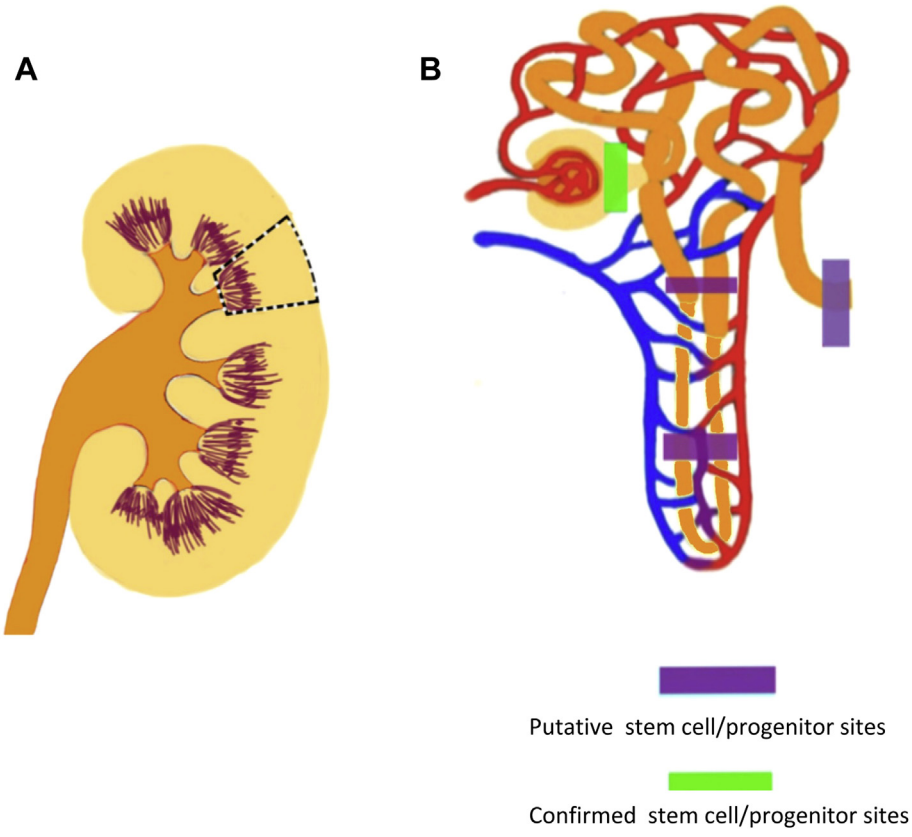

Figure 1 Possible sources of endogenous renal stem cells in the kidney. (A) The dotted area depicts the potential existence of renal stem cells, which are possibly the sources of urine-derived stem cells. (B) A detailed depiction of possible locations of urine stem cells.