

## Urine stem cells - A novel Insight

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Stem cells are a class of undifferentiated cells that are able to differentiate into specialized cell types that have capacity to serve any function making them powerful enough to regenerate damaged tissue under right conditions. Stem cells commonly come from 2 main sources:

1. Embryo(blastocyst)
2. Adult tissue (adult stem cells)

Harvesting stem cells for therapy one day could be as simple as asking patient for a urine sample. (1) Tissue engineering is a promising field offering the possibility of providing scaffolds in order to structurally and functionally restore the altered pathological tissue. (2) Stem cell research has remained to be an exploding and exciting area possessing the potential of improving healthcare.

Two types of stem cells known 1. Pluripotent stem cells(PSCs) 2. Somatic stem cells. Most commonly investigated PSCs include Embryonic Stem Cells (ESCs) and Induced Pluripotent stem cells(iPSCs). iPSCs, which bypass the ethical issue of ESCs resulting from destroying an early embryo, however some obstacles including long term manipulation, low reprogramming and differentiation efficiency and tumorigenicity have prevented iPSCs from a broad range of clinical applications. (2)

The somatic stem cells, bone marrow derived stem cells(BMSCs) and Adipose derived (2) stem cells(ADSCs) have been investigated for long periods of time. Although they have potential to differentiate into various cells types, they are obtained through an invasive procedure and could bring damage to the patients.

Therefore, within last decade urine derived stem cells(UDSCS) are emerging as a promising cell source due to following several advantages:

1. They can be obtained regardless of persons' age, gender, or health condition (except those in urinary tract infection and anuria)
2. Cells can be obtained using simple, safe, low cost and non-invasive procedure.
3. It is easy to isolate pure stem cells, which do not require an enzyme digestion process
4. Display telomerase activity so that they are able to generate more cells, but not teratomas or tumours.
5. They differentiate into podocytes, smooth muscle, endo epithelial and uroepithelial cells with higher efficacy. (3)

Successfully directed stem cells from urine can potentially become not only bladder type cells but could also form bone, cartilage, fat, skeletal muscle, nerve and endothelial cells. The multipotent nature of cells suggests their potential use in variety of therapies. (1)

UDSCs have been selected as alternative starting cells to generate iPSCs. UDSCs derived disease specific iPSCs have already been established preliminarily in cardiac diseases, abnormal endocrine diseases, abnormal haemorrhagic diseases, aneuploidy disease such as Downs syndrome, neural disease, muscular disease, systemic lupus erythematosus, cryptorchidism and hypercholesterolemia. (2)

Kidney epithelial cells, a common component of urine, could be converted into induced Pluripotent stem cells (iPS), which have the ability to differentiate into any cell type found in the body. (4) iPS cells reprogrammed from urine developed at twice speed of iPS cells made from blood or skin cells. Combined with relative simplicity of collecting urine sample, the use of human urine cells in the therapies for neurodegenerative disease could become highly viable. After forming iPS from urine cells, Pei and colleagues formed neural progenitor cells by introducing them in a neuron growth medium. (4) Thus with a potentially safer, more abundant, and more personalised source of neurons, therapies for neurodegenerative diseases could be potentially revolutionized in coming years.

The source of stem cells in urine may be the renal tubules or papilla in kidney. Glomerular parietal cells in glomeruli, function as stem cell as they possess potential to give rise to podocytes and proximal tubular cells. Further more, USCs expressed CD146+/CD31 similar to that expressed in parietal cells and podocytes in glomerulus, while renal tubules epithelial cells, bladder and ureter

urothelial and smooth muscle cells did not, implying that USCs are likely transitional cells at the parietal /podocytes interface originating from renal tissue. (3)

USCs express telomerase activity and are highly expandable, but unlike iPS cells or Embryonic Stem cells the Urine derived stem cells do not form tumour when implanted in body. (3) UDSCs also secrete a battery of growth factors and cytokines have been positive in models of diabetic erectile dysfunction, stress urinary incontinence, bladder reconstruction and renal insufficiency.

Different donor specific cells isolated from blood, skin, hair require invasive methods for isolation and complex costly reagents to culture. (5) UDSCs can be obtained through a simple, non invasive low cost approach that avoids surgical procedures and can be differentiated into three layers (ectoderm, mesoderm, endoderm) that are a hallmark of true stem cells (1) and also differentiate into specific cell types making it a novel cell source. And as being able to use patients own stem cells for therapy is considered advantageous because they do not induce immune responses and rejection.

Thus USDs due to its minimally invasive, cost effective, easy isolation, superior favourable gene profile than conventional stem and inherent multipotent potential make them a new source of seed cells in tissue engineering.

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