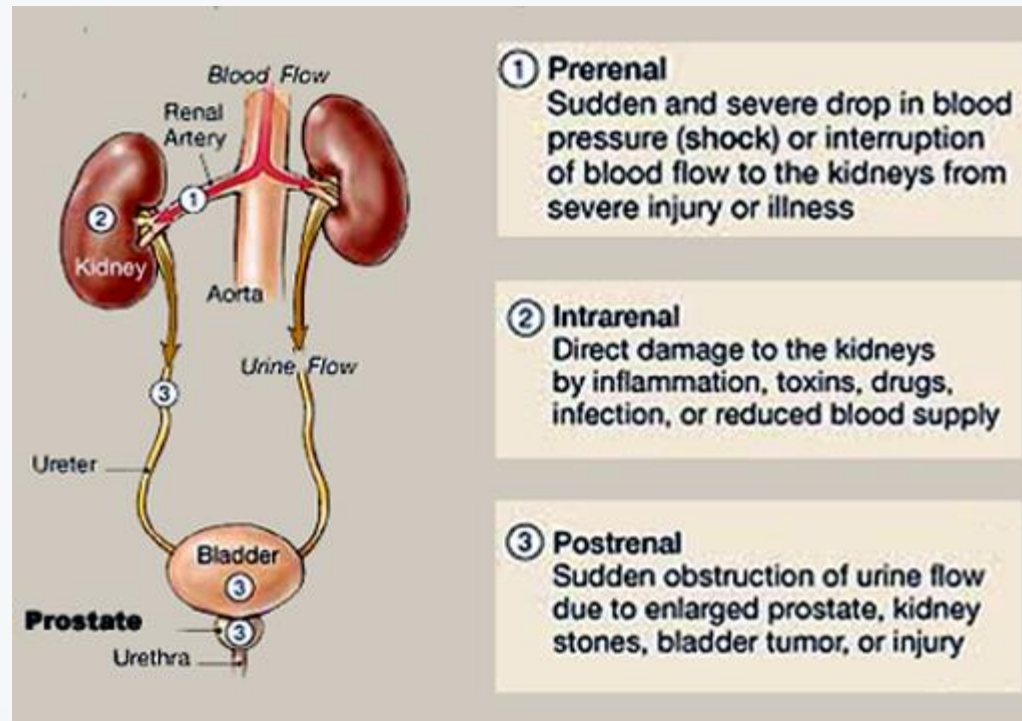


A decorative vertical bar on the left side of the slide, featuring horizontal stripes in various colors (green, blue, purple, pink, red, orange, yellow, green, blue, purple, pink) and several translucent, 3D-style bubbles of different sizes.

Introduction

Acute kidney injury (AKI)

- Definition
- Etiology

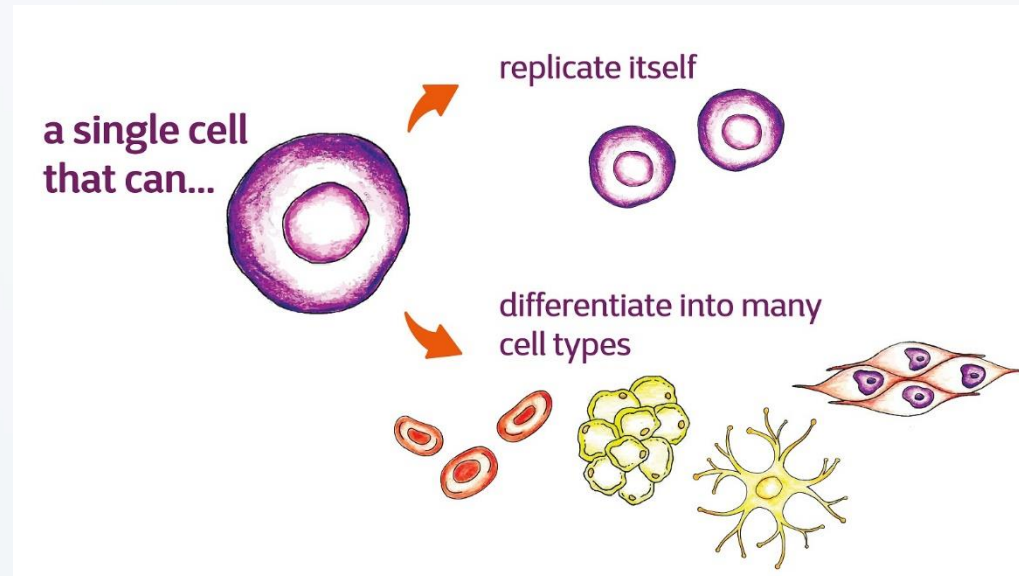


- Cisplatin-induced AKI
- Treatment (drug, dialysis, transplantation, stem cell) 2

Stem cell-based therapy

Types:

- Embryonic stem cells (ESCs)
- induced-pluripotent stem cells (iPSCs)
- Adult stem cells (ASCs)
- ✓ Endometrial stromal/stem cells (EnSCs)



Stem/stromal cell therapy in renal diseases

Preclinical studies
and clinical trials

AKI induced by ischemia/reperfusion
AKI induced by cisplatin
Polycystic kidney disease
Diabetic nephropathy
Kidney transplantation

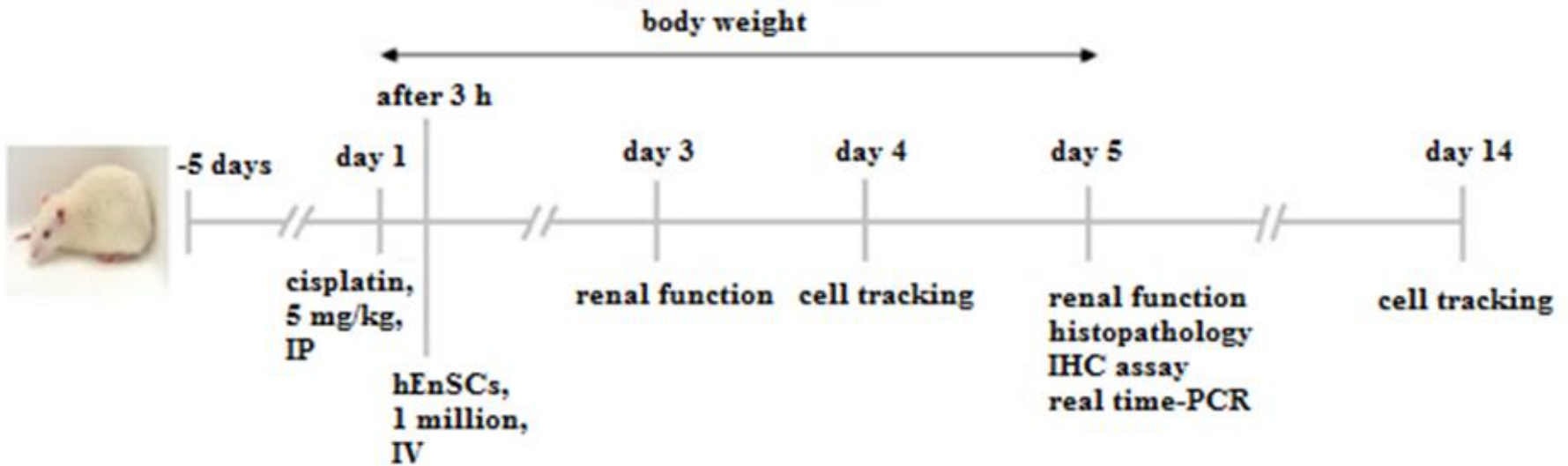
- ↓ Acute tubular necrosis
- ↓ Macrophage activation and migration
- ↓ Interstitial fibrosis and myofibroblast formation

- ↓ Apoptosis
- ↑ Tubular cell proliferation
- ↑ Renal function and morphology

- ↓ Creatinine clearance
- ↓ Peritubular fibrosis and glomerulosclerosis
- ↓ Kidney weights
- ↑ Cortical and medullary vascular density

- ↓ Extracellular matrix deposition
- ↓ Urinary albumin/creatinine ratio

- Suppression of T cell activation
- ↓ Interstitial fibrosis
- ↑ Allograft viability and survival
- ↑ FOXP3+ Tregs

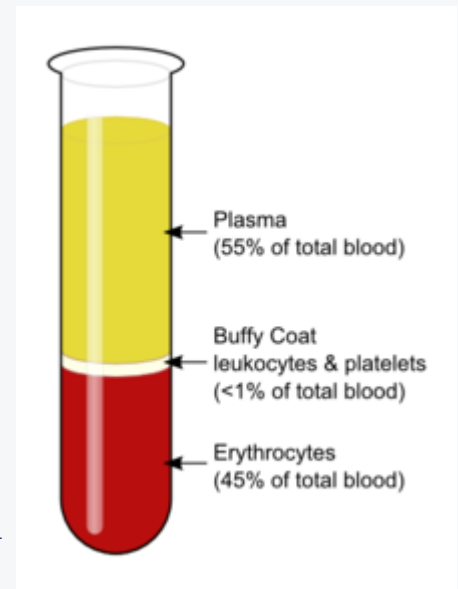


Groups

- Intact: No treatment
- Model: 5 mg/kg wb, IP
- PBS: 5 mg/kg wb, IP; 200 μ l PBS, IV
- Cell: 5 mg/kg wb, IP; 1 million hEnSCs , IV

Biochemical markers of renal function

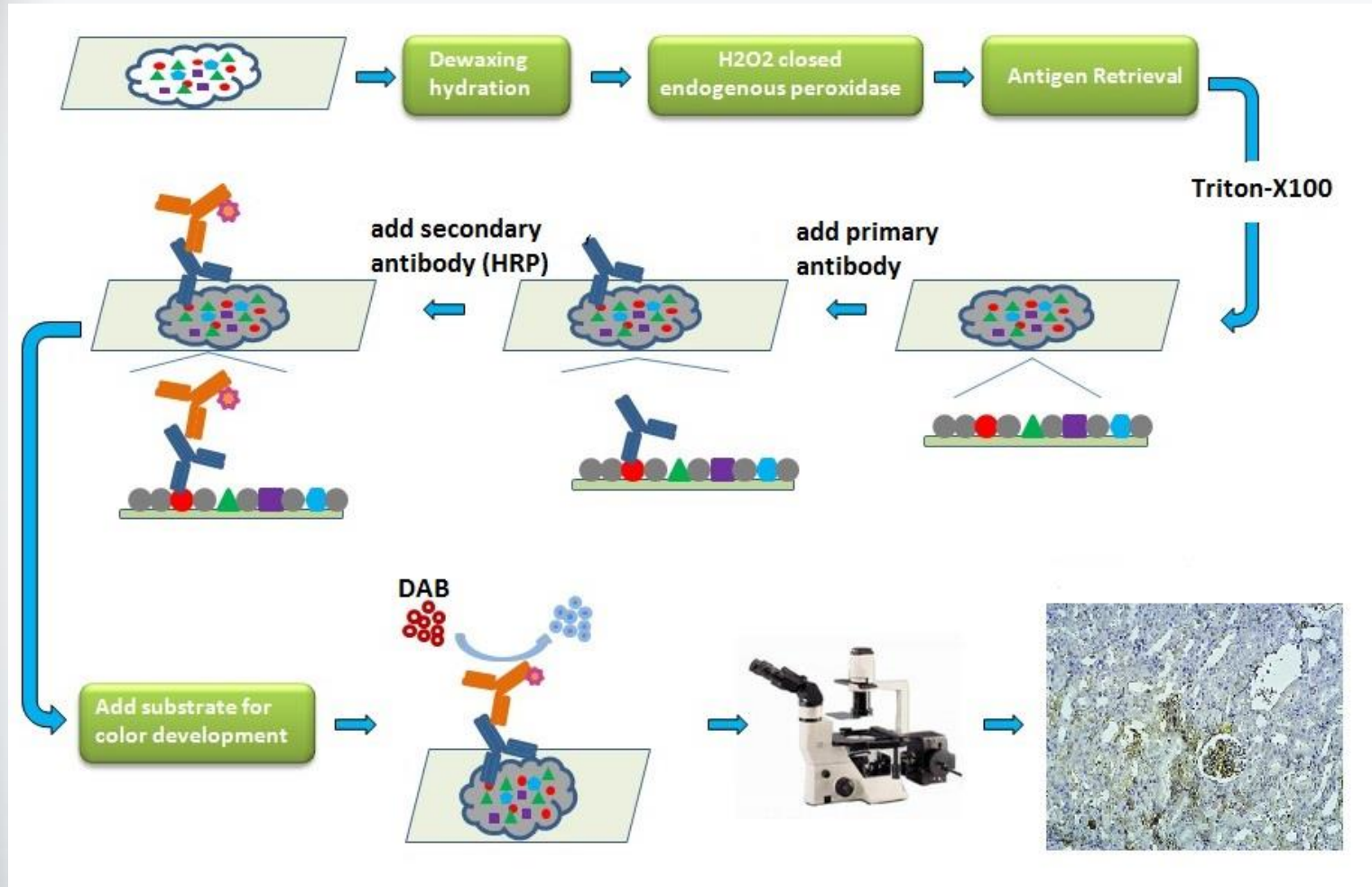
- Anesthesia with ketamine-xylazine
- Blood collection from the heart
- Clotting at room temperature
- Centrifuge (3000 rpm, 10-15 min)
- Separation of serum
- Measurement of BUN, SCr, Na and K



Renal histology

Steps	Solution
Deparaffinization and rehydration	Xylene I Xylene II Absolute alcohol 90% alcohol 70% alcohol Water wash
Staining	Hematoxylin Water wash Eosin Water wash
Dehydration	70% alcohol 90% alcohol Absolute alcohol Xylene I Xylene II

Immunohistochemical staining of Ki-67

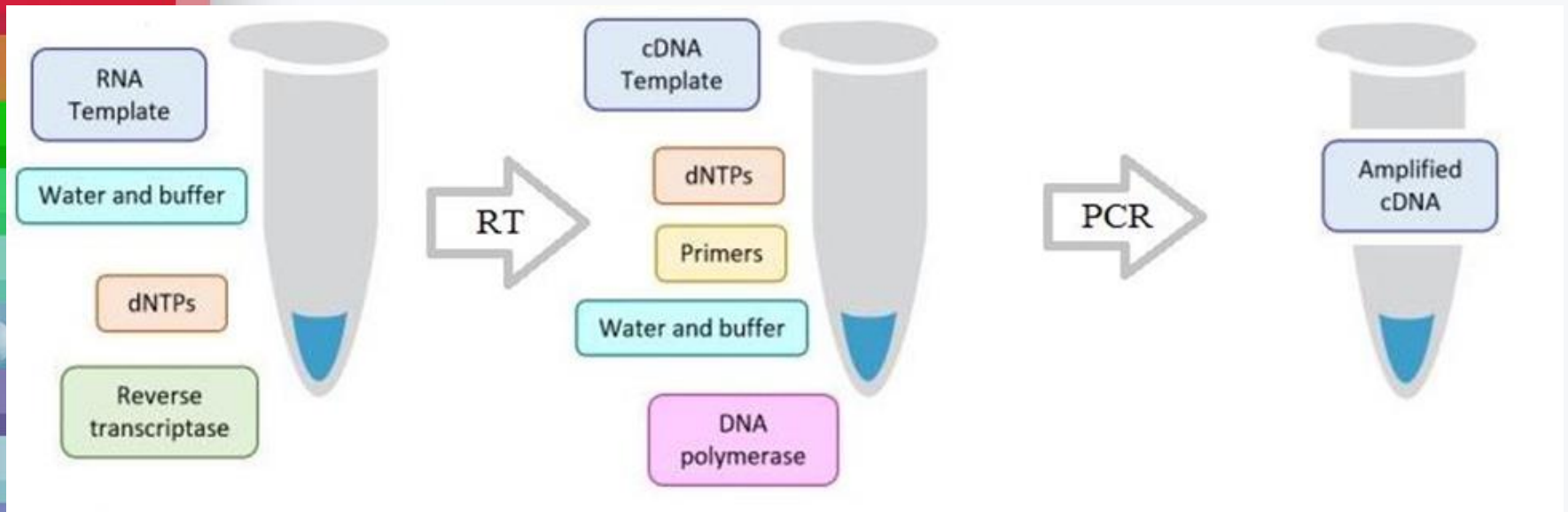


RT-qPCR

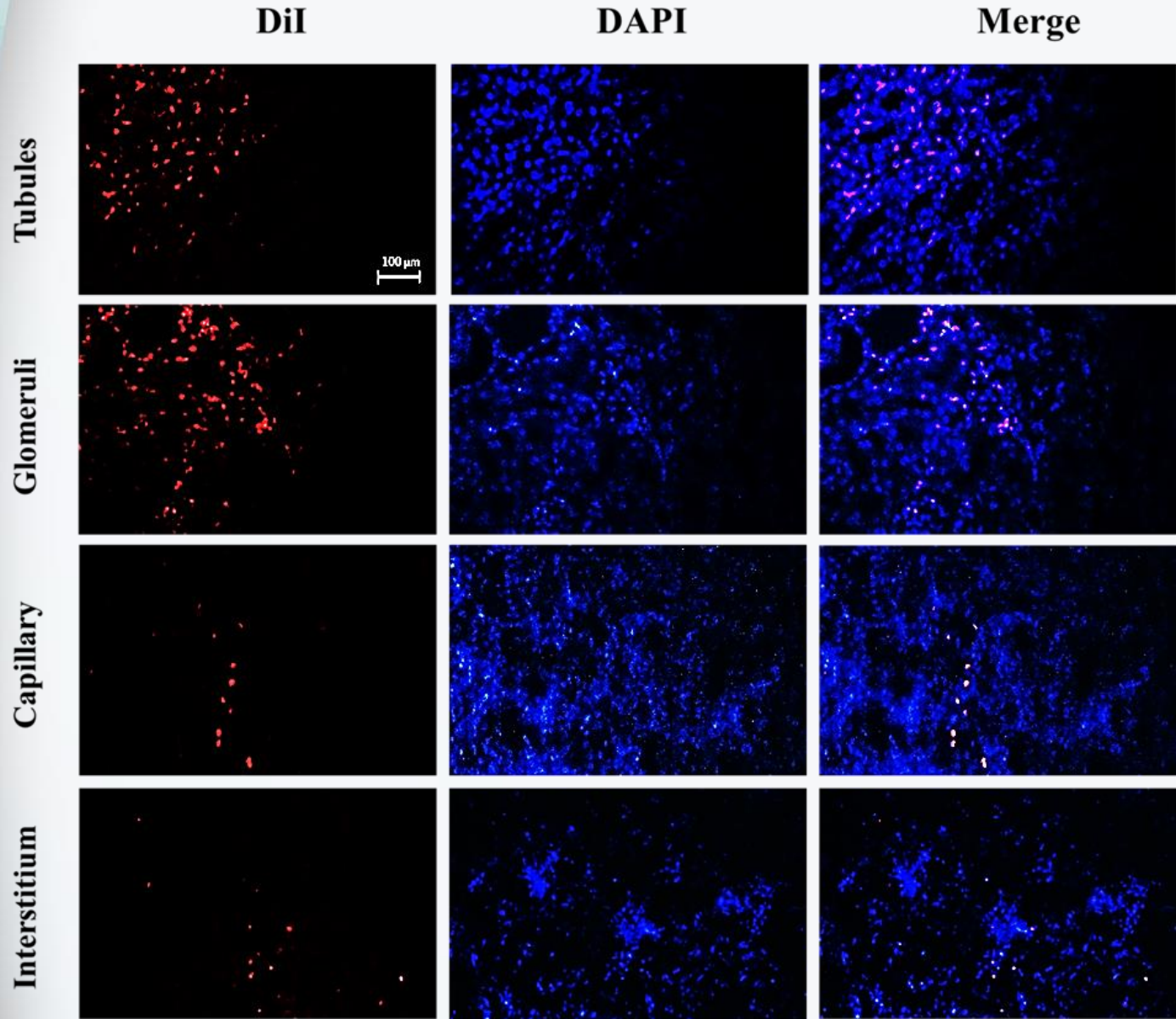
Two-step

1- Total RNA extraction and cDNA synthesis

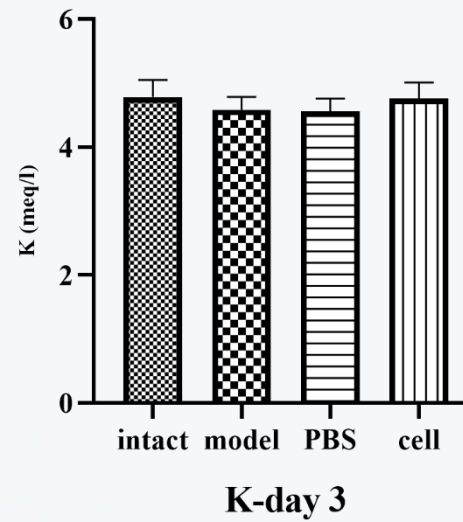
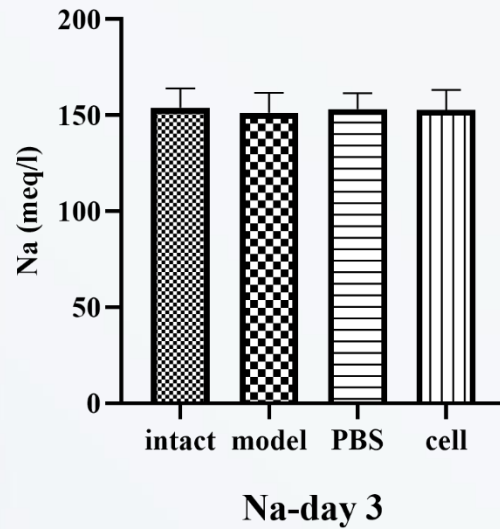
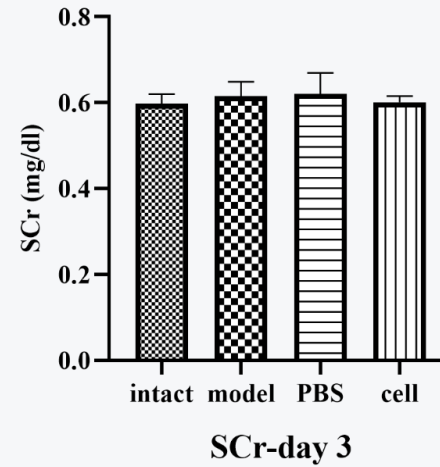
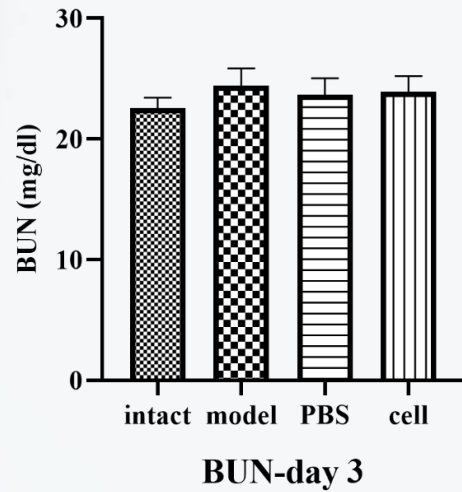
2- qPCR



Results, cell tracking in kidney



Results, renal function (day 3)



Discussion, biochemical markers of renal function

Researchers	Year	Cause of injury	Results	Cell therapy	Results
Mostafa <i>et al.</i>	2016	Cisplatin (5 mg/kg, day 4)	↑BUN, SCr	5 million MSC	↓ BUN, SCr
Lim <i>et al.</i>	2016	Cisplatin (dog, day 4)	↑BUN, SCr, ↓Na ↓K	1 million BM-MSc	↑ BUN, SCr ↓Na, K
Moghadasali <i>et al.</i>	2014	Cisplatin (5 mg/kg, monkey)	↑Urea, SCr, ↓K ↓Na	5 million/ 1 Kg WB Autologous BM-MSc	↓ Urea, SCr, ↓K ↑Na
Zeinali <i>et al.</i>	2021	Cisplatin (5 mg/kg, day 5)	↑BUN, SCr ↓Na, K	1 million Xenogeneic hEnSC	↓BUN, SCr ↑Na, K

Discussion, histological analysis

- ✓ Moghadasali et al. (2014): Cisplatin caused significant changes in the renal histology of the **monkey** on day 4. Injection of BM-MSCs into renal artery on days 4 and 28 had no significant effect on pathological scores, hyaline casts, and fibrosis scores.
- ✓ Lim et al. (2016): In **dogs**, BM-MSCs **decreased fibrotic changes** significantly, but this was not the case for tubular and glomerular injuries.
- ✓ Sun et al. (2019): Injection of urine-derived stem cells resulted in a significant **decrease in the tubular and glomerular damage** in **rats** with cisplatin (5mg/kg)-induced AKI on day 4.

Transplantation of hEnSCs significantly reduced the rate of cast formation and also decreased pathological scores on day 5.

- ✓ Differences in effects suggest differences in the behavior of stem cells and their regenerative potential between species.



Thanks for your attention