Cell-based Therapies in Kidney Disease

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Medical School

Driven to Discover℠

Kidney International, Vol. 61 (2002), pp. 2228–2234

Predictors of renal function following lung or heart-lung transplantation

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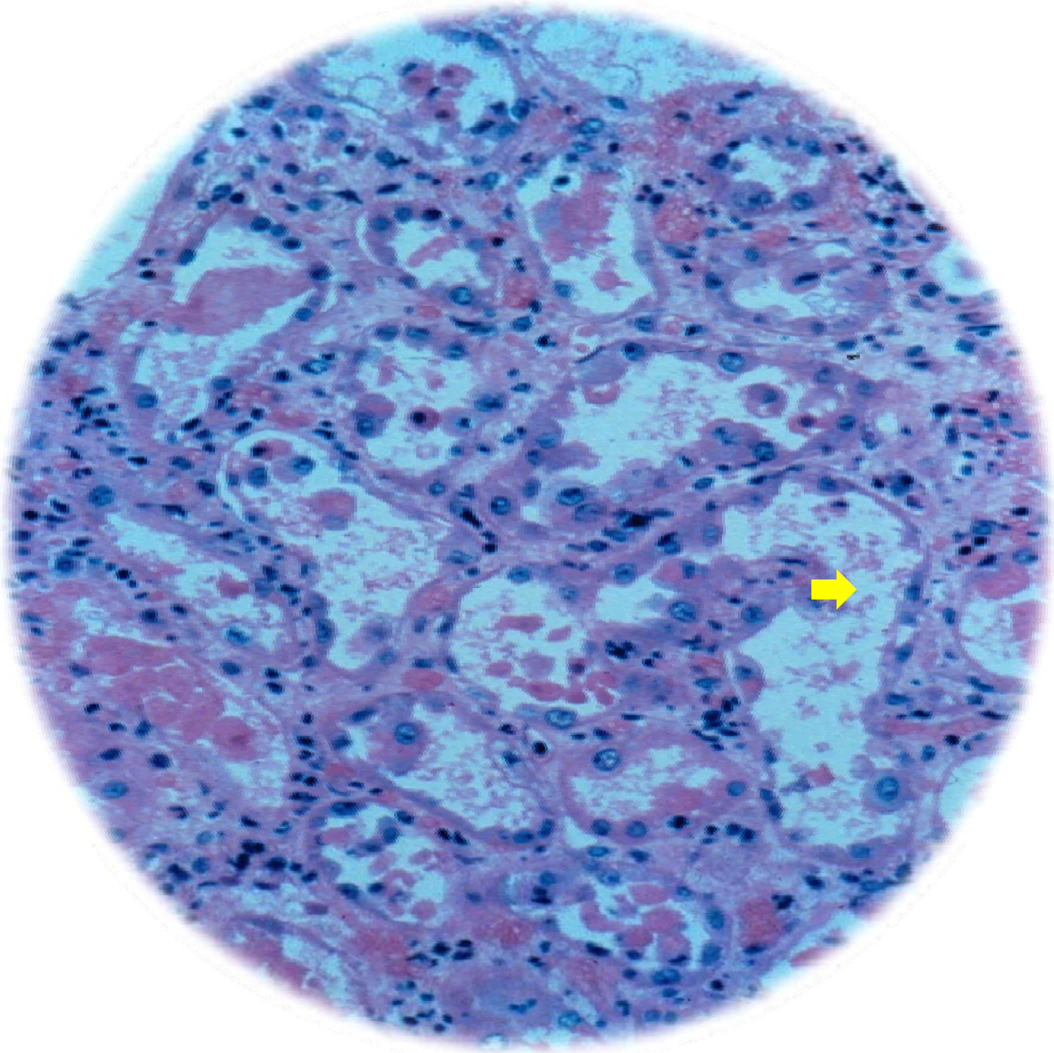
Case Presentation

- 58 year old diabetic man admitted to the ICU with an acute anterior MI
- Baseline creatinine 3.1 (diabetic nephropathy)
- Persistent chest pain $\Rightarrow$ angiography and emergent CABG
- Post-op hypotension (80/45) responds to pressors
- Progressive increase in serum creatinine over the next few days 3.1 to 3.4 to 3.8 to 4.2

Evaluation and Treatment

- Optimization of hemodynamics
- Initiation of dialysis on POD 4 because of K=6, oliguria, and 30 pound weight gain with serum creatinine 4.2
- Every other day dialysis to maintain electrolyte and volume status
- Discharged POD 22 off dialysis
- Chronic dialysis initiated 6 months later

Looking under the microscope

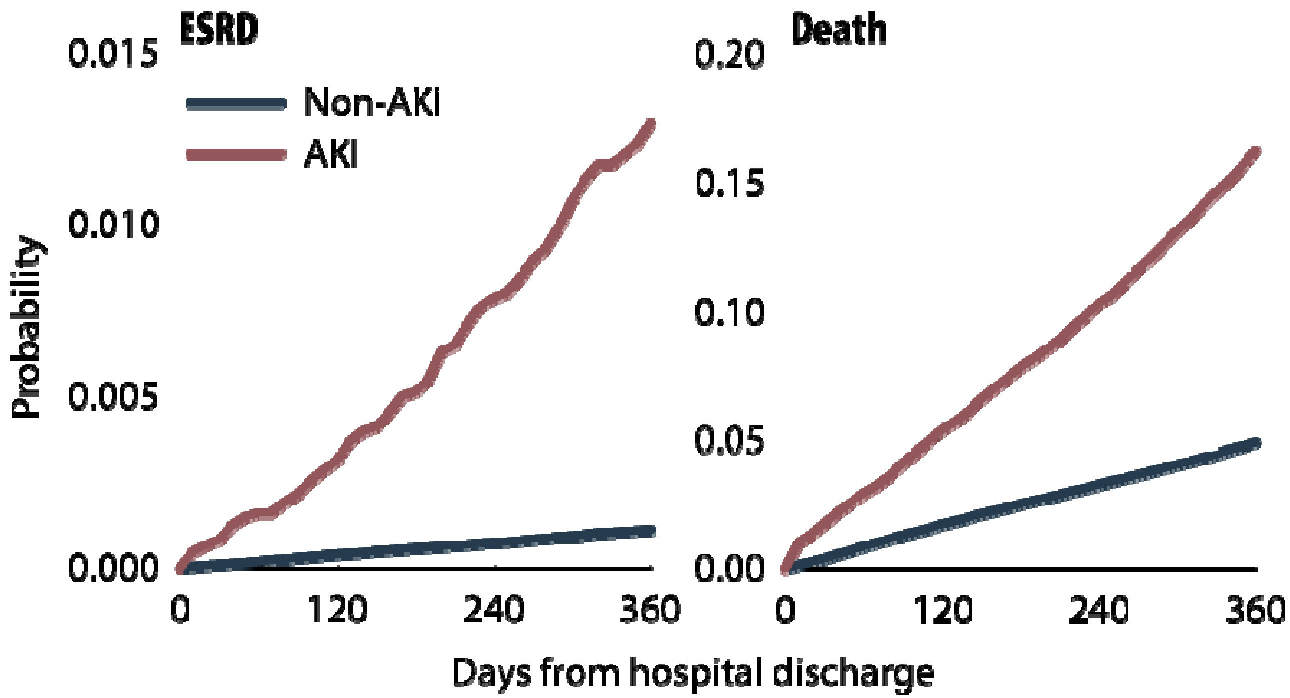


ATN

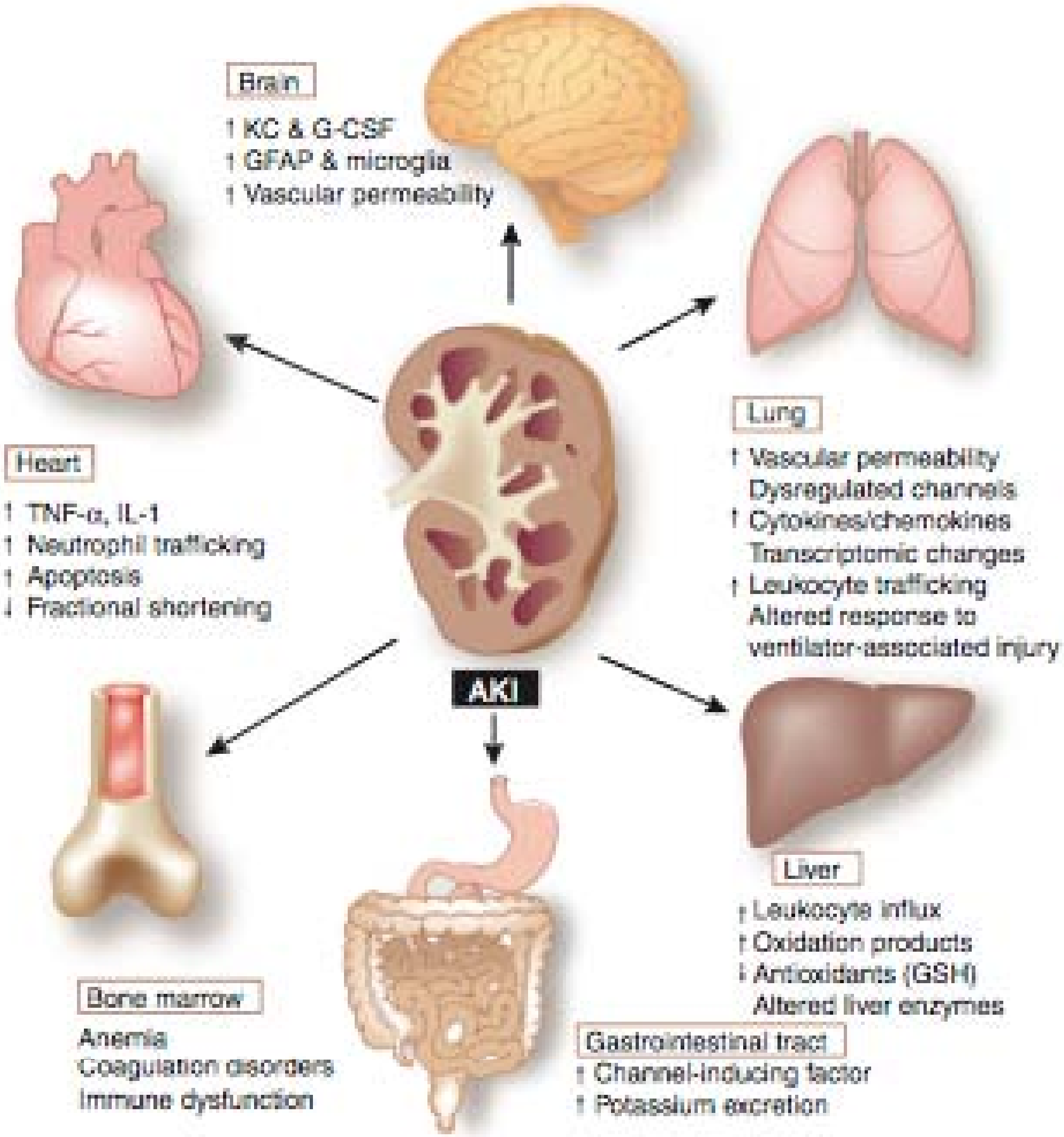
Acute Kidney Injury

- Incidence 30 cases per 1 million population
- 5% of hospitalized patients
- 30% of ICU patients
- High short-term mortality
  - 40 to 70% mortality rate
  - Mortality dependent on underlying disease
  - Prognosis not significantly improved despite dialysis
    - Mortality rate:
    - WWII 91%
    - Korea 68%
    - Vietnam 67%

Probability of ESRD & death after live hospital discharge, by AKI status



General Medicare patients age 66 & older on 12/31/2006, continuously enrolled in Medicare inpatient/outpatient & physician/supplier coverage, & with no HMO coverage, surviving in 2006. AKI defined in 2006. Excludes patients whose ESRD date is on or before the AKI discharge date. Patients followed to a maximum of one year after AKI discharge date for those with AKI or Jan.1, 2007 for those without AKI. A one-year entry period before follow-up is used to define CKD status and comorbid conditions.

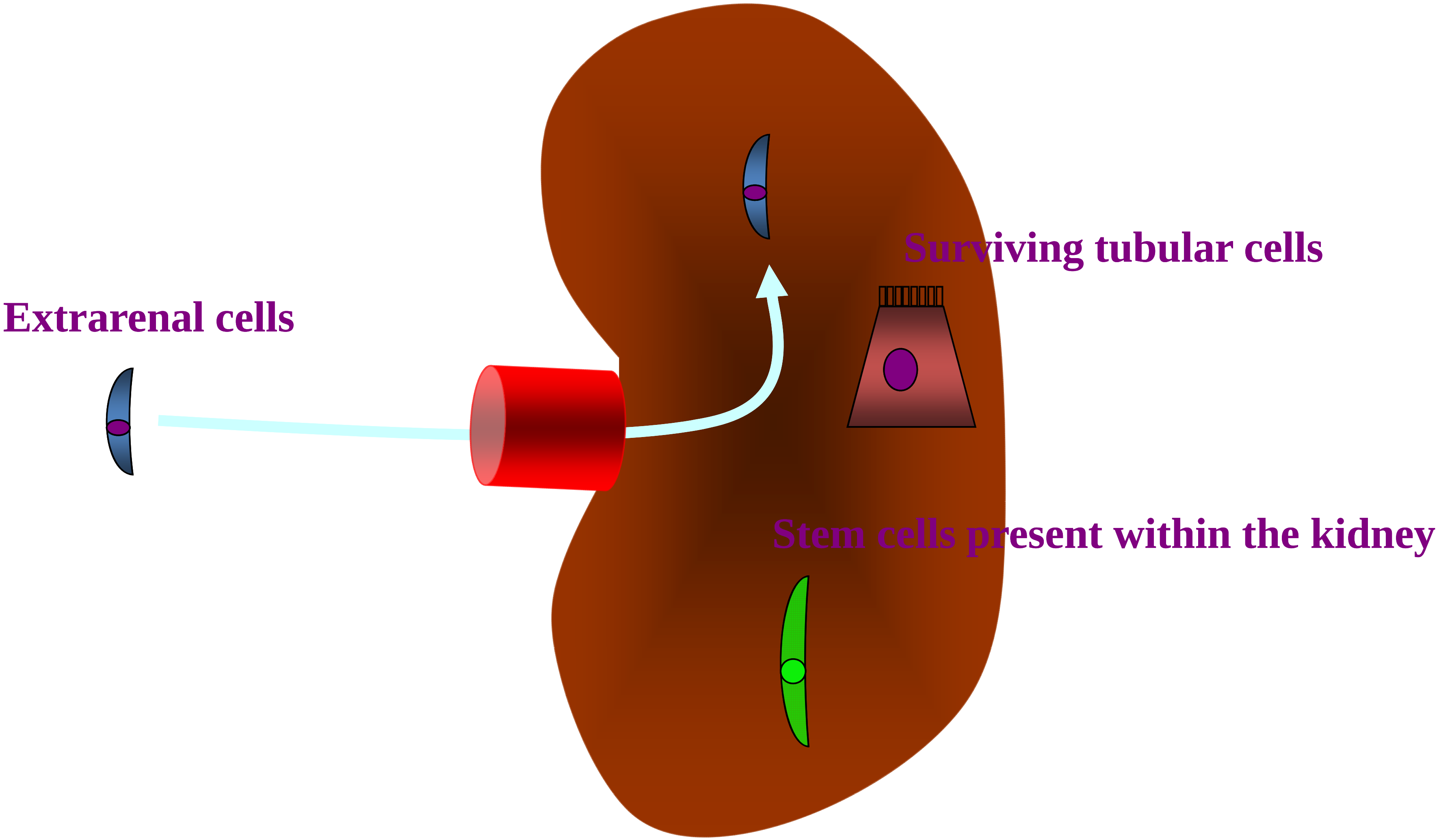


Kidney International (2008) **74**, 849–851. doi:10.1038/ki.2008.390

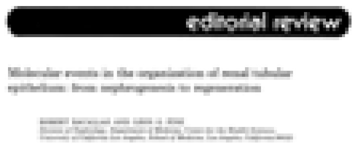
Acute Tubular Necrosis

- Injury phase
- Recovery phase
  - Regeneration of necrotic tubules
  - Growth factors (EGF, IGF) accelerate recovery in experimental models not humans
  - Other failed therapies: ANP, erythropoietin

Potential Source of Regenerating Cells

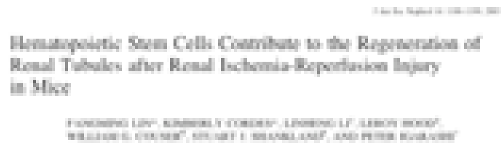


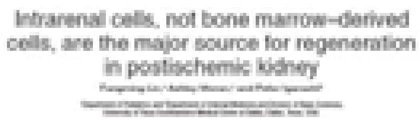
Renal Regeneration



Poulsom R, Forbes SJ, Hodivala-Dilke K, *et al* . J Pathol 2001; 195:229-235

Grimm PC, Nickerson P, Jeffery J, et al . N Engl J Med 2001; 345:93-97.





1989: Dedifferentiaton

2001: Extrarenal cells

2003: Cellular therapy

2004: Renal stem cells

2005: Dedifferentiaton

Kidney and beyond – Review Article

American Journal of Nephrology

Am J Nephrol 2008;28:607–613
DOI: 10.1159/000117311

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Do Stem Cells Exist in the Adult Kidney?

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Cellular Therapy of Kidney Disease

Cellular Therapy of Kidney Disease

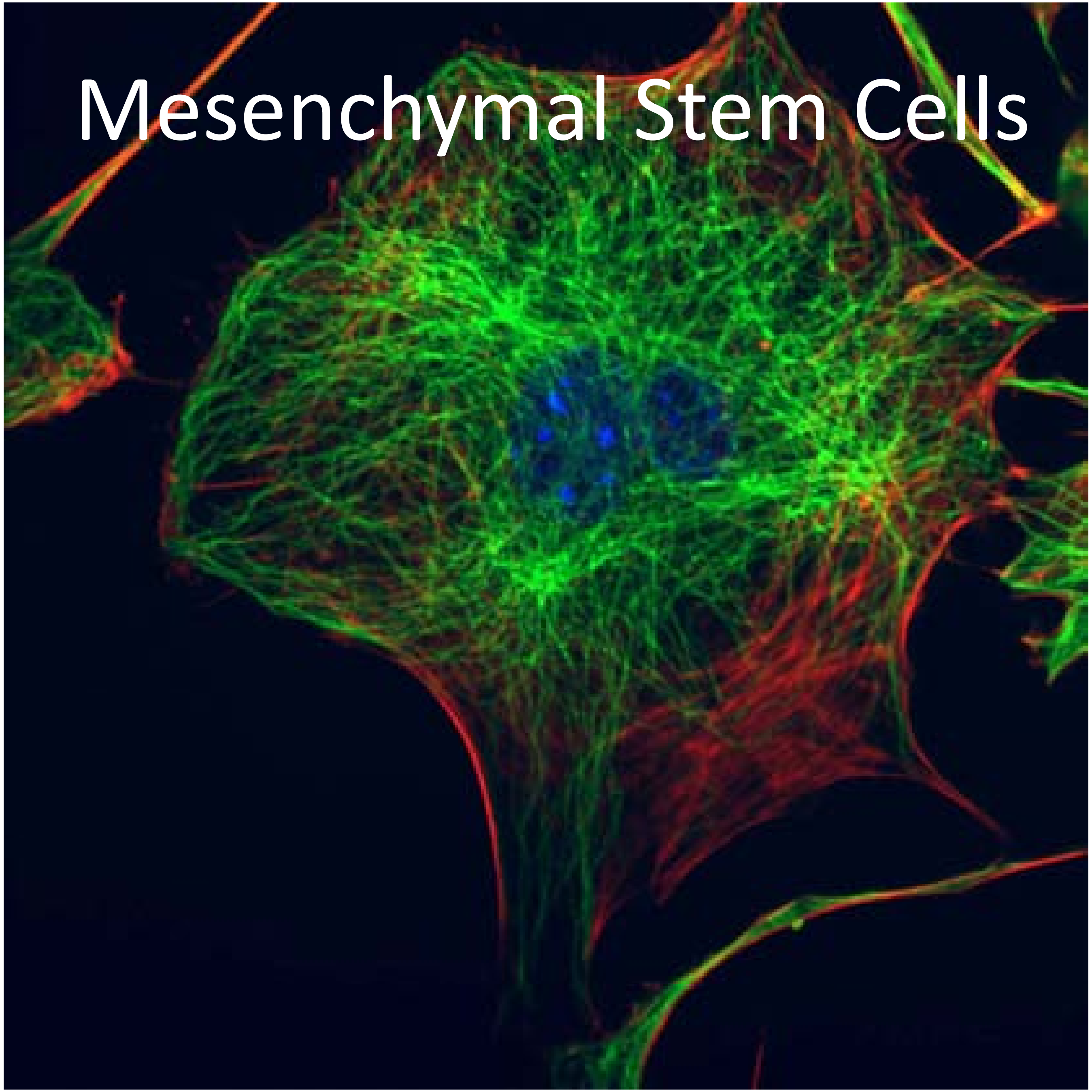
- Acute kidney injury
  - Ischemia reperfusion
  - Cisplatin
  - Rhabdomyolysis
- Kidney transplantation
  - Induction therapy
  - Subclinical rejection
- Diabetes
- SLE
- Nephrotic syndrome
  - Doxorubicin
  - FSGS
- Genetic kidney diseases

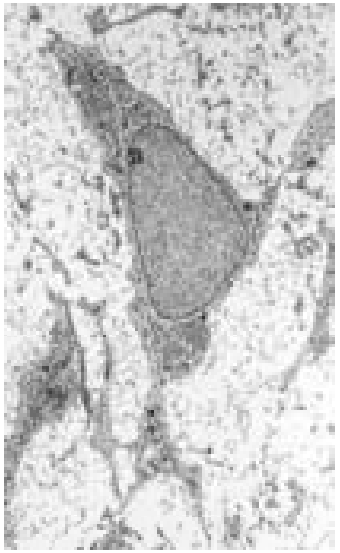
Table 1. Nephrology-Related Trials of MSCs

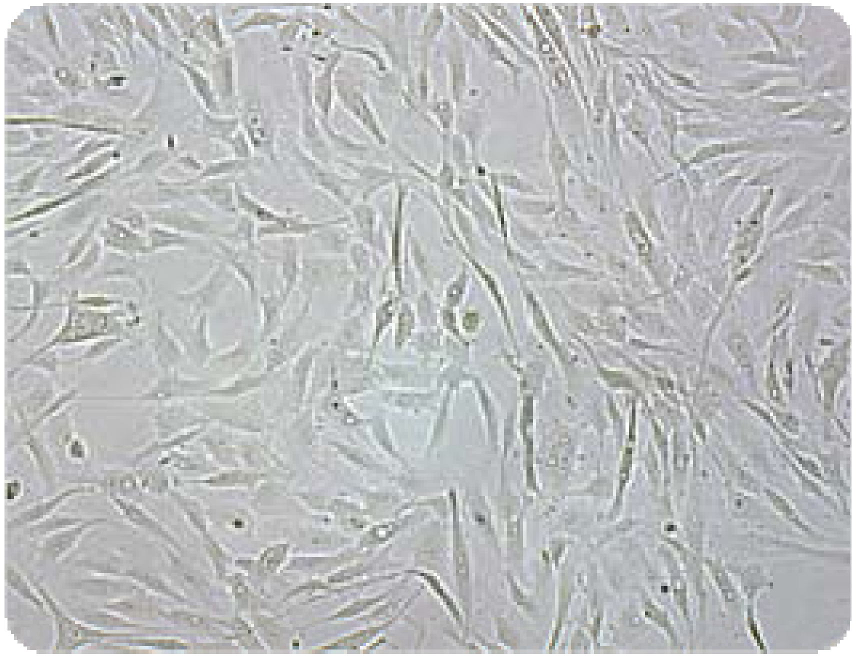
Trial/Registration No.	Cell Type	Primary End Point	Design	Site
Induction therapy recipient of living kidney allograft; NCT00658073	Autologous MSCs	Safety and efficacy	Randomized, open-label, active control	Fuzhou General Hospital, China
Subclinical rejection; NCT00734396	Autologous MSCs	Safety and feasibility	Nonrandomized, open-label, uncontrolled	Leiden University Medical Center, the Netherlands
MSC under basiliximab; low-dose RATG; NCT00752479	Autologous MSCs	Safety and efficacy to induce kidney transplant tolerance	Randomized, open-label, active control	Mario Negri Institute, Italy
Chronic allograft nephropathy; NCT00659620	Autologous and allogeneic MSCs	Safety and efficacy	Treatment, open-label, historical control	Fuzhou General Hospital, China
Refractory systemic lupus erythematosus; NCT00698191	Allogeneic MSCs	Safety and efficacy	Treatment, nonrandomized, open-label	Nanjing Medical University, China
Cisplatin-induced AKI in patients with solid-organ cancers; NCT01275612	Allogeneic MSCs	Safety and efficacy	Treatment, open-label	Mario Negri Institute, Italy

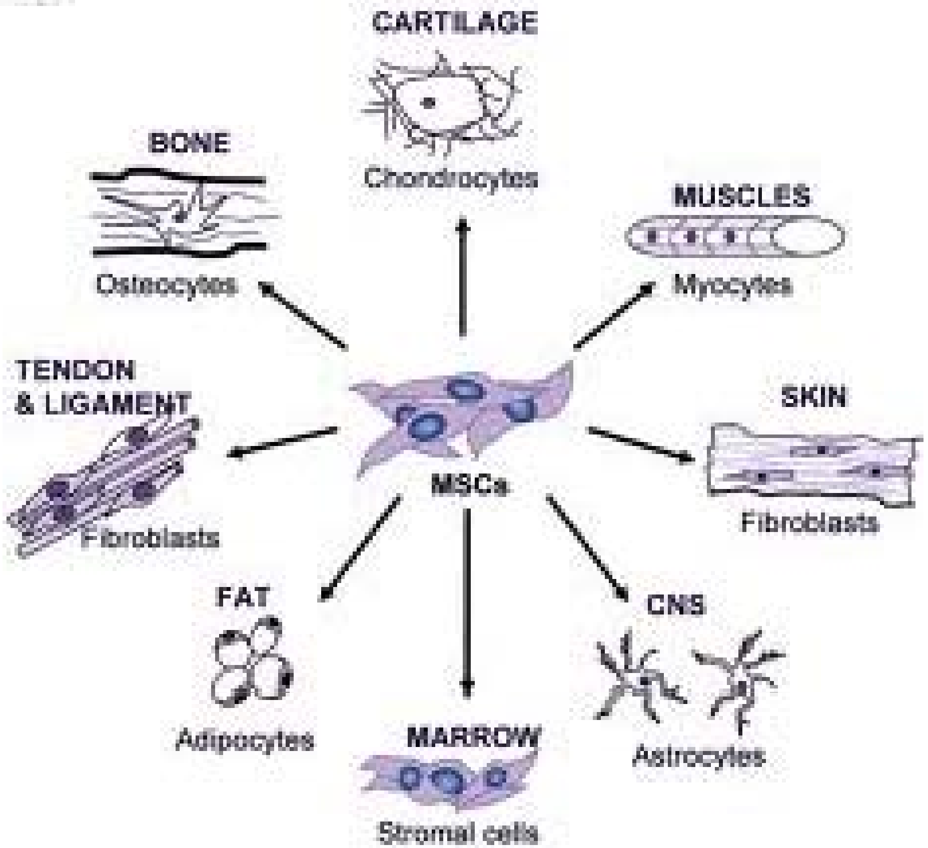
Note: Listed are phase 1/2 trials available in ClinicalTrials.gov.

Abbreviations: AKI, acute kidney injury; MSC, multipotent mesenchymal stromal cell; RATG, rabbit antithymocyte globulin induction.


Mesenchymal Stem Cells






CARTILAGE
Chondrocytes
BONE
Osteocytes
MUSCLES
Myocytes
TENDON
& LIGAMENT
Fibroblasts
MSCs
SKIN
Fibroblasts
FAT
Adipocytes
MARROW
Stromal cells
CNS
Astrocytes

Why MSCs?

- Migrate to site of injury
- Release factors (paracrine and endocrine):
  - Influence cell survival and proliferation
  - Modulate immune response
  - Anti-inflammatory actions
- Pre-clinical studies
- Safe in other diseases (Phase 1):
  - Amyotrophic lateral sclerosis
  - Multiple sclerosis
  - Stroke
  - Crohn disease
  - Acute graft-vs-host disease

J Am Soc Nephrol 15: 1794–1804, 2004

Mesenchymal Stem Cells Are Renotropic, Helping to Repair the Kidney and Improve Function in Acute Renal Failure

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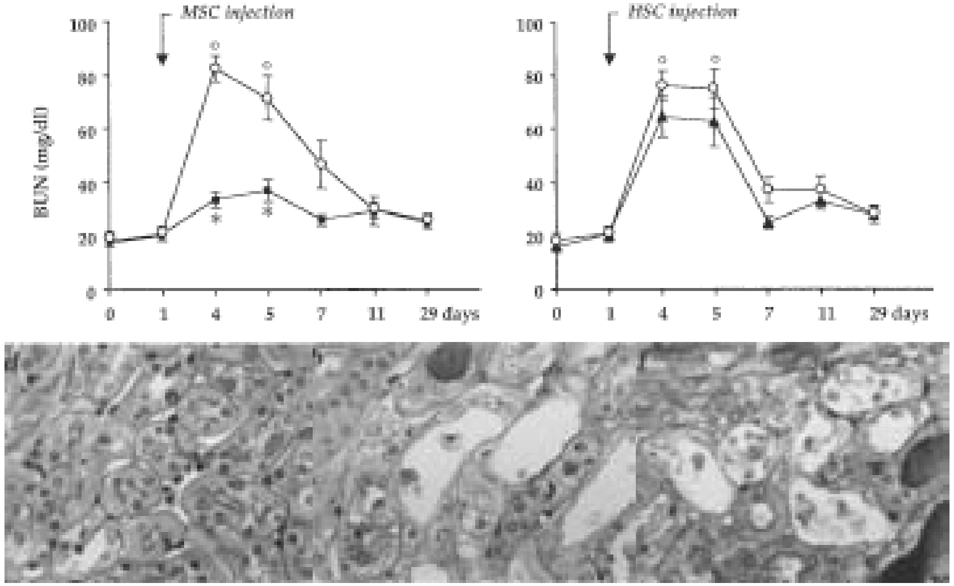
Cisplatin induced ARF

MSC

or

HSC



MSC

saline

HSC

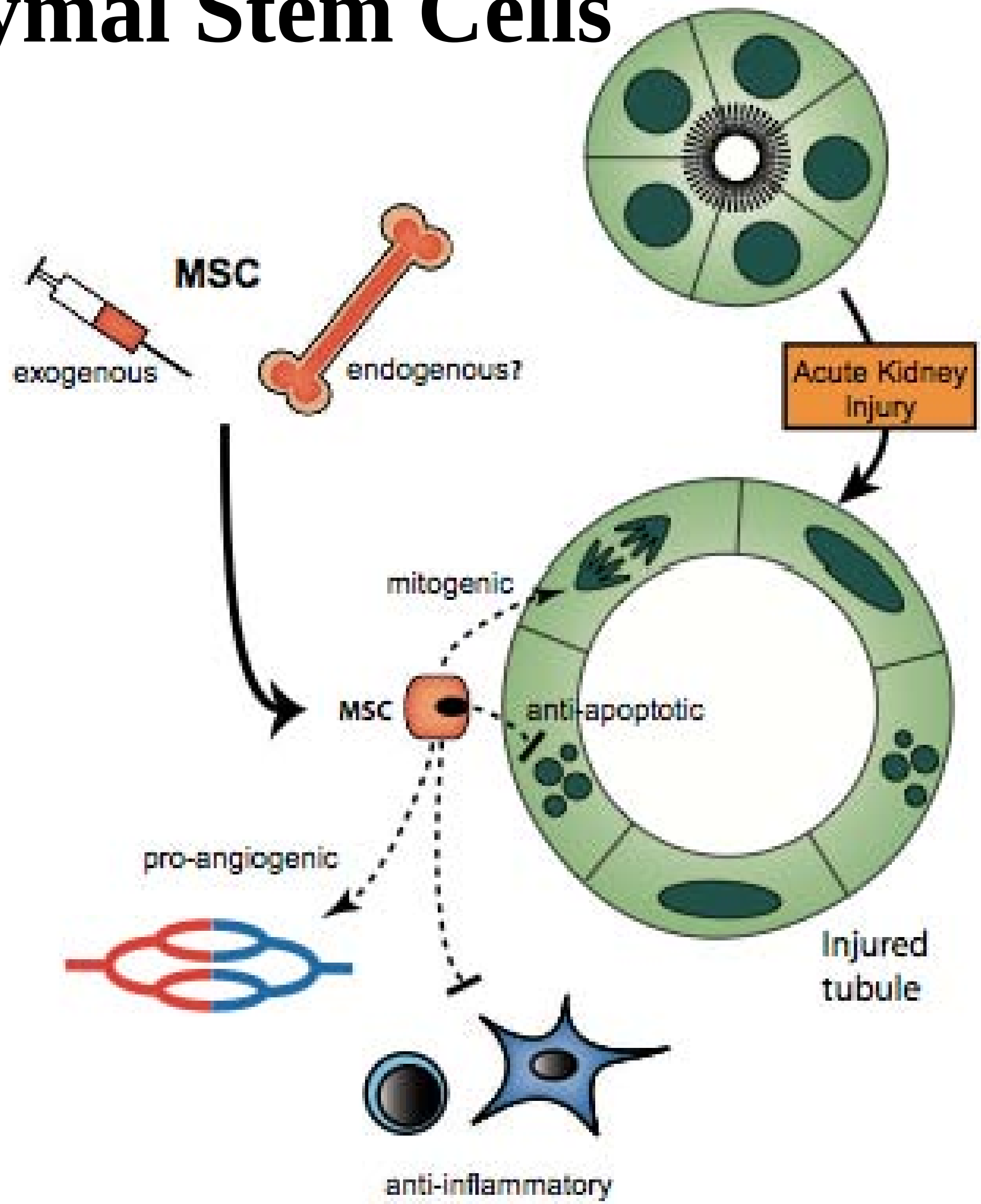
Am J Physiol Renal Physiol 289: F31–F42, 2005.
First published February 15, 2005; doi:10.1152/ajprenal.00007.2005.

Administered mesenchymal stem cells protect against ischemic acute renal failure through differentiation-independent mechanisms

Florian Tögel,[1,2] Zhuma Hu,[1] Kathleen Weiss,[1] Jorge Isaac,[3] Claudia Lange,[4] and Christof Westenfelder[1,2]

[1]*Division of Nephrology, Department of Medicine, University of Utah, and Veterans Affairs Medical Center, and Departments of [2]Physiology and [3]Pathology, University of Utah, Salt Lake City, Utah; and [4]Bone Marrow Transplantation Center, Hamburg, Germany*

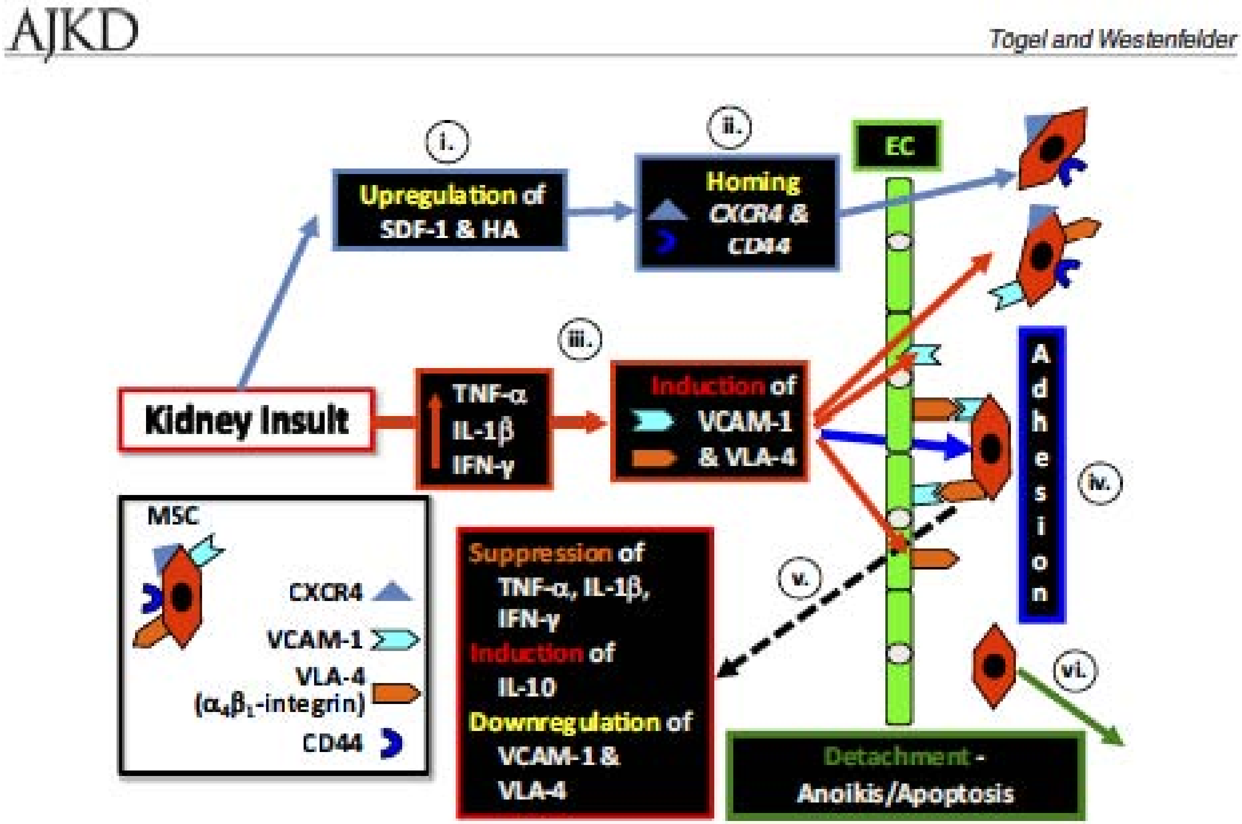
Mesenchymal Stem Cells



Mesenchymal Stem Cells in Acute Kidney Injury

Benjamin D. Humphreys[1,2] and Joseph V. Bonventre[1,2,3]

Annu. Rev. Med. 2008. 59:311–25



Mode of Action: paracrine and endocrine

Other Cell Therapies

- Embryonic stem cells (ESC) – risk of teratoma
- Induced pluripotent stem cells (iPS) – can be autologous
- Endothelial precursors
- Amniotic fluid stem cells
- Adipose-derived stem cells

Also studies on engineering MSCs (e.g. overexpress CD44 to increase homing to the kidney.

Nephrology

In-Depth Topic Review

Am J Nephrol 2013;37:16–29
DOI: [illegible]

Stem Cells and Their Role in Renal Ischaemia Reperfusion Injury

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Table 1. Studies highlighting benefits of SC therapy in small animal models

Reference	SC source	Animal	Mode of action	Features
Brodsky et al. [50]	human umbilical vein endothelial cells	rat	homing of SC (H)	↑ renal functional protection of ischaemic kidney
Lin et al. [31]	mouse HSC	mouse	H	↑ renal function ↑ β-galactosidase-positive cells ↑ tubular cell differentiation
Arriero et al. [32]	mouse skeletal muscle-derived SC	mouse	H	↑ short-term renal function ↑ differentiation into endothelial cell lineage
Jiang et al. [51]	rat BM-MSC	rat	H	↑ engraftment (20%) of BM-MSC seen by Y chromosome in situ hybridisation ↑ improvement in functional and histological parameters
Morigi et al. [81]	mouse BM-MSC	mouse	paracrine and endocrine effects (P/E)	↑ proliferation ↑ morphological recovery ↑ renal function
Tögel et al. [23]	rat BM-MSC	rat	P/E	↑ renal function ↓ apoptosis and renal injury ↓ IL-1β, TNF-α, IFN-γ, iNOS ↑ IL-10, bFGF, TGF-α, Bcl-2
Tögel et al. [52]	rat BM-MSC	rat	P/E	↓ apoptosis and inflammation ↓ IL-1β, TNF-α, IFN-γ, iNOS
Imberti et al. [120]	mouse BM-MSC	mouse	P/E	↑ renal function and ↓ tubular injury ↑ VEGF, HGF, IGI-1
Bi et al. [84]	mouse BM-MSC	mouse	P/E	↑ renal function ↑ tubular cell proliferation ↓ tubular cell atrophy
Semedo et al. [53]	rat BM-MSC	rat	P/E	↓ serum creatinine and plasma urea ↑ PCNA nuclei in MSC-treated kidney ↑ IL-4, ↓ IL-1β
Semedo et al. [13]	rat BM-MSC	rat	P/E	↑ renal function and proliferation ↓ apoptosis and renal injury ↑ Bcl-2/Bad ratio change to Thy-2 inflammatory profile ↓ IL-1β, IL-6, TNF-α ↑ IL-4, IL-10
Westenfelder et al. [115]	rat VEGF knockout BM-MSC	rat	P/E	↑ VEGF, HGF, IGF-1 ↓ mortality and ↑ functional recovery
Hara et al. [55]	rat BM-MSC	rat	P/E	↓ IL-1β, TNF-α, IFN-γ inhibition of ICAM-1 ↓ macrophage infiltration (CD68+, CD3+, CD25+) ↓ DC attracting chemokines (CCL19, CCL21) ameliorates inflammation
Patel et al. [54]	rat GTSC	rat	P/E	↑ 2- to 8-fold of growth factors (FGF2, HGF, IGF-1, VEGF) and anti-inflammatory factors (IL-4, IL-10) abundance and easy accessibility compared to other SC

Original Report: Laboratory Investigation

American Journal of Nephrology

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Use of Mesenchymal Stem Cells and Darbepoetin Improve Ischemia-Induced Acute Kidney Injury Outcomes

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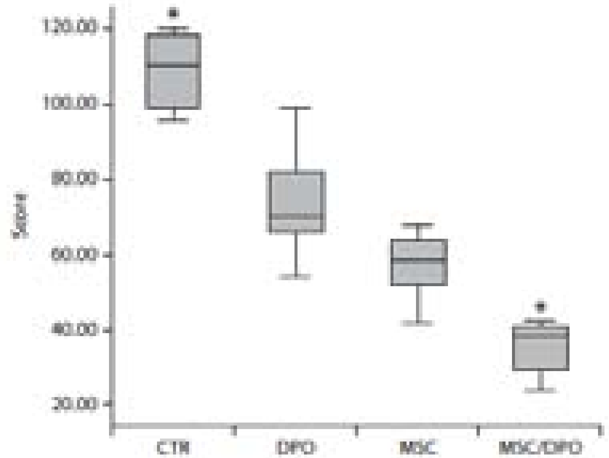
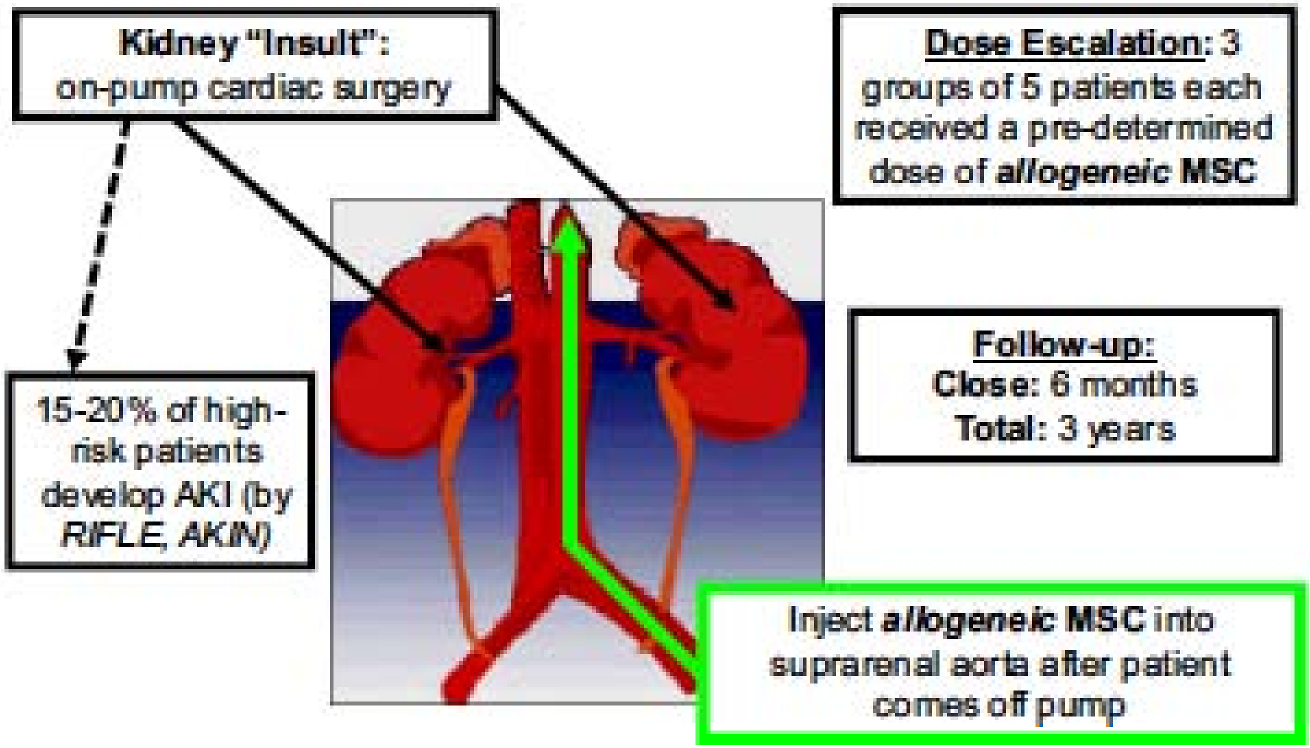
Serhan Piskinpasa[a] Duygu Uckan[d] Nuhan Purali[e] Petek Korkusuz[c] Cetin Turgan[a]

Departments of [a]Nephrology, [b]Urology, [c]Histology and Embryology, [d]Pediatric Hematology, and [e]Biophysics, Hacettepe University Faculty of Medicine, Ankara, Turkey

Table 1. Measurements of the renal function and histologic scores in the study groups

Parameter	CTR (n = 7)	DPO (n = 7)	MSC (n = 7)	MSC/DPO (n = 7)	p value*
Cre, mg/dl					
Baseline	0.60 ± 0.18	0.50 ± 0.13	0.50 ± 0.14	0.60 ± 0.10	0.37
24 h	2.80 ± 0.54[a]	3.30 ± 0.49[b]	3.10 ± 0.33[c]	1.90 ± 0.56[a, b, c]	0.002
48 h	2.70 ± 0.58[d, e, f]	2.00 ± 0.07[d, g]	1.90 ± 0.10[e, h]	1.70 ± 0.29[g, f, h]	0.001
72 h	2.00 ± 0.12[i, j, k]	1.40 ± 0.31[i, l]	1.10 ± 0.11[j, m]	0.82 ± 0.32[k, l, m]	0.0003





Phase 1 clinical trial: on-pump cardiac surgery patients at high risk of postop AKI treated with allogeneic MSC

Mesenchymal Stem Cells In Cisplatin-Induced Acute Renal Failure In Patients With Solid Organ Cancers (CIS/MSC08)

This study is currently recruiting participants.

Verified February 2013 by Mario Negri Institute for Pharmacological Research

Sponsor:
Mario Negri Institute for Pharmacological Research

Information provided by (Responsible Party):
Mario Negri Institute for Pharmacological Research

ClinicalTrials.gov Identifier:
NCT01275612

First received: January 11, 2011
Last updated: February 22, 2013
Last verified: February 2013
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

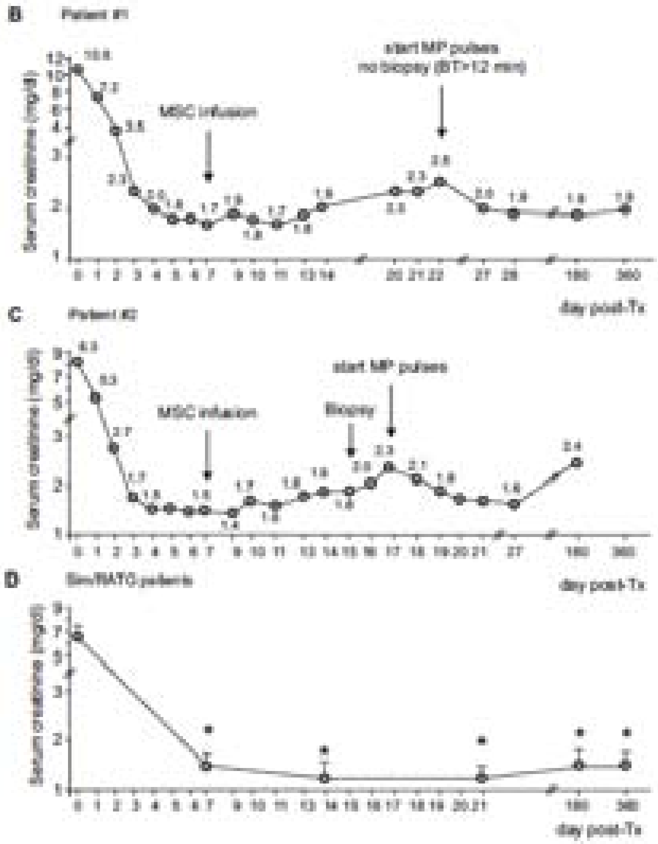
Purpose

This is a pilot, explorative, study to test the feasibility and safety of systemic infusion of donor ex-vivo expanded Mesenchymal Stem Cells to repair the kidney and improve function in patients with solid organ cancers who develop acute renal failure after chemotherapy with cisplatin.

Kidney Transplantation

Autologous Mesenchymal Stromal Cells and Kidney Transplantation: A Pilot Study of Safety and Clinical Feasibility

Norberto Perico,[*,†] *Federica Casiraghi,*[*,†] *Martino Introna,*[*,‡] *Eliana Gotti,*[†] *Marta Todeschini,*[*,†] *Regiane Aparecida Cavinato,*[*,†] *Chiara Capelli,*[‡] *Alessandro Rambaldi,*[§] *Paola Cassis,*[*,†] *Paola Rizzo,*[†] *Monica Cortinovis,*[*,†] *Maddalena Marasà,*[†] *Josee Golay,*[‡] *Marina Noris,*[*,†] *and Giuseppe Remuzzi*[*,†]



www.cjasn.org Vol 6 February, 2011

ORIGINAL CONTRIBUTION

Induction Therapy With Autologous Mesenchymal Stem Cells in Living-Related Kidney Transplants

A Randomized Controlled Trial

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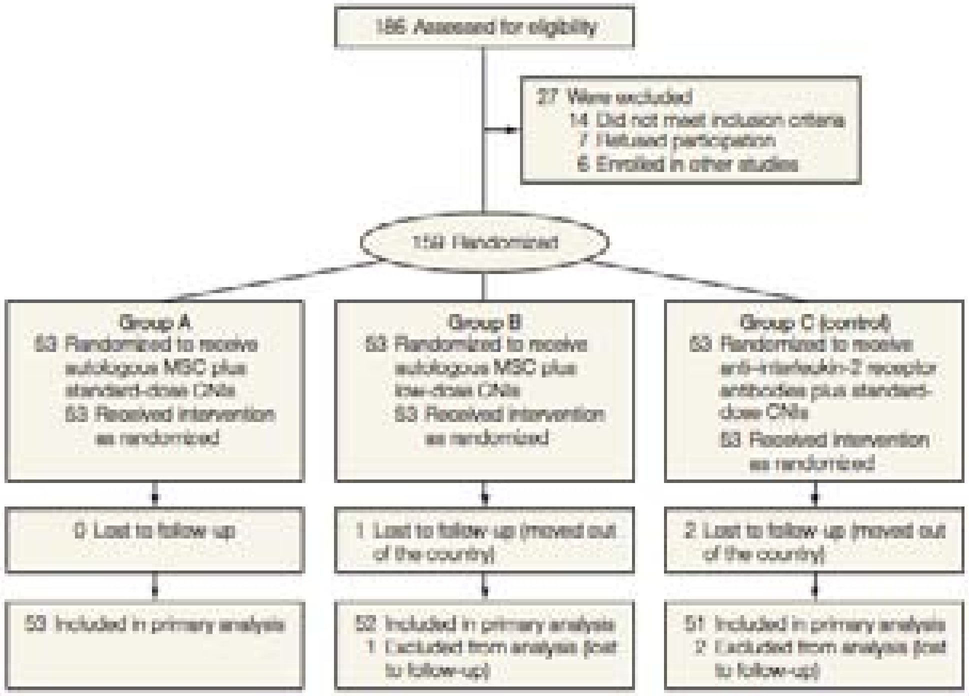


- Primary outcome: incidence of bx proven AR and eGFR within first year
- Secondary outcome: 1-year patient and graft survival and incidence of adverse events

JAMA, March 21, 2012—Vol 307, No. 11
Corrected on March 21, 2012

Induction Therapy With Autologous Mesenchymal Stem Cells in Living-Related Kidney Transplants

A Randomized Controlled Trial

- MSC groups had faster renal recovery during first month
- DGF not different
- AR not different at 1 year (better at 6 months with MSC)
- Patient and graft survival similar
- Less risk of opportunistic infection in MSC donors

Table 2. Estimated eGFR Differences Between Groups

Time Point, d	eGFR Difference (95% CI), mL/min per 1.73 m²	*P* Value[a]
Autologous MSC + Standard-Dose CNI vs Control Group		
0	1.0 (−2.0 to 4.0)	.51
7	24.4 (11.9 to 37.0)	<.001
14	15.3 (2.3 to 28.3)	.02
30	12.1 (0.3 to 23.8)	.045
60	7.8 (−2.2 to 17.8)	.13
90	3.1 (−6.3 to 12.4)	.52
180	1.2 (−7.9 to 10.3)	.80
360	7.7 (−2.4 to 17.8)	.14
7-30[b]	6.2 (0.4 to 11.9)	.04
0−360[b]	9.1 (1.6 to 16.5)	.02
Autologous MSC + Low-Dose CNI vs Control Group		
0	−0.5 (−3.6 to 2.7)	.78
7	22.4 (10.8 to 34.0)	<.001
14	8.2 (−3.9 to 20.3)	.18
30	2.4 (−9.3 to 14.1)	.69
60	3.3 (−6.5 to 13.0)	.51
90	2.1 (−8.0 to 12.1)	.69
180	−6.7 (−15.4 to 2.0)	.13
360	1.1 (−9.3 to 11.6)	.83
7-30[b]	10.0 (3.8 to 16.2)	.002
0-360[b]	4.0 (−2.9 to 10.9)	.25
Autologous MSC + Standard-Dose vs Low-Dose CNI		
0	1.5 (−1.3 to 4.2)	.30
7	2.1 (−10.7 to 14.8)	.75
14	7.1 (−5.8 to 20.0)	.28
30	9.7 (−0.7 to 20.1)	.07
60	4.6 (−3.4 to 12.6)	.26
90	1.0 (−8.5 to 10.5)	.84
180	7.9 (−0.7 to 16.5)	.07
360	6.5 (−3.7 to 16.7)	.21
7-30[b]	−3.8 (−9.4 to 1.8)	.19
0-360[b]	5.0 (−1.8 to 11.9)	.15

Induction Therapy With Autologous Mesenchymal Stem Cells in Living-Related Kidney Transplants

A Randomized Controlled Trial

	logous Mesenchymal Stem Cell Treatment			
	dard-Dose CNI (n = 53)	Low-Dose CNI (n = 52)	Control (n = 51)	*P* Value Overall Type 3[b]
Primary end point				
eGFR, mean (95% CI), mL/min per 1.73 m^2,[c]				
Posttransplant				
0 d	6.8 (4.7-8.8)	5.3 (3.1-7.6)	5.8 (3.0-8.6)	.56
7 d	77.0 (67.4-86.6)[d]	74.9 (66.3-83.6)[d]	52.6 (44.5-60.7)	<.001
14 d	84.9 (75.2-94.6)[e]	77.8 (69.0-86.6)	69.6 (61.0-78.3)	.07
1 mo	91.1 (83.7-98.4)[f]	81.4 (73.8-89.0)	79.0 (69.9-88.1)	.08
2 mo	90.1 (84.3-96.0)	85.6 (79.9-91.3)	82.3 (74.1-90.5)	.28
3 mo	88.9 (82.8-95.0)	87.9 (80.5-95.3)	85.8 (78.8-92.9)	.81
6 mo	90.6 (84.2-97.1)	82.7 (76.6-88.8)	89.4 (83.0-95.9)	.62
12 mo	93.2 (86.2-100.2)	86.7 (79.0-94.3)	85.5 (78.2-92.9)	.49
Acute rejection, No. (%) [95% CI]				
At 6 mo				
Biopsy-confirmed	4 (7.5) [0.4-14.7][g]	4 (7.7) [0.5-14.9][h]	11 (21.6) [10.5-32.6]	.02
Corticosteroid-resistant	0	0	4 (7.8) [0.6-15.1]	
Histological severity				
Banff I/II	4 (7.5) [0.4-14.7]	4 (7.7) [0.5-14.9]	7 (13.7) [4.5-23.0]	.007
Banff III	0	0	4 (7.8) [0.6-15.1]	
At 12 mo				
Biopsy-confirmed	8 (15.1) [5.5-24.7]	9 (17.3) [7.1-27.5]	13 (25.5) [13.8-37.2]	.37
Corticosteroid-resistant	0	1 (1.9) [0-5.6]	4 (7.8) [0.6-15.1]	.06
Histological severity				
Banff I/ II	8 (15.1) [5.5-24.7]	8 (15.4) [5.7-25.1]	7 (13.7) [4.5-23.0]	.07
Banff III	0	1 (1.9) [0-5.6]	4 (7.8) [0.6-15.1]	
Secondary, No. (%) [95% CI]				
Delayed graft function	5 (9.4) [1.6-17.3]	4 (7.7) [0.5-14.9]	4 (7.8) [0.6-15.1]	.94
Duration of dialysis, mean (range), d	17.4 (10.5-24.3)	15.3 (7.9-23.1)	16.3 (10.0-22.5)	.28
Graft loss	1 (1.9) [0-5.5]	2 (3.8) [0-9.0]	1 (2.0) [0-5.7]	.85
Acute rejection	0	1 (1.9) [0-5.6]	1 (2.0) [0-5.7]	.85
Chronic rejection	1 (1.9) [0-5.5]	1 (1.9) [0-5.6]	0	
Death	0	0	0	

STEM CELLS TRANSLATIONAL MEDICINE

TISSUE-SPECIFIC PROGENITOR AND STEM CELLS

Autologous Bone Marrow-Derived Mesenchymal Stromal Cells for the Treatment of Allograft Rejection After Renal Transplantation: Results of a Phase I Study

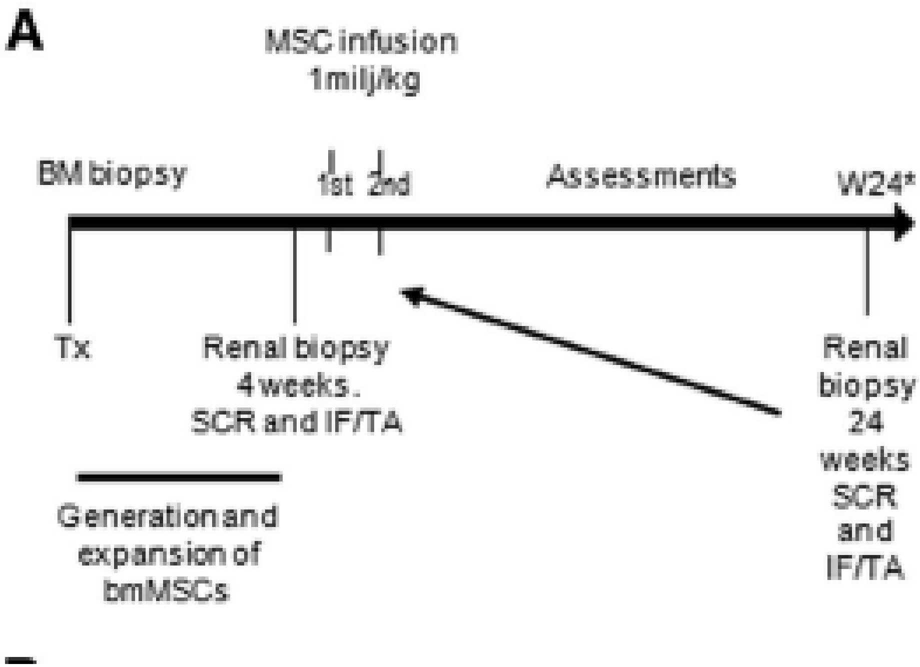
MARLIES E.J. REINDERS,[a,b] JOHAN W. DE FIJTER,[a] HELENE ROELOFS,[c] INGEBORG M. BAJEMA,[d] DOROTTYA K. DE VRIES,[e] ALEXANDER F. SCHAAPHERDER,[e] FRANS H.J. CLAAS,[c] PAULA P.M.C. VAN MIERT,[c] DAVE L. ROELEN,[c] CEES VAN KOOTEN,[a] WILLEM E. FIBBE,[c] TON J. RABELINK[a,b]

Key Words. Mesenchymal stem cells • Kidney • Immunosuppression • Transplantation


Stem Cells Translational Medicine

Tissue-Specific Progenitor and Stem Cells

Autologous Bone Marrow-Derived Mesenchymal Stromal Cells for the Treatment of Allograft Rejection After Renal Transplantation: Results of a Phase I Study



6 HLA mismatched LD kidney recipients

Table 1. Patients

Recipient (gender, age)	Primary kidney disease	Immunologic status	CMV status (D/R)	Protocol biopsy (time post-Tx)[a]	Renal biopsy (time post-MSCs)	Virus infection (time post-MSCs)
1. M, 66 years	IgAN	HLA 1-2-2 mm PRAs 0% Cross-match: neg Anti-donor Abs: neg	−/−	Newly developed IF/TA (Banff IF/TA, I) (10 months)	BK nephropathy (+21 weeks)	BK virus activation (+21 weeks)
2. F, 61 years	AKI	HLA 1-1-2 mm PRAs 4% Cross-match: neg Anti-donor Abs: neg	+/−	Progressive IF/TA (Banff IF/TA, I) (9.5 months)		Primo CMV (+2 weeks)
3. M, 67 years	Nephrosclerosis	HLA 2-2-2 mm PRAs 0% Cross-match: neg Anti-donor Abs: neg	+/−	SCR and IF/TA (Banff borderline changes and IF/TA, I) (8 months)		Enhanced CMV viral load (+7 months)
4. M, 41 years	ADPKD	HLA 1-2-2 mm PRAs 0% Cross-match: neg Anti-donor Abs: neg	+/+	Borderline SCR and IF/TA (Banff Borderline changes and IF/TA, I) (6 months)	No SCR no IF/TA (+10 weeks)	
5. F, 54 years	ADPKD	HLA 1-2-2 mm PRAs 0% Cross-match: neg Anti-donor Abs: neg	+/−	SCR (Banff T-cell mediated rejection, IB) (6 months)	No SCR/no IF/TA (+6 weeks)	
6. F, 58 years	Hypertensive nephropathy	HLA 1-2-2 mm PRAs 4% Cross-match: neg Anti-donor Abs: neg	−/−	Increase in IF/TA (Banff IF/TA, I) (6 months)		

[a]Banff score according to Banff 97 diagnostic categories for renal allograft biopsies [16].

Abbreviations: Abs, antibodies; ADPKD, adult polycystic kidney disease; AKI, acute kidney injury; CMV, cytomegalovirus; D, donor; F, female; HLA, human leukocyte antigen; IF/TA, interstitial fibrosis tubular atrophy; IgAN, IgA nephropathy; M, male; mm, human leukocyte antigen mismatch; MSC, mesenchymal stromal cell; neg, negative; NODAT, new onset diabetes after transplantation; PRAs, panel reactive antibodies; R, recipient; SCR, subclinical rejection; Tx, transplantation.

Other Kidney Diseases

Repairing the Chronic Damaged Kidney: The Role of Regenerative Medicine

H.C. Caldas, A.P.C. Hayashi, and M. Abbud-Filho

Table 1. Model, Amount of Cells, Routes of Cell Administration, and Results of Studies Using Cell-Based Therapies for Treatment of Experimental Chronic Renal Failure

Reference	Model	Number and Cell Type	Functional Outcome	Delivery Method	Histology
18	COL4A3 KO	MSC (1×10^6)	No change in renal function	Tail vein	↓ Interstitial fibrosis
24	Anti-Thy1.1 (GN)	MSC (2×10^6)	Improved renal function and decreased proteinuria	Intra-arterially	↓ Glomerulosclerosis
29	5/6 nephrectomy	MSC (1×10^6)	No change in creatinine and decreased proteinuria	Tail vein	↓ Glomerulosclerosis
27	5/6 nephrectomy	MSC (2×10^6)	Increased albuminuria and serum creatinine	Subcapsule	↓ Glomerulosclerosis
30	5/6 nephrectomy	Lin—(2×10^6)	Decreased proteinuria	Tail vein	↓ Glomerulosclerosis ↓ Interstitial fibrosis
28	5/6 nephrectomy	MSC (2×10^5)	Amelioration of renal function	Tail vein	↓ Glomerulosclerosis ↓ Interstitial fibrosis
26	5/6 nephrectomy	MSC—MO (1×10^6)	Amelioration of renal function	Renal parenchyma	↓ Glomerulosclerosis
31	5/6 and 2/3 nephrectomy	MSC—MO (1×10^6)	Amelioration of renal function	BM seeded with MSC or MO implanted in the renal parenchyma	↓ Glomerulosclerosis ↓ Interstitial fibrosis ↓ Lymphocytic infiltration

COL4A3, collagen4A3 knockout; GN, glomerulonephritis; MO, mononuclear cell; MSC, mesenchymal stem cells; BM, biomaterial.

Transplantation Proceedings, 43, 3573–3576 (2011)

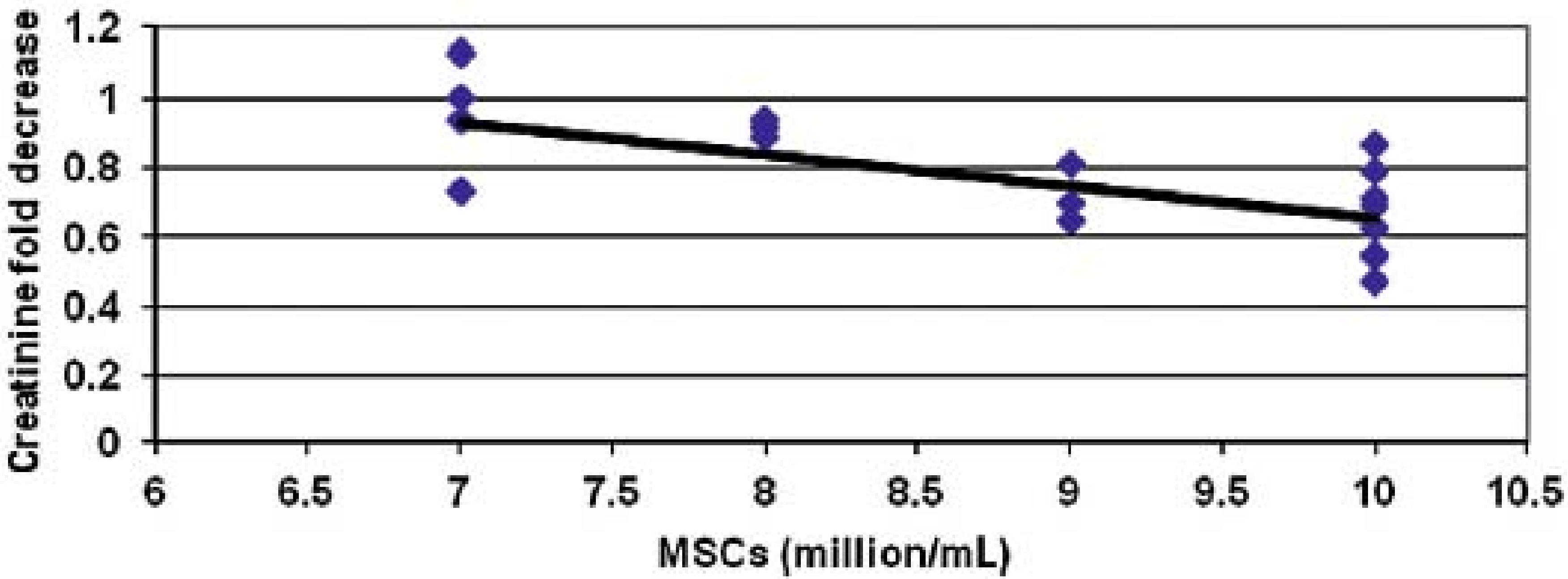
NEPHROLOGY

Original Article

Mesenchymal stem cells are a rescue approach for recovery of deteriorating kidney function

MERVAT EL-ANSARY, GAMAL SAADI and SAMAH M ABD EL-HAMID

Table 1 Clinical and laboratory data of all groups at diagnosis



Present	2; 20%	0; 0%	0; 0%	0.09
Absent	8; 80%	10; 100%	10; 100%	NS

NS, not significant; SD, standard deviation.

MSC in 2 divided doses 1 week apart

Followed for 6 months

Effect of stem cells seeded onto biomaterial on the progression of experimental chronic kidney disease

Heloisa C Caldas[1], Ida M M Fernandes[1], Rosa S Kawasaki-Oyama[1], Maria Alice S F Baptista[1], Ana Maria G Plepis[2], Virginia A Martins[2], Terezila M Coimbra[3], Eny M Goloni-Bertollo[4], Domingo M Braile[1] and Mario Abbud-Filho[1]

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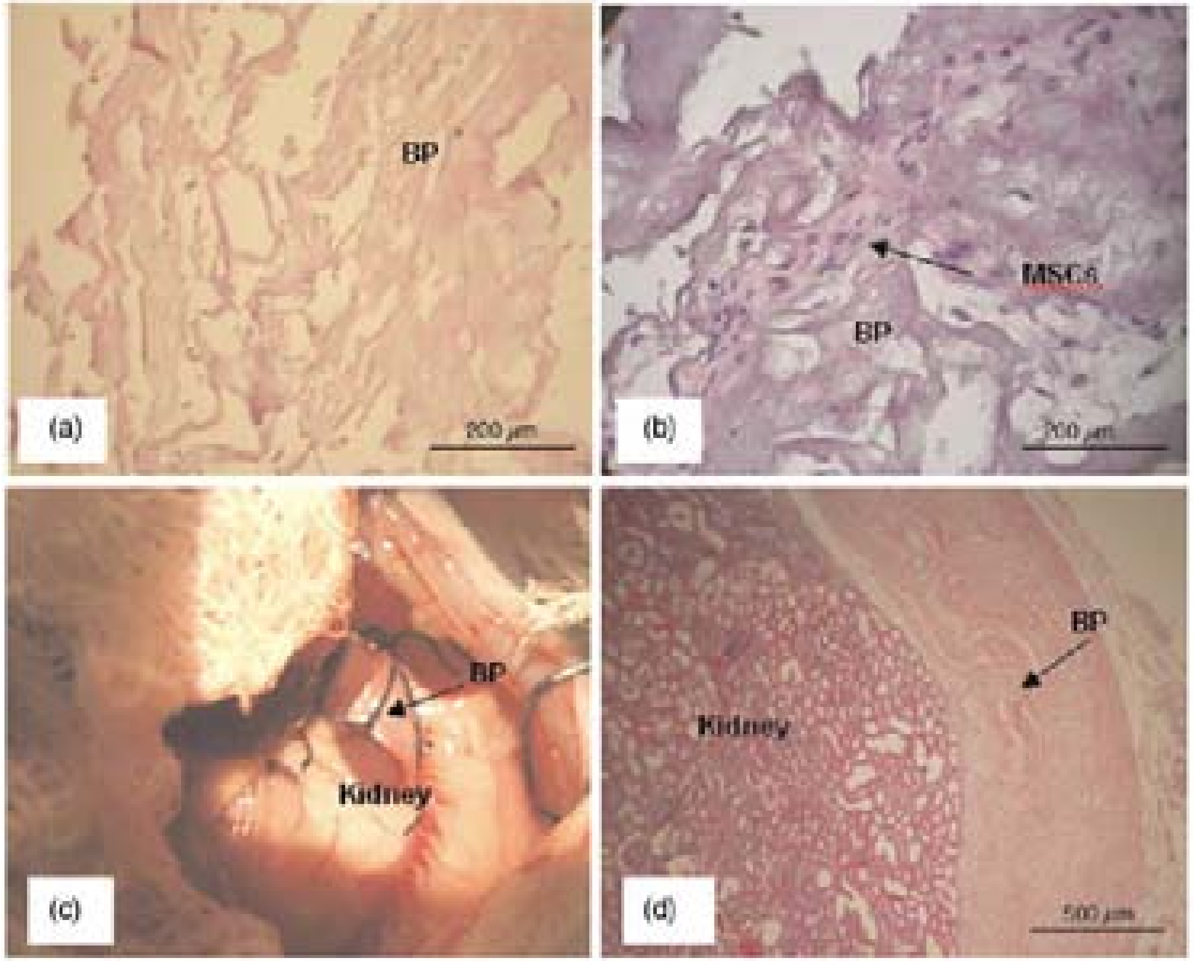
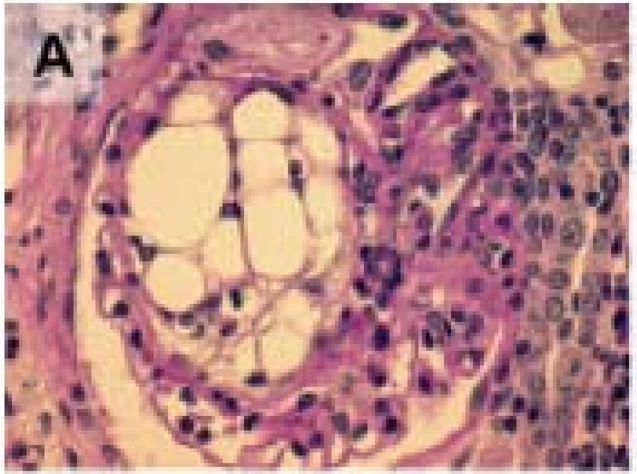
Email: mabbud@terra.com.br

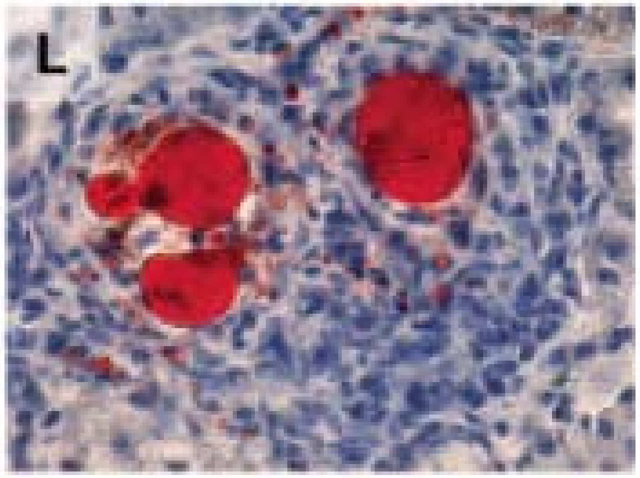


Mesenchymal Stem Cells Prevent Progressive Experimental Renal Failure but Maldifferentiate into Glomerular Adipocytes

Uta Kunter,* Song Rong,* Peter Boor,*† Frank Eitner,* Gerhard Müller-Newen,‡ Zivka Djuric,* Claudia R. van Roeyen,* Andrzej Konieczny,* Tammo Ostendorf,* Luigi Villa,* Maja Milovanceva-Popovska,* Dontscho Kerjaschki,§ and Jürgen Floege*

*Division of Nephrology, University Hospital RWTH Aachen, Aachen, Germany; †Department of Clinical and Experimental Pharmacotherapy, Slovak Medical University, Bratislava, Slovakia; ‡Institute of Biochemistry, University Hospital Rheinisch-Westfälische Technische Hochschule Aachen, Aachen, Germany; and §Department of Pathology, University of Vienna, Vienna, Austria





J Am Soc Nephrol 18: 1754–1764, 2007

Human Umbilical Mesenchymal Stem Cells Attenuate the Progression of Focal Segmental Glomerulosclerosis

Hualin Ma, PhD, Yaojiong Wu, MD, PhD, Ying Xu, MS, Liping Sun, PhD and Xinzhou Zhang, MD, PhD

TABLE 2. Comparison of urine protein concentration in every group

	Pretreatment urine protein (mg/d)	4 Week urine protein (mg/d)	8 Week urine protein (mg/d)	12 Week urine protein (mg/d)
No intervention	10.00 ± 5.20	9.75 ± 4.13	14.51 ± 1.88	22.49 ± 5.36
ADR	10.19 ± 4.09	204.82 ± 45.96[a]	149.01 ± 90.84[a]	28.07 ± 12.60
ADR + MSC iv low	12.59 ± 3.91	99.65 ± 18.88[a,b]	63.76 ± 33.66[b]	48.82 ± 17.61
ADR + MSC iv high	11.63 ± 7.22	55.82 ± 24.33[a,b]	45.45 ± 11.40[b]	37.92 ± 10.49

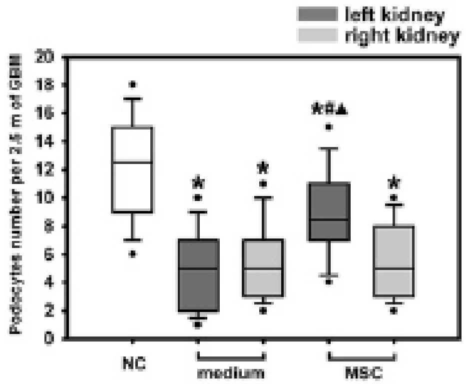
Values represent mean ± SEM.
[a] $P < 0.05$ vs. control group.
[b] $P < 0.05$ vs. ADR group.

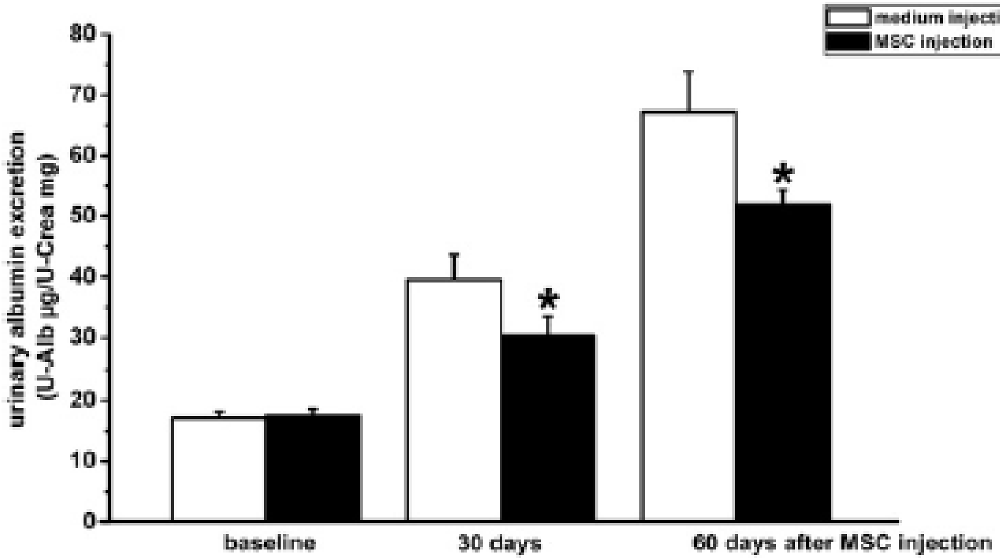
Biol Blood Marrow Transplant 19 (2013) 538–546

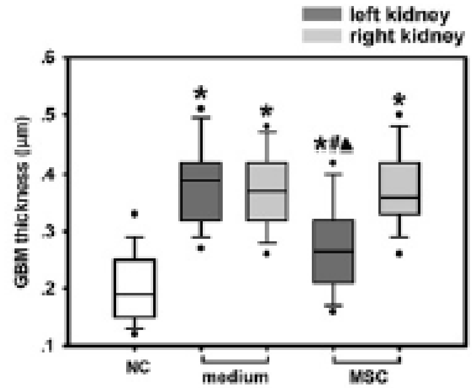
Mesenchymal Stem Cells Ameliorate Podocyte Injury and Proteinuria in a Type 1 Diabetic Nephropathy Rat Model

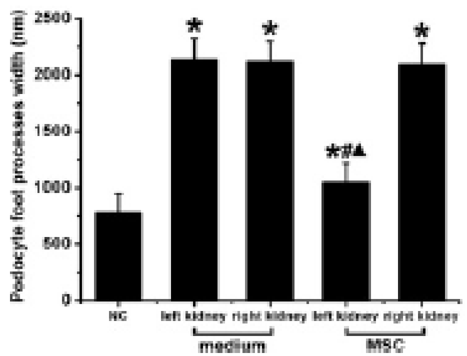
Shuai Wang [1,2], Yi Li [1], Jinghong Zhao [1], Jingbo Zhang [1], Yunjian Huang [1,*]

[1] Institute of Nephrology of Chongqing and Department of Nephrology, Xinqiao Hospital, Third Military Medical University, Chongqing, China
[2] Department of Nephrology, Chengdu Military General Hospital, Chengdu, Sichuan, China







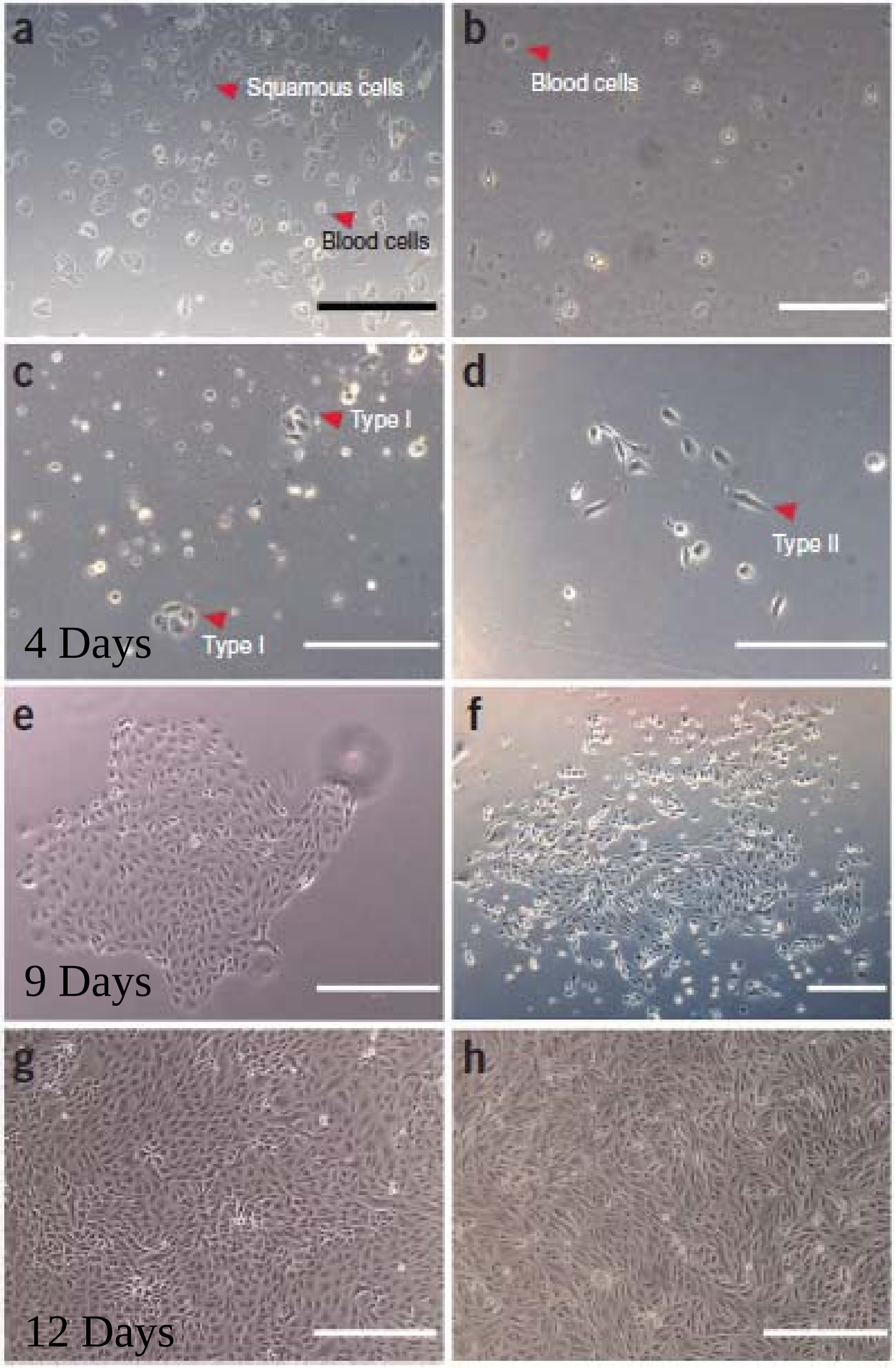


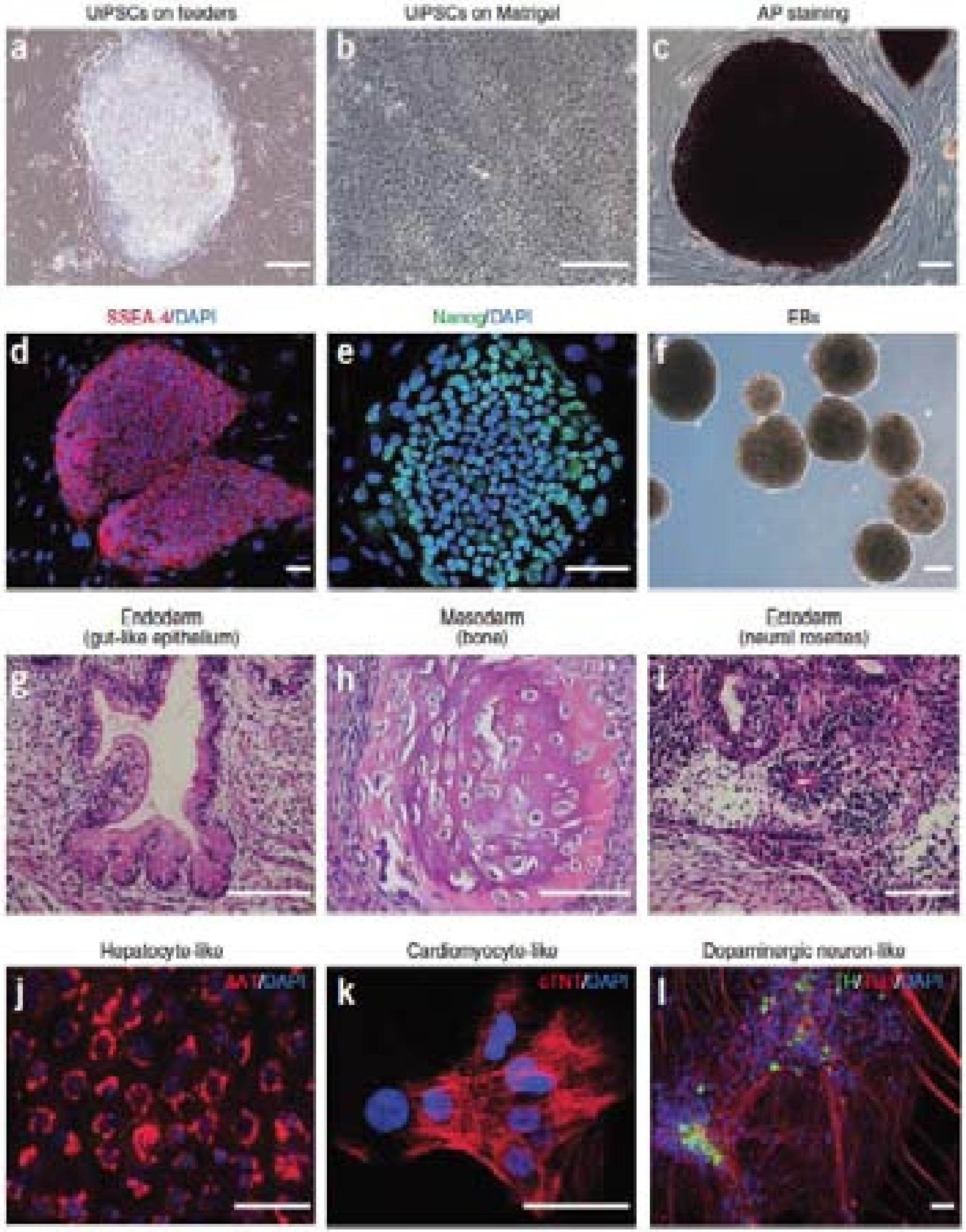
Risks of Cellular Therapy

- Immunosuppression
- Chromosomal abberations
- Neoplastic transformation
- Pulmonary emboli
- Lack of standardization of cell preparations
- Lack of efficacy

Generation of human induced pluripotent stem cells from urine samples

Ting Zhou[1,7], Christina Benda[1,7], Sarah Dunzinger[2], Yinghua Huang[1], Jenny Cy Ho[3], Jiayin Yang[1], Yu Wang[1], Yu Zhang[1], Qiang Zhuang[1], Yanhua Li[1], Xichen Bao[1], Hung-Fat Tse[3,5], Johannes Grillari[2,6], Regina Grillari-Voglauer[2,6], Duanqing Pei[1] & Miguel A Esteban[1,4,5]

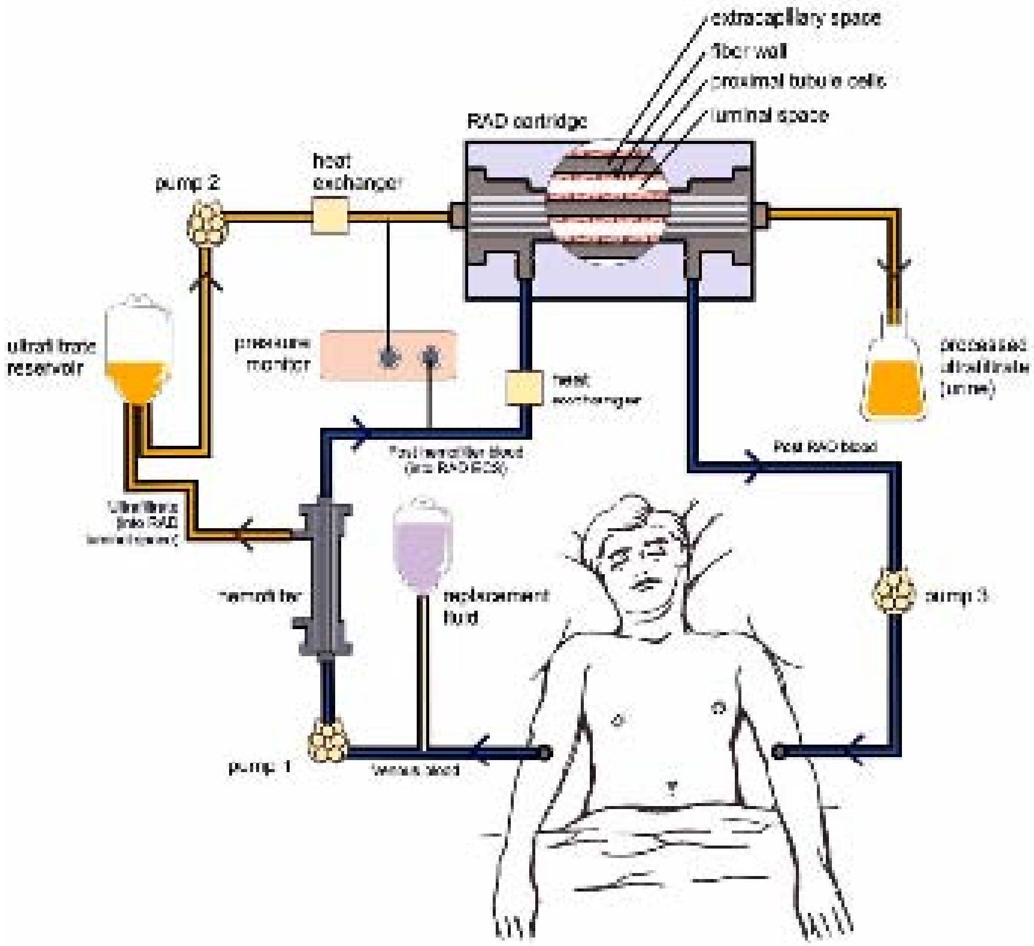



UiPSCs on feeders
UiPSCs on Matrigel
AP staining
a
b
c
SSEA-4/DAPI
Nanog/DAPI
EBs
d
e
f
Endoderm
(gut-like epithelium)
Mesoderm
(bone)
Ectoderm
(neural rosettes)
g
h
i
Hepatocyte-like
Cardiomyocyte-like
Dopaminergic neuron-like
j
k
l
AAT/DAPI
cTNT/DAPI
TH/Tuj1/DAPI

Current Drug Targets, 2009, *10*, 1227-1234

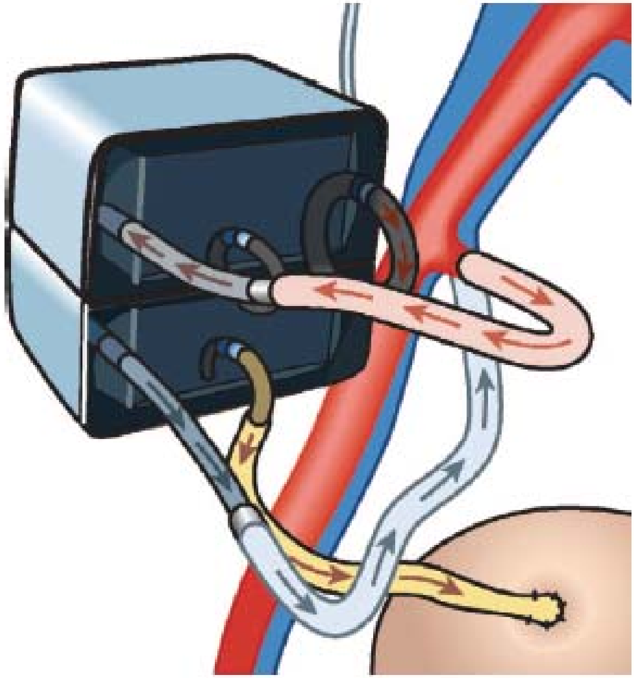
The Bioartificial Kidney in the Treatment of Acute Kidney Injury

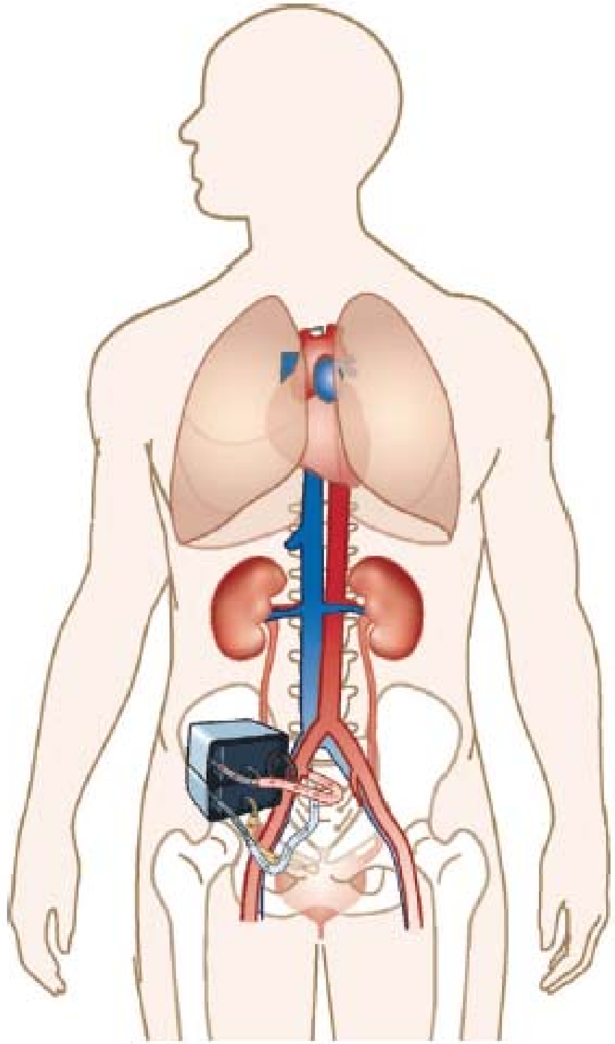
Joon Ho Song[1] and H. David Humes[*,2]



Achieving more frequent and longer dialysis for the majority: wearable dialysis and implantable artificial kidney devices

William H. Fissell[1], Shuvo Roy[2] and Andrew Davenport[3]



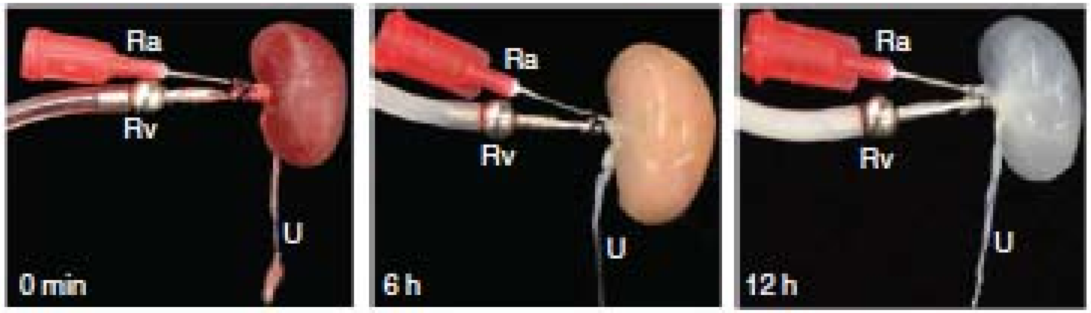


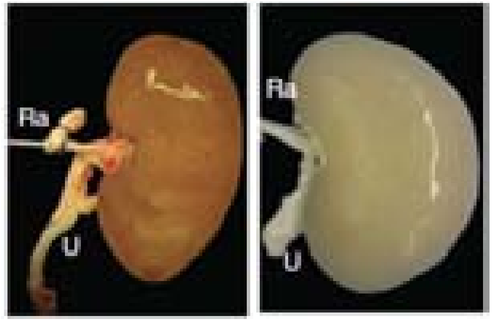
Kidney International advance online publication, 13 February 2013;
doi:10.1038/ki.2012.466

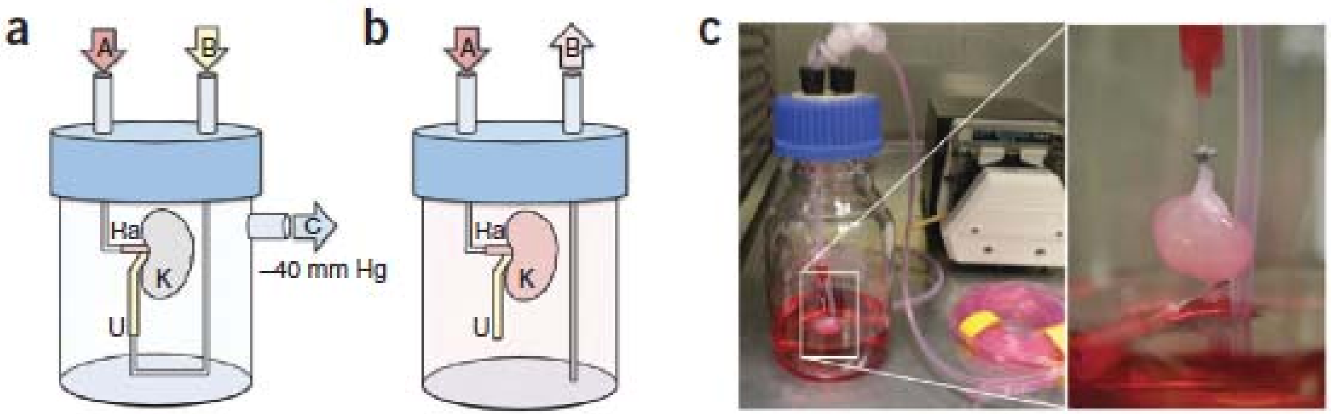
nature medicine

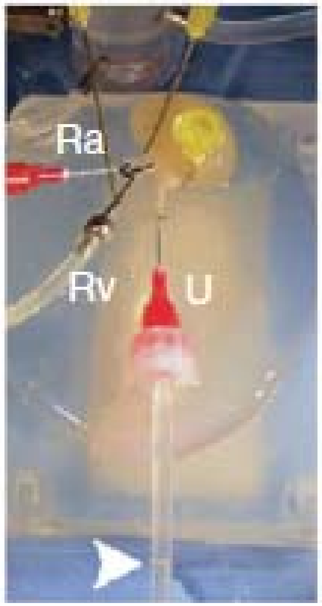
Regeneration and experimental orthotopic transplantation of a bioengineered kidney

Jeremy J Song[1,2], Jacques P Guyette[1,2], Sarah E Gilpin[1,2], Gabriel Gonzalez[1,2], Joseph P Vacanti[1–3] & Harald C Ott[1,2,4]





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Rv
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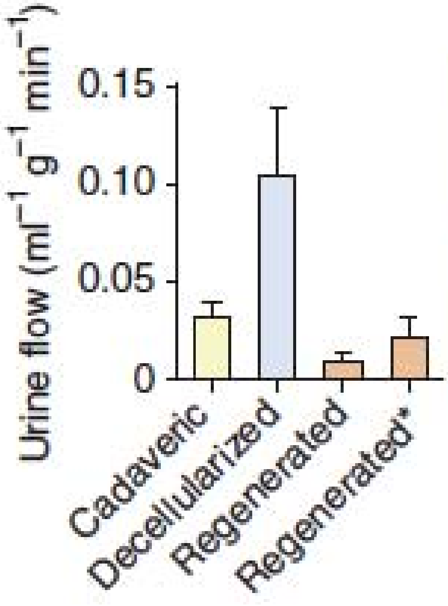
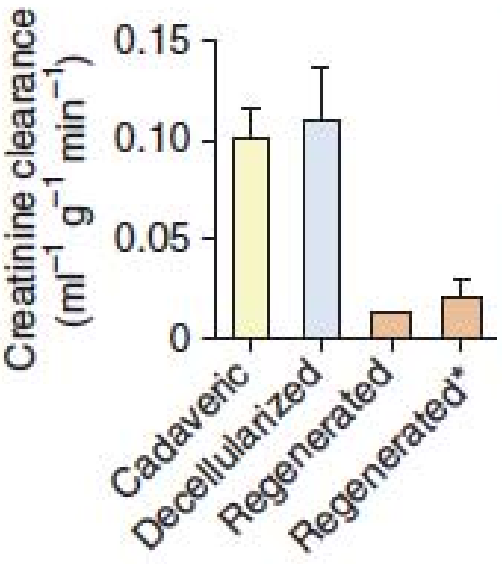
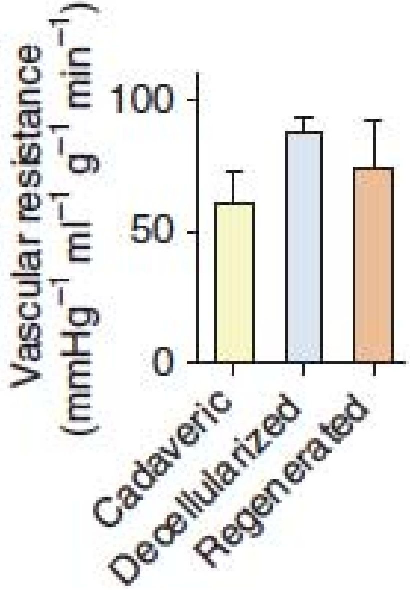
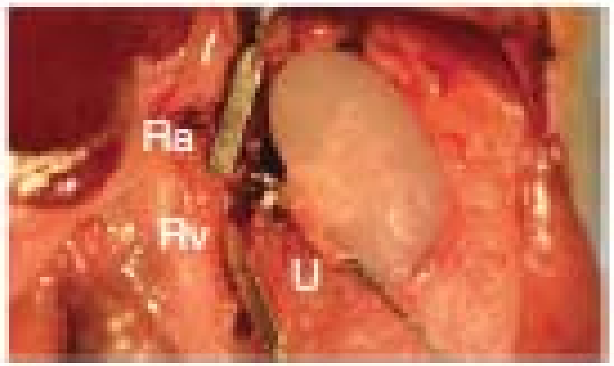

Urine flow (ml^{-1} g^{-1} min^{-1})
0.15
0.10
0.05
0
Cadaveric
Decellularized
Regenerated
Regenerated*


Creatinine clearance (ml^{-1} g^{-1} min^{-1})
0.15
0.10
0.05
0
Cadaveric
Decellularized
Regenerated
Regenerated*


Vascular resistance (mmHg^{-1} ml^{-1} g^{-1} min^{-1})
100
50
0
Cadaveric
Decellularized
Regenerated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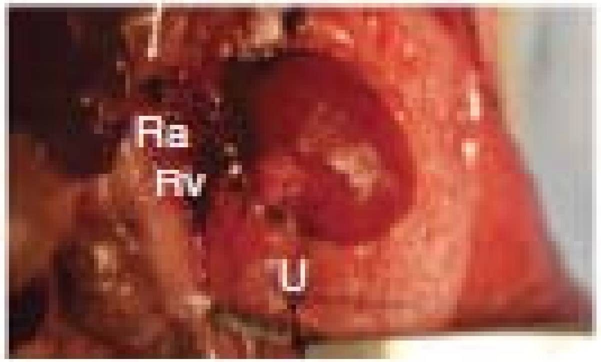
Ra
Rv
U

Case Presentation

- 58 year old diabetic man admitted to the ICU with an acute anterior MI
- Baseline creatinine 3.1 (diabetic nephropathy)
- Persistent chest pain $\Rightarrow$ angiography and emergent CABG
- Post-op hypotensive (80/45), hypoxemic, wedge 31, CXR pulmonary edema, anuric with Cr 4.2 and K 6.0

Evaluation and Treatment 2020

- Preoperative genomic screen demonstrates increased susceptibility to AKI genotype
- Serial perioperative biomarker screens demonstrate early ATN
- Autologous mesenchymal stem cells ordered from Cell Bank and infused into suprarenal aorta
- Biomarker screen demonstrate good response to stem cells with all markers decreasing 12 hours following surgery
- Housestaff attend History of Medicine lecture on use of serum creatinine to monitor kidney function


TAKE TWO STEM CELLS AND CALL ME IN THE MORNING.
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The End

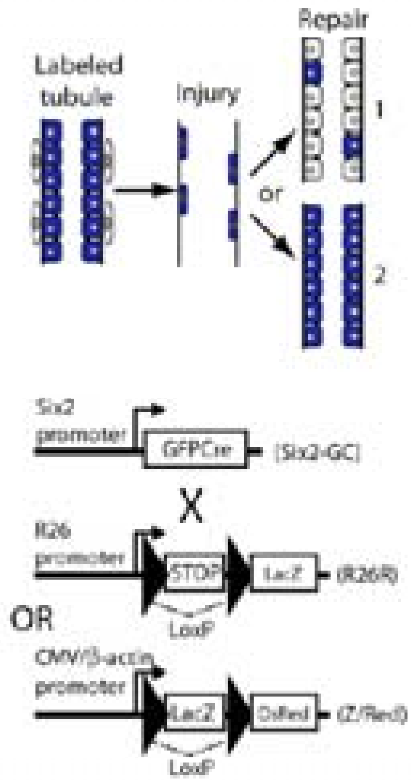

Worth1000.com

Acute Kidney Injury

Cell Stem Cell
Short Article

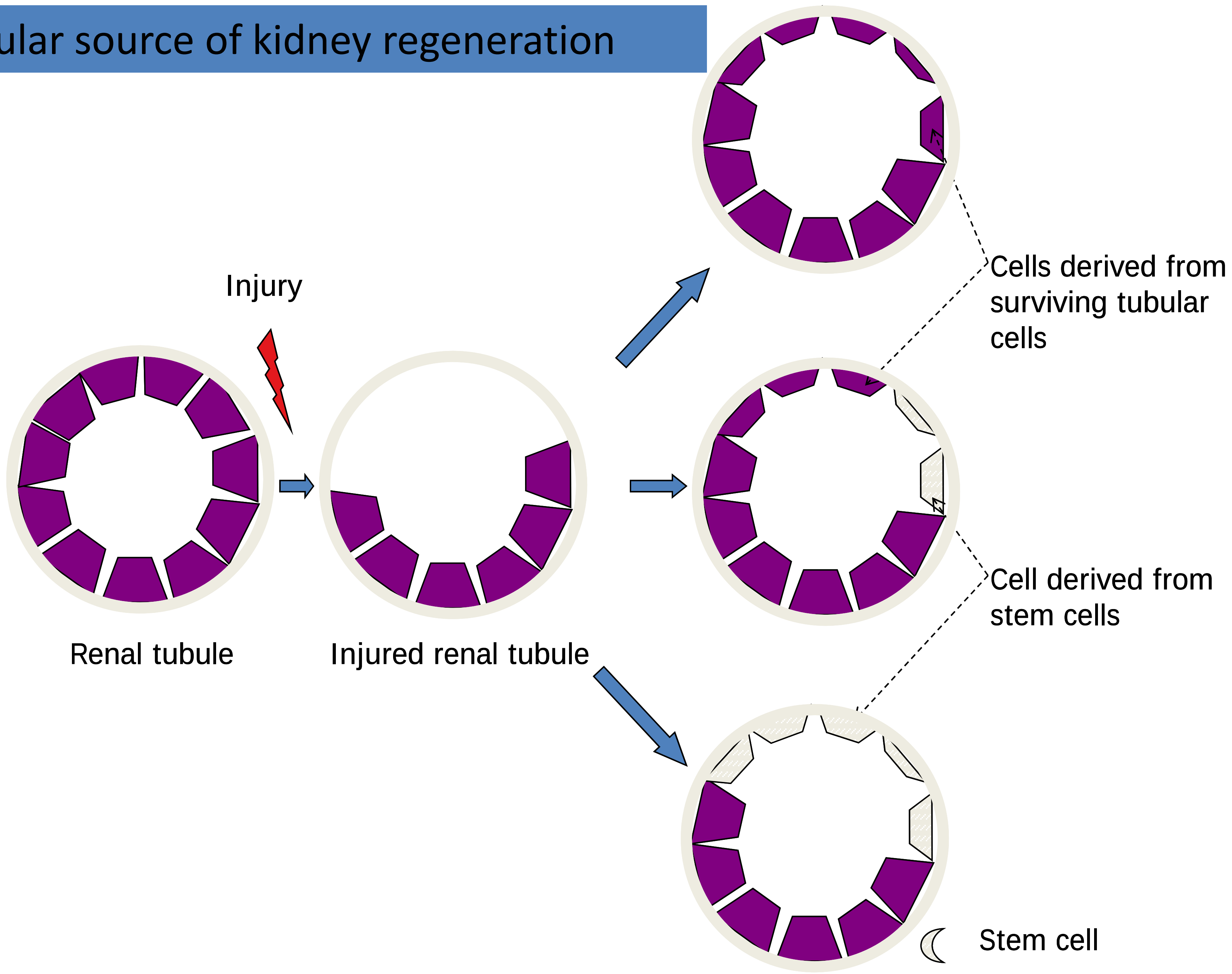
Intrinsic Epithelial Cells Repair the Kidney after Injury

Benjamin D. Humphreys, M. Todd Valerius, Akio Kobayashi, Joshua W. Mugford, Saruth Soeung, Jeremy S. Duffield, Andrew P. McMahon, and Joseph V. Bonventre



Cell Stem Cell 2, 284–291, March 2008

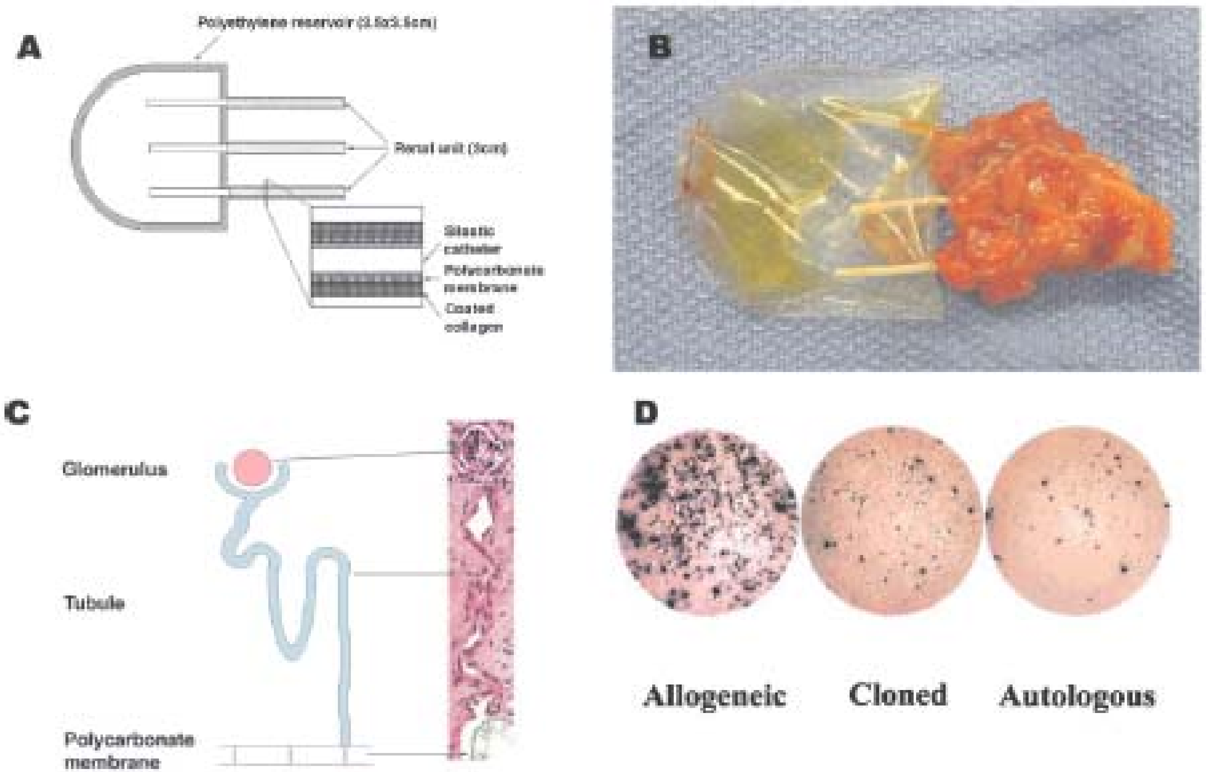
Cellular source of kidney regeneration



J Am Soc Nephrol 15: 1113–1125, 2004

Tissue Engineering, Stem Cells, and Cloning: Opportunities for Regenerative Medicine

CHESTER J. KOH and ANTHONY ATALA
Institute for Regenerative Medicine, Wake Forest University School of Medicine, Winston Salem, North Carolina.



OPEN ACCESS Freely available online

PLoS one

Human Embryonic Mesenchymal Stem Cell-Derived Conditioned Medium Rescues Kidney Function in Rats with Established Chronic Kidney Disease

Arianne van Koppen[1], Jaap A. Joles[1], Bas W. M. van Balkom[1], Sai Kiang Lim[2], Dominique de Kleijn[3], Rachel H. Giles[1], Marianne C. Verhaar[1*]

gapore, Republic