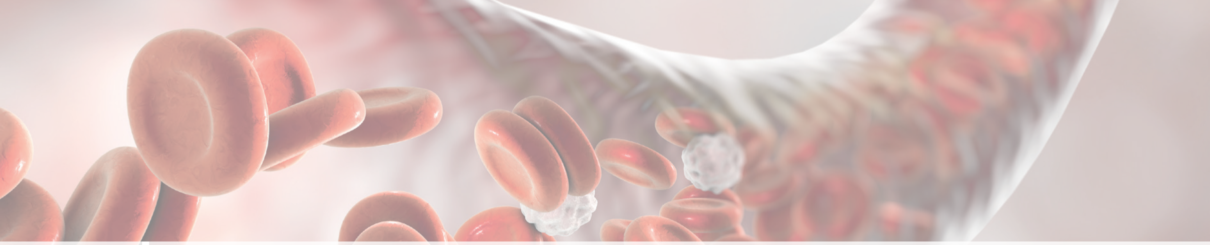

5. Bölüm

BÖBREK İSKEMİ REPERFÜZYONU

Ayşegül KÜÇÜK[1]
Ümmü Gülşen BOZOK[2]
Ali Can KURTİPEK[3]

5.1. Böbrek Fizyolojisi

Böbrekler vücut ağırlığının yaklaşık % 0.5'i olmasına rağmen, fonksiyonları sebebiyle en yoğun çalışan düzenleyici organlardan biridir. Böbrek vücut sıvı ozmolaritesi ve hacminin düzenlenmesi, su ve elektrolit dengesi, asit baz dengesi, kan basıncının düzenlenmesi, metabolik atıklar ve yabancı maddelerin atılması, bazı hormonların üretilmesi ve salgılanması işlemlerini gerçekleştirerek metabolizmanın düzenlenmesinde rol alır.

Vücut sıvılarının ozmolarite ve hacminin düzenlenmesi, dokularda normal hücre hacminin sürdürülmesi ve dolaşım sisteminin normal fonksiyonu için gereklidir. Homeostazın devamı için de elektrolitlerin ve suyun atılan miktarı ile alınan miktarı dengede olmalıdır. Elektrolit ve su dengesi böbrekler tarafından günlük atılımın günlük alımla dengelenmesi ile sağlanır. Vücudun metabolik fonksiyonlarının çoğu pH'a duyarlıdır. Bu yüzden vücut sıvılarının pH'ı çok dar sınırlar içinde tutulmalıdır. Bu düzenlemede akciğerler ve böbrekler rol oynar. Böbrekler üre, ürik asit, kreatinin, hemoglobin (Hb) yıkım son ürünleri, hormon metabolitleri gibi çok sayıda metabolik son ürünü atar. Ayrıca, ilaçlar ve yiyeceklerle alınan be-

[1] Prof. Dr., Kütahya Sağlık Bilimleri Üniversitesi Tıp Fakültesi, Fizyoloji AD., kucukaysegul@hotmail.com
[2] Öğr. Gör. Dr., Kütahya Sağlık Bilimleri Üniversitesi Tıp Fakültesi, Fizyoloji AD., gulsenozsoy07@gmail.com
[3] Uzm. Dr., Ankara Şehir Hastanesi, İç Hastalıkları Kliniği, akurtipeka@gmail.com

Kaynaklar

1. Köylü H. Klinik Anlatımlı Tıbbi Fizyoloji. 2. Baskı, 2016:283-85
2. Rojas-Morales P, León-Contreras JC, Aparicio-Trejo OE, Reyes-Ocampo JG, Medina-Campos ON, Jiménez-Osorio AS, et al. Fasting reduces oxidative stress, mitochondrial dysfunction and fibrosis induced by renal ischemia-reperfusion injury. Free Radic Biol Med 2019;135:60-7.
3. Hoste EAJ, Kellum JA, Selby NM, Zarbock A, Palevsky PM, Bagshaw SM, et al. Global epidemiology and outcomes of acute kidney injury. Nat Rev Nephrol 2018;14(10):607-25.
4. Lameire NH, Bagga A, Cruz D, De Maeseneer J, Endre Z, Kellum JA, et al. Acute kidney injury: an increasing global concern. Lancet 2013;382(9887):170-9.
5. Beker BM, Corleto MG, Fieiras C, Musso CG. Novel acute kidney injury biomarkers: their characteristics, utility and concerns. Int Urol Nephrol 2018;50(4):705-13.
6. Jensen D, Kierulf-Lassen C, Kristensen MLV, Nørregaard R, Weyer K, Nielsen R, et al. Megalin dependent urinary cystatin C excretion in ischemic kidney injury in rats. PLoS One 2017;12(6):e0178796. doi: 10.1371/journal.pone.0178796.
7. Price PM, Megyesi J, Saggi S, Safirstein RL. Regulation of transcription by the rat EGF gene promoter in normal and ischemic murine kidney cells. Am J Physiol 1995;268(4 Pt 2):F664-70.
8. Hosgood SA, Bagul A, Nicholson ML. Minimising cold ischaemic injury in an experimental model of kidney transplantation. Eur J Clin Invest 2011;41(3):233-40.
9. Lane BR, Babitz SK, Vlasakova K, Wong A, Noyes SL, Boshoven W, et al. Evaluation of Urinary Renal Biomarkers for Early Prediction of Acute Kidney Injury Following Partial Nephrectomy: A Feasibility Study. Eur Urol Focus 2020;6(6):1240-7.
10. Nguan CY, Guan Q, Gleave ME, Du C. Promotion of cell proliferation by clusterin in the renal tissue repair phase after ischemia-reperfusion injury. Am J Physiol Renal Physiol 2014;306(7):F724-33.
11. Dekker SEI, Ruhaak LR, Romijn FPHTM, Meijer E, Cobbaert CM, de Fijter JW, et al; DIPAK Consortium. Urinary Tissue Inhibitor of Metalloproteinases-2 and Insulin-Like Growth Factor-Binding Protein 7 Do Not Correlate With Disease Severity in ADPKD Patients. Kidney Int Rep 2019;4(6):833-41.
12. Greenberg JH, Zappitelli M, Jia Y, Thiessen-Philbrook HR, de Fontnouvelle CA, Wilson FP, et al. Biomarkers of AKI Progression after Pediatric Cardiac Surgery. J Am Soc Nephrol 2018;29(5):1549-56.
13. Bennett M, Dent CL, Ma Q, Dastrala S, Grenier F, Workman R, et al. Urine NGAL predicts severity of acute kidney injury after cardiac surgery: a prospective study. Clin J Am Soc Nephrol 2008;3(3):665-73.
14. Kocan H, Citgez S, Yucetas U, Yucetas E, Yazici M, Amasyali AS, et al. Can ischemia-modified albumin be used as an objective biomarker for renal ischemic damage? An experimental study with Wistar albino rats. Transplant Proc 2014;46(10):3326-9.
15. Bao YW, Yuan Y, Chen JH, Lin WQ. Kidney disease models: tools to identify mechanisms and potential therapeutic targets. Zool Res 2018;39(2):72-86.
16. Shiva N, Sharma N, Kulkarni YA, Mulay SR, Gaikwad AB. Renal ischemia/reperfusion injury: An insight on in vitro and in vivo models. Life Sci 2020;256:117860. doi: 10.1016/j.lfs.2020.117860.
17. Galli F, Piroddi M, Annetti C, Aisa C, Floridi E, Floridi A. Oxidative stress and reactive oxygen species. Contrib Nephrol 2005;149:240-60.
18. Alejandro V, Scandling JD Jr, Sibley RK, Dafoe D, Alfrey E, Deen W, et al. Mechanisms of filtration failure during postischemic injury of the human kidney. A study of the reperfused renal allograft. J Clin Invest 1995;95(2):820-31.

19. Basile DP, Anderson MD, Sutton TA. Pathophysiology of acute kidney injury. Compr Physiol 2012;2(2):1303-53.
20. Saikumar P, Venkatachalam MA. Role of apoptosis in hypoxic/ischemic damage in the kidney. Semin Nephrol 2003;23(6):511-21.
21. Ashworth SL, Sandoval RM, Tanner GA, Molitoris BA. Two-photon microscopy: visualization of kidney dynamics. Kidney Int 2007;72(4):416-21.
22. Burne-Taney MJ, Rabb H. The role of adhesion molecules and T cells in ischemic renal injury. Curr Opin Nephrol Hypertens 2003;12(1):85-90.
23. Zuk A, Bonventre JV, Brown D, Matlin KS. Polarity, integrin, and extracellular matrix dynamics in the postischemic rat kidney. Am J Physiol 1998;275(3):C711-31.
24. Molitoris BA, Geerdes A, McIntosh JR. Dissociation and redistribution of Na+,K(+)-ATPase from its surface membrane actin cytoskeletal complex during cellular ATP depletion. J Clin Invest 1991;88(2):462-9.
25. Imamura R, Isaka Y, Sandoval RM, Ori A, Adamsky S, Feinstein E, et al. Intravital two-photon microscopy assessment of renal protection efficacy of siRNA for p53 in experimental rat kidney transplantation models. Cell Transplant 2010;19(12):1659-70.
26. Sogabe K, Roeser NF, Davis JA, Nurko S, Venkatachalam MA, Weinberg JM. Calcium dependence of integrity of the actin cytoskeleton of proximal tubule cell microvilli. Am J Physiol 1996;271(2 Pt 2):F292-303.
27. Goligorsky MS, Brodsky SV, Noiri E. NO bioavailability, endothelial dysfunction, and acute renal failure: new insights into pathophysiology. Semin Nephrol 2004;24(4):316-23.
28. Sutton TA, Kelly KJ, Mang HE, Plotkin Z, Sandoval RM, Dagher PC. Minocycline reduces renal microvascular leakage in a rat model of ischemic renal injury. Am J Physiol Renal Physiol 2005;288(1):F91-7.
29. Jang HR, Rabb H. Immune cells in experimental acute kidney injury. Nat Rev Nephrol 2015;11(2):88-101.
30. Ozkok A, Edelstein CL. Pathophysiology of cisplatin-induced acute kidney injury. Biomed Res Int 2014;2014:967826. doi: 10.1155/2014/967826.
31. Perše M, Večerić-Haler Ž. Cisplatin-Induced Rodent Model of Kidney Injury: Characteristics and Challenges. Biomed Res Int 2018;2018:1462802. doi: 10.1155/2018/1462802.
32. Gautier JC, Riefke B, Walter J, Kurth P, Mylecraine L, Guilpin V, et al. Evaluation of novel biomarkers of nephrotoxicity in two strains of rat treated with Cisplatin. Toxicol Pathol 2010;38(6):943-56.
33. Vinken P, Starckx S, Barale-Thomas E, Looszova A, Sonee M, Goeminne N, et al. Tissue Kim-1 and urinary clusterin as early indicators of cisplatin-induced acute kidney injury in rats. Toxicol Pathol 2012;40(7):1049-62.
34. Yamate J, Tatsumi M, Nakatsuji S, Kuwamura M, Kotani T, Sakuma S. Immunohistochemical observations on the kinetics of macrophages and myofibroblasts in rat renal interstitial fibrosis induced by cis-diamminedichloroplatinum. J Comp Pathol 1995;112(1):27-39.
35. Behling EB, Sendão MC, Francescato HD, Antunes LM, Costa RS, Bianchi Mde L. Comparative study of multiple dosage of quercetin against cisplatin-induced nephrotoxicity and oxidative stress in rat kidneys. Pharmacol Rep 2006;58(4):526-32.
36. Yamate J, Ishida A, Tsujino K, Tatsumi M, Nakatsuji S, Kuwamura M, et al. Immunohistochemical study of rat renal interstitial fibrosis induced by repeated injection of cisplatin, with special reference to the kinetics of macrophages and myofibroblasts. Toxicol Pathol 1996;24(2):199-206.
37. Yamate J, Sato K, Ide M, Nakanishi M, Kuwamura M, Sakuma S, et al. Participation of different macrophage populations and myofibroblastic cells in chronically developed renal interstitial fibrosis after cisplatin-induced renal injury in rats. Vet Pathol 2002;39(3):322-33.

38. Zhang J, Goering PL, Espandiari P, Shaw M, Bonventre JV, Vaidya VS, et al. Differences in immunolocalization of Kim-1, RPA-1, and RPA-2 in kidneys of gentamicin-, cisplatin-, and valproic acid-treated rats: potential role of iNOS and nitrotyrosine. Toxicol Pathol 2009;37(5):629-43.
39. Santos NA, Catão CS, Martins NM, Curti C, Bianchi ML, Santos AC. Cisplatin-induced nephrotoxicity is associated with oxidative stress, redox state unbalance, impairment of energetic metabolism and apoptosis in rat kidney mitochondria. Arch Toxicol 2007;81(7):495-504.
40. Kishore BK, Krane CM, Di Iulio D, Menon AG, Cacini W. Expression of renal aquaporins 1, 2, and 3 in a rat model of cisplatin-induced polyuria. Kidney Int 2000;58(2):701-11.
41. Price PM, Safirstein RL, Megyesi J. The cell cycle and acute kidney injury. Kidney Int 2009;76(6):604-13.
42. Yang C, Kaushal V, Shah SV, Kaushal GP. Autophagy is associated with apoptosis in cisplatin injury to renal tubular epithelial cells. Am J Physiol Renal Physiol 2008;294(4):F777-87.
43. Daugaard G, Abildgaard U, Larsen S, Holstein-Rathlou NH, Amtorp O, Olesen HP, et al. Functional and histopathological changes in dog kidneys after administration of cisplatin. Ren Physiol 1987;10(1):54-64.
44. Akcay A, Nguyen Q, He Z, Turkmen K, Won Lee D, Hernando AA, et al. IL-33 exacerbates acute kidney injury. J Am Soc Nephrol 2011;22(11):2057-67.
45. Morigi M, Rota C, Montemurro T, Montelatici E, Lo Cicero V, Imberti B, et al. Life-sparing effect of human cord blood-mesenchymal stem cells in experimental acute kidney injury. Stem Cells 2010;28(3):513-22.
46. Wei Q, Wang MH, Dong Z. Differential gender differences in ischemic and nephrotoxic acute renal failure. Am J Nephrol 2005;25(5):491-9.
47. Wei Q, Dong Z. Mouse model of ischemic acute kidney injury: technical notes and tricks. Am J Physiol Renal Physiol 2012;303(11):F1487-94.
48. Skrypnyk NI, Harris RC, de Caestecker MP. Ischemia-reperfusion model of acute kidney injury and post injury fibrosis in mice. J Vis Exp 2013;(78):50495. doi: 10.3791/50495.
49. Fu Y, Tang C, Cai J, Chen G, Zhang D, Dong Z. Rodent models of AKI-CKD transition. Am J Physiol Renal Physiol 2018;315(4):F1098-106.
50. Nemoto T, Burne MJ, Daniels F, O'Donnell MP, Crosson J, Berens K, et al. Small molecule selectin ligand inhibition improves outcome in ischemic acute renal failure. Kidney Int 2001;60(6):2205-14.
51. Masola V, Zaza G, Gambaro G, Onisto M, Bellin G, Vischini G, et al. Heparanase: A Potential New Factor Involved in the Renal Epithelial Mesenchymal Transition (EMT) Induced by Ischemia/Reperfusion (I/R) Injury. PLoS One 2016;11(7):e0160074. doi: 10.1371/journal.pone.0160074.
52. Wei J, Zhang J, Wang L, Jiang S, Fu L, Buggs J, et al. New mouse model of chronic kidney disease transitioned from ischemic acute kidney injury. Am J Physiol Renal Physiol 2019;317(2):F286-95.
53. Kim J, Padanilam BJ. Renal denervation prevents long-term sequelae of ischemic renal injury. Kidney Int 2015;87(2):350-8.
54. Danelli L, Madjene LC, Madera-Salcedo I, Gautier G, Pacreau E, Ben Mkaddem S, et al. Early Phase Mast Cell Activation Determines the Chronic Outcome of Renal Ischemia-Reperfusion Injury. J Immunol 2017;198(6):2374-82.
55. Lu X, Li N, Shushakova N, Schmitt R, Menne J, Susnik N, et al. C57BL/6 and 129/Sv mice: genetic difference to renal ischemia-reperfusion. J Nephrol 2012;25(5):738-43.
56. Adachi T, Sugiyama N, Gondai T, Yagita H, Yokoyama T. Blockade of Death Ligand TRAIL Inhibits Renal Ischemia Reperfusion Injury. Acta Histochem Cytochem 2013;46(6):161-70.

57. Le Clef N, Verhulst A, D'Haese PC, Vervaet BA. Unilateral Renal Ischemia-Reperfusion as a Robust Model for Acute to Chronic Kidney Injury in Mice. PLoS One 2016;11(3):e0152153. doi: 10.1371/journal.pone.0152153.
58. Park Y, Hirose R, Dang K, Xu F, Behrends M, Tan V, et al. Increased severity of renal ischemia-reperfusion injury with venous clamping compared to arterial clamping in a rat model. Surgery 2008;143(2):243-51.
59. Owji SM, Nikeghbal E, Moosavi SM. Comparison of ischaemia-reperfusion-induced acute kidney injury by clamping renal arteries, veins or pedicles in anaesthetized rats. Exp Physiol 2018;103(10):1390-402.
60. Finn WF. Enhanced recovery from postischemic acute renal failure. Micropuncture studies in the rat. Circ Res 1980;46(3):440-8.
61. Lech M, Gröbmayr R, Ryu M, Lorenz G, Hartter I, Mulay SR, et al. Macrophage phenotype controls long-term AKI outcomes--kidney regeneration versus atrophy. J Am Soc Nephrol 2014;25(2):292-304.
62. Shrestha B, Haylor J. Experimental rat models of chronic allograft nephropathy: a review. Int J Nephrol Renovasc Dis 2014;7:315-22.
63. Ahmadi AR, Qi L, Iwasaki K, Wang W, Wesson RN, Cameron AM, et al. Orthotopic Rat Kidney Transplantation: A Novel and Simplified Surgical Approach. J Vis Exp 2019;(147). doi: 10.3791/59403.
64. D'Silva M, Gittes RF, Wolf P, Pirenne J, Munger K, Pascual J, et al. Rat kidney transplantation update with special reference to vesical calculi. Microsurgery 1990;11(2):169-76.
65. Yin M, Booster MH, vd Bogaard AE, Kootstra G. A simple technique to harvest two kidneys from one donor rat for transplantation. Lab Anim 1994;28(4):387-90.
66. Halazun KJ, Al-Mukhtar A, Aldouri A, Willis S, Ahmad N. Warm ischemia in transplantation: search for a consensus definition. Transplant Proc 2007;39(5):1329-31.
67. Feuillu B, Cormier L, Frimat L, Kessler M, Amrani M, Mangin P, et al. Kidney warming during transplantation. Transpl Int 2003;16(5):307-12.
68. Szostek M, Kosieradzki M, Chmura A, Pacholczyk M, Lagiewska B, Adadyński L, et al. Does "second warm ischemia time" play a role in kidney allograft function? Transplant Proc 1999;31(1-2):1037-8.
69. Florack G, Sutherland DE, Ascherl R, Heil J, Erhardt W, Najarian JS. Definition of normothermic ischemia limits for kidney and pancreas grafts. J Surg Res 1986;40(6):550-63.
70. Ahmad N, Pratt JR, Potts DJ, Lodge JP. Comparative efficacy of renal preservation solutions to limit functional impairment after warm ischemic injury. Kidney Int 2006;69(5):884-93.
71. Stubenitsky BM, Booster MH, Nederstigt AP, Kievit JK, Jacobs RW, Kootstra G. Kidney preservation in the next millenium. Transpl Int 1999;12(2):83-91.
72. Toscano MG, Ganea D, Gamero AM. Cecal ligation puncture procedure. J Vis Exp 2011;(51):2860. doi: 10.3791/2860.
73. Kono H, Chen CJ, Ontiveros F, Rock KL. Uric acid promotes an acute inflammatory response to sterile cell death in mice. J Clin Invest 2010;120(6):1939-49.
74. Chen SW, Kim M, Kim M, Song JH, Park SW, Wells D, et al. Mice that overexpress human heat shock protein 27 have increased renal injury following ischemia reperfusion. Kidney Int 2009;75(5):499-510.
75. Rosenberger C, Griethe W, Gruber G, Wiesener M, Frei U, Bachmann S, et al. Cellular responses to hypoxia after renal segmental infarction. Kidney Int 2003;64(3):874-86.
76. Bernhardt WM, Câmpean V, Kany S, Jürgensen JS, Weidemann A, Warnecke C, et al. Preconditional activation of hypoxia-inducible factors ameliorates ischemic acute renal failure. J Am Soc Nephrol 2006;17(7):1970-8.
77. Matsumoto M, Makino Y, Tanaka T, Tanaka H, Ishizaka N, Noiri E, et al. Induction of renoprotective gene expression by cobalt ameliorates ischemic injury of the kidney in rats. J Am Soc Nephrol 2003;14(7):1825-32.

78. Kelly KJ, Williams WW Jr, Colvin RB, Meehan SM, Springer TA, Gutierrez-Ramos JC, et al. Intercellular adhesion molecule-1-deficient mice are protected against ischemic renal injury. J Clin Invest 1996;97(4):1056-63.
79. Takada M, Nadeau KC, Shaw GD, Marquette KA, Tilney NL. The cytokine-adhesion molecule cascade in ischemia/reperfusion injury of the rat kidney. Inhibition by a soluble P-selectin ligand. J Clin Invest 1997;99(11):2682-90.
80. Donnahoo KK, Meng X, Ayala A, Cain MP, Harken AH, Meldrum DR. Early kidney TNF-alpha expression mediates neutrophil infiltration and injury after renal ischemia-reperfusion. Am J Physiol 1999;277(3):R922-9.
81. Hiroyoshi T, Tsuchida M, Uchiyama K, Fujikawa K, Komatsu T, Kanaoka Y, et al. Splenectomy protects the kidneys against ischemic reperfusion injury in the rat. Transpl Immunol 2012;27(1):8-11.
82. Anders HJ, Vielhauer V, Schlöndorff D. Chemokines and chemokine receptors are involved in the resolution or progression of renal disease. Kidney Int 2003;63(2):401-15.
83. Furuichi K, Wada T, Iwata Y, Kitagawa K, Kobayashi K, Hashimoto H, et al. CCR2 signaling contributes to ischemia-reperfusion injury in kidney. J Am Soc Nephrol 2003;14(10):2503-15.
84. Wu H, Chen G, Wyburn KR, Yin J, Bertolino P, Eris JM, et al. TLR4 activation mediates kidney ischemia/reperfusion injury. J Clin Invest 2007;117(10):2847-59.
85. Ysebaert DK, De Greef KE, Vercauteren SR, Ghielli M, Verpooten GA, Eyskens EJ, et al. Identification and kinetics of leukocytes after severe ischaemia/reperfusion renal injury. Nephrol Dial Transplant 2000;15(10):1562-74.
86. De Greef KE, Ysebaert DK, Dauwe S, Persy V, Vercauteren SR, Mey D, et al. Anti-B7-1 blocks mononuclear cell adherence in vasa recta after ischemia. Kidney Int 2001;60(4):1415-27.
87. Jo SK, Sung SA, Cho WY, Go KJ, Kim HK. Macrophages contribute to the initiation of ischaemic acute renal failure in rats. Nephrol Dial Transplant 2006;21(5):1231-9.
88. Persy VP, Verhulst A, Ysebaert DK, De Greef KE, De Broe ME. Reduced postischemic macrophage infiltration and interstitial fibrosis in osteopontin knockout mice. Kidney Int 2003;63(2):543-53.
89. Alikhan MA, Jones CV, Williams TM, Beckhouse AG, Fletcher AL, Kett MM, et al. Colony-stimulating factor-1 promotes kidney growth and repair via alteration of macrophage responses. Am J Pathol 2011;179(3):1243-56.
90. Lee S, Huen S, Nishio H, Nishio S, Lee HK, Choi BS, et al. Distinct macrophage phenotypes contribute to kidney injury and repair. J Am Soc Nephrol 2011;22(2):317-26.
91. Zhang MZ, Yao B, Yang S, Jiang L, Wang S, Fan X, et al. CSF-1 signaling mediates recovery from acute kidney injury. J Clin Invest 2012;122(12):4519-32.
92. Loverre A, Capobianco C, Stallone G, Infante B, Schena A, Ditonno P, et al. Ischemia-reperfusion injury-induced abnormal dendritic cell traffic in the transplanted kidney with delayed graft function. Kidney Int 2007;72(8):994-1003.
93. Zhang ZX, Shek K, Wang S, Huang X, Lau A, Yin Z, et al. Osteopontin expressed in tubular epithelial cells regulates NK cell-mediated kidney ischemia reperfusion injury. J Immunol 2010;185(2):967-73.
94. Ascon DB, Lopez-Briones S, Liu M, Ascon M, Savransky V, Colvin RB, et al. Phenotypic and functional characterization of kidney-infiltrating lymphocytes in renal ischemia reperfusion injury. J Immunol 2006;177(5):3380-7.
95. Sakr M, Zetti G, McClain C, Gavaler J, Nalesnik M, Todo S, et al. The protective effect of FK506 pretreatment against renal ischemia/reperfusion injury in rats. Transplantation 1992;53(5):987-91.
96. Jones EA, Shoskes DA. The effect of mycophenolate mofetil and polyphenolic bioflavonoids on renal ischemia reperfusion injury and repair. J Urol 2000;163(3):999-1004.

97. Takada M, Chandraker A, Nadeau KC, Sayegh MH, Tilney NL. The role of the B7 costimulatory pathway in experimental cold ischemia/reperfusion injury. J Clin Invest 1997;100(5):1199-203.
98. Day YJ, Huang L, Ye H, Li L, Linden J, Okusa MD. Renal ischemia-reperfusion injury and adenosine 2A receptor-mediated tissue protection: the role of CD4+ T cells and IFN-gamma. J Immunol 2006;176(5):3108-14.
99. Yokota N, Burne-Taney M, Racusen L, Rabb H. Contrasting roles for STAT4 and STAT6 signal transduction pathways in murine renal ischemia-reperfusion injury. Am J Physiol Renal Physiol 2003;285(2):F319-25.
100. Wang S, Diao H, Guan Q, Cruikshank WW, Delovitch TL, Jevnikar AM, et al. Decreased renal ischemia-reperfusion injury by IL-16 inactivation. Kidney Int 2008;73(3):318-26.
101. Ascon DB, Ascon M, Satpute S, Lopez-Briones S, Racusen L, Colvin RB, et al. Normal mouse kidneys contain activated and CD3+CD4- CD8- double-negative T lymphocytes with a distinct TCR repertoire. J Leukoc Biol 2008;84(6):1400-9.
102. Jang HR, Gandolfo MT, Ko GJ, Racusen L, Rabb H. The effect of murine anti-thymocyte globulin on experimental kidney warm ischemia-reperfusion injury in mice. Transpl Immunol 2009;22(1-2):44-54.
103. Gandolfo MT, Jang HR, Bagnasco SM, Ko GJ, Agreda P, Satpute SR, et al. Foxp3+ regulatory T cells participate in repair of ischemic acute kidney injury. Kidney Int 2009;76(7):717-29.
104. Ascon M, Ascon DB, Liu M, Cheadle C, Sarkar C, Racusen L, et al. Renal ischemia-reperfusion leads to long term infiltration of activated and effector-memory T lymphocytes. Kidney Int 2009;75(5):526-35.
105. Jang HR, Gandolfo MT, Ko GJ, Satpute SR, Racusen L, Rabb H. B cells limit repair after ischemic acute kidney injury. J Am Soc Nephrol 2010;21(4):654-65.
106. Stromski ME, Cooper K, Thulin G, Gaudio KM, Siegel NJ, Shulman RG. Chemical and functional correlates of postischemic renal ATP levels. Proc Natl Acad Sci U S A 1986;83(16):6142-5.
107. Ichimura T, Asseldonk EJ, Humphreys BD, Gunaratnam L, Duffield JS, Bonventre JV. Kidney injury molecule-1 is a phosphatidylserine receptor that confers a phagocytic phenotype on epithelial cells. J Clin Invest 2008;118(5):1657-68.
108. Li B, Castano AP, Hudson TE, Nowlin BT, Lin SL, Bonventre JV, et al. The melanoma-associated transmembrane glycoprotein Gpnmb controls trafficking of cellular debris for degradation and is essential for tissue repair. FASEB J 2010;24(12):4767-81.
109. Lin SL, Li B, Rao S, Yeo EJ, Hudson TE, Nowlin BT, et al. Macrophage Wnt7b is critical for kidney repair and regeneration. Proc Natl Acad Sci U S A 2010;107(9):4194-9.
110. Vannay A, Fekete A, Adori C, Tóth T, Losonczy G, László L, et al. Divergence of renal vascular endothelial growth factor mRNA expression and protein level in post-ischaemic rat kidneys. Exp Physiol 2004;89(4):435-44.
111. Han SJ, Lee HT. Mechanisms and therapeutic targets of ischemic acute kidney injury. Kidney Res Clin Pract 2019;38(4):427-40.
112. Gupta S, Verfaillie C, Chmielewski D, Kren S, Eidman K, Connaire J, et al. Isolation and characterization of kidney-derived stem cells. J Am Soc Nephrol 2006;17(11):3028-40.
113. Tongers J, Losordo DW. Frontiers in nephrology: the evolving therapeutic applications of endothelial progenitor cells. J Am Soc Nephrol 2007;18(11):2843-52.
114. Bussolati B, Bruno S, Grange C, Buttiglieri S, Deregibus MC, Cantino D, et alG. Isolation of renal progenitor cells from adult human kidney. Am J Pathol 2005;166(2):545-55.
115. De Broe ME. Tubular regeneration and the role of bone marrow cells: 'stem cell therapy'--a panacea? Nephrol Dial Transplant 2005;20(11):2318-20.
116. Lange C, Tögel F, Ittrich H, Clayton F, Nolte-Ernsting C, Zander AR, et al. Administered mesenchymal stem cells enhance recovery from ischemia/reperfusion-induced acute renal failure in rats. Kidney Int 2005;68(4):1613-7.

117. Li B, Cohen A, Hudson TE, Motlagh D, Amrani DL, Duffield JS. Mobilized human hematopoietic stem/progenitor cells promote kidney repair after ischemia/reperfusion injury. Circulation 2010;121(20):2211-20.
118. Park KM, Chen A, Bonventre JV. Prevention of kidney ischemia/reperfusion-induced functional injury and JNK, p38, and MAPK kinase activation by remote ischemic pretreatment. J Biol Chem 2001;276(15):11870-6.
119. Kinsey GR, Huang L, Vergis AL, Li L, Okusa MD. Regulatory T cells contribute to the protective effect of ischemic preconditioning in the kidney. Kidney Int 2010;77(9):771-80.
120. Munshi R, Hsu C, Himmelfarb J. Advances in understanding ischemic acute kidney injury. BMC Med 2011;9:11. doi: 10.1186/1741-7015-9-11.
121. Rosenberger C, Mandriota S, Jürgensen JS, Wiesener MS, Hörstrup JH, Frei U, et al. Expression of hypoxia-inducible factor-1alpha and -2alpha in hypoxic and ischemic rat kidneys. J Am Soc Nephrol 2002;13(7):1721-32.
122. Kojima I, Tanaka T, Inagi R, Kato H, Yamashita T, Sakiyama A, et al. Protective role of hypoxia-inducible factor-2alpha against ischemic damage and oxidative stress in the kidney. J Am Soc Nephrol 2007;18(4):1218-26.
123. Hill P, Shukla D, Tran MG, Aragones J, Cook HT, Carmeliet P, et al. Inhibition of hypoxia inducible factor hydroxylases protects against renal ischemia-reperfusion injury. J Am Soc Nephrol 2008;19(1):39-46.
124. Park KM, Byun JY, Kramers C, Kim JI, Huang PL, Bonventre JV. Inducible nitric-oxide synthase is an important contributor to prolonged protective effects of ischemic preconditioning in the mouse kidney. J Biol Chem 2003;278(29):27256-66.
125. Yeh CH, Hsu SP, Yang CC, Chien CT, Wang NP. Hypoxic preconditioning reinforces HIF-alpha-dependent HSP70 signaling to reduce ischemic renal failure-induced renal tubular apoptosis and autophagy. Life Sci 2010;86(3-4):115-23.
126. Hölzen JP, August C, Bahde R, Minin E, Lang D, Heidenreich S, et al. Influence of heme oxygenase-1 on microcirculation after kidney transplantation. J Surg Res 2008;148(2):126-35.
127. Kim J, Jang HS, Park KM. Reactive oxygen species generated by renal ischemia and reperfusion trigger protection against subsequent renal ischemia and reperfusion injury in mice. Am J Physiol Renal Physiol 2010;298(1):F158-66.
128. Hung CC, Ichimura T, Stevens JL, Bonventre JV. Protection of renal epithelial cells against oxidative injury by endoplasmic reticulum stress preconditioning is mediated by ERK1/2 activation. J Biol Chem 2003;278(31):29317-26.
129. Zarbock A, Kellum JA. Remote Ischemic Preconditioning and Protection of the Kidney--A Novel Therapeutic Option. Crit Care Med 2016;44(3):607-16.
130. Er F, Nia AM, Dopp H, Hellmich M, Dahlem KM, Caglayan E, et al. Ischemic preconditioning for prevention of contrast medium-induced nephropathy: randomized pilot RenPro Trial (Renal Protection Trial). Circulation 2012;126(3):296-303.
131. Hu S, Dong H, Zhang H, Wang S, Hou L, Chen S, et al. Noninvasive limb remote ischemic preconditioning contributes neuroprotective effects via activation of adenosine A1 receptor and redox status after transient focal cerebral ischemia in rats. Brain Res 2012;1459:81-90.
132. Hale SL, Kloner RA. Protection of myocardium by transient, preischemic administration of phenylephrine in the rabbit. Coron Artery Dis 1994;5(7):605-10.