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SUPPLEMENTARY MATERIAL

Hemostasis and the kidney: an unforeseen initial opportunity to create a small research group that grew into an institute

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SELECTED PUBLICATIONS FROM THE GROUP

1. T. Bertani, G. Rocchi, G. Sacchi, G. Mecca, G. Remuzzi. Adriamycin-induced glomerulosclerosis in the rat. *Am J Kidney Dis* 1986;7:12-19.
2. M. Livio, A. Benigni, G. Viganò, G. Mecca, G. Remuzzi. Moderate doses of aspirin and risk of bleeding in renal failure. *Lancet* 1986;1:414-416.
3. C. Zoja, L. Furci, F. Ghilardi, P. Zilio, A. Benigni, G. Remuzzi. Cyclosporin-induced endothelial cell injury. *Lab Invest* 1986;55:455-462.
4. F. Gaspari, G. Viganò, S. Orisio, M. Bonati, M. Livio, G. Remuzzi. Aspirin prolongs bleeding time in uremia by a mechanism distinct from platelet cyclooxygenase inhibition. *J Clin Invest* 1987;79:1788-1797.
5. G. Remuzzi. HUS and TTP: Variable expression of a single entity. *Kidney Int* 1987;32:292-308.
6. M. Livio, A. Benigni, C. Zoja, R. Begnis, C. Morelli, M. Rossini, S. Garattini, G. Remuzzi. Differential inhibition by aspirin of platelet thromboxane and renal prostaglandins in the rat. *J Pharmacol Exp Ther* 1989;248:334-341.
7. A. Benigni, G. Gregorini, T. Frusca, C. Chiabrando, S. Ballerini, A. Valcamonico, S. Orisio, A. Piccinelli, V. Pincioli, R. Fanelli, A. Gastaldi, G. Remuzzi. Effect of low-dose aspirin on fetal and maternal generation of thromboxane by platelets in women at risk for pregnancy-induced hypertension. *N Engl J Med* 1989;321:357-362.
8. A. Remuzzi, S. Puntorieri, C. Battaglia, T. Bertani, G. Remuzzi. Angiotensin converting enzyme inhibition ameliorates glomerular filtration of macromolecules and water and lessens glomerular injury in the rat. *J Clin Invest* 1990;85:541-549.
9. G. Remuzzi, T. Bertani. Is glomerulosclerosis a consequence of altered glomerular permeability to macromolecules? *Kidney Int* 1990;38:384-394.
10. G. Remuzzi, M. Rossini, O. Imberti, N. Perico. Kidney graft survival in rats without immunosuppressive drugs after intrathymic glomerular transplantation. *Lancet* 1991;337:750-752.
11. A. Benigni, C. Zoja, D. Corna, S. Orisio, L. Longaretti, T. Bertani, G. Remuzzi. A specific endothelin subtype A receptor antagonist protects against injury in renal disease progression. *Kidney Int* 1993;44:440-444.
12. A. Remuzzi, A. Benigni, B. Malanchini, I. Bruzzi, C. Foglieni, G. Remuzzi. ACE inhibition prevents renal failure and death in uninephrectomized MWF/Ztm rats. *Kidney Int* 1995;47:1319-1326.
13. A. Benigni, C. Zoja, G. Remuzzi. The renal toxicity of sustained glomerular protein traffic. *Lab Invest* 1995;73:461-468.
14. G. Remuzzi, P. Ruggenenti, A. Benigni. Understanding the nature of renal disease progression. *Kidney Int* 1997;51:2-15.

15. A. Benigni, V. Colosio, C. Brena, I. Bruzzi, T. Bertani, G. Remuzzi. Unselective inhibition of endothelin receptors reduces renal dysfunction in experimental diabetes. *Diabetes* 1998;47:450-456.
16. P. Ruggenenti, A. Perna, L. Mosconi, R. Pisoni, G. Remuzzi, on behalf of the (GISEN). Urinary protein excretion rate is the best independent predictor of ESRF in non-diabetic proteinuric chronic nephropathies. *Kidney Int* 1998;53:1209-1216.
17. C. Zojá, R. Donadelli, S. Colleoni, M. Figliuzzi, S. Bonazzola, M. Morigi, G. Remuzzi. Protein overload stimulates RANTES production by proximal tubular cells depending on NF- κ B activation. *Kidney Int* 1998;53:1608-1615.
18. A. Benigni, D. Corna, R. Maffi, G. Benedetti, C. Zojá, G. Remuzzi. Renoprotective effect of contemporary blocking of angiotensin II and endothelin-1 in rats with membranous nephropathy. *Kidney Int* 1998;54:353-359.
19. M. Abbate, C. Zojá, D. Rottoli, D. Corna, N. Perico, T. Bertani, G. Remuzzi. Antiproteinuric therapy while preventing the abnormal protein traffic in proximal tubule abrogates protein- and complement-dependent interstitial inflammation in experimental renal disease. *J Am Soc Nephrol* 1999;10:804-813.
20. M. Galbusera, A. Benigni, S. Paris, P. Ruggenenti, C. Zojá, C. Rossi, G. Remuzzi. Unrecognized pattern of von Willebrand Factor abnormalities in hemolytic uremic syndrome and thrombotic thrombocytopenic purpura. *J Am Soc Nephrol* 1999;10:1234-1241.
21. A. Remuzzi, A. Fassi, T. Bertani, N. Perico, G. Remuzzi. ACE inhibition induces regression of proteinuria and halts progression of renal damage in a genetic model of progressive nephropathy. *Am J Kidney Dis* 1999;34:626-632.
22. S. Tomasoni, N. Azzollini, F. Casiraghi, M.C. Capogrossi, G. Remuzzi, A. Benigni. CTLA4Ig gene transfer prolongs survival and induces donor-specific tolerance in a rat renal allograft. *J Am Soc Nephrol* 2000;11:747-752.
23. C. Zojá, A. Benigni, M. Noris, D. Corna, F. Casiraghi, M. Pagnoncelli, D. Rottoli, M. Abbate, G. Remuzzi. Mycophenolate mofetil combined with a cyclooxygenase-2 inhibitor ameliorates murine lupus nephritis and prolongs animal life. *Kidney Int* 2001;60:653-663.
24. M. Morigi, M. Galbusera, E. Binda, B. Imberti, S. Gastoldi, A. Remuzzi, C. Zojá, G. Remuzzi. Verotoxin-1-induced upregulation of adhesive molecules renders microvascular endothelial cells thrombogenic at high shear stress. *Blood* 2001;98(6):1828-1835.
25. C. Zojá, S. Angioletti, R. Donadelli, C. Zanchi, S. Tomasoni, E. Binda, B. Imberti, M. te Loo, L. Monnens, G. Remuzzi, M. Morigi. Shiga toxin-2 triggers endothelial leukocyte adhesion and transmigration via NF- κ B dependent up-regulation of IL-8 and MCP-1. *Kidney Int* 2002;62:846-856.
26. C. Zojá, D. Corna, D. Camozzi, D. Cattaneo, D. Rottoli, C. Batani, C. Zanchi, M. Abbate, G. Remuzzi. How to fully protect the kidney in a severe model of progressive

nephropathy: a multidrug approach. J Am Soc Nephrol 2002;13:2898-2908.

27. A. Benigni, C. Zoja, D. Corna, C. Zatelli, S. Conti, M. Campana, E. Gagliardini, D. Rottoli, C. Zanchi, M. Abbate, S. Ledbetter, G. Remuzzi. Add-on anti-TGF- β antibody to ACE inhibitor arrests progressive diabetic nephropathy in the rat. J Am Soc Nephrol 2003;14:1816-1824.
28. A. Remuzzi, E. Gagliardini, F. Sangalli, M. Bonomelli, M. Piccinelli, A. Benigni, G. Remuzzi. ACE inhibition reduces glomerulosclerosis and regenerates glomerular tissue in a model of progressive renal disease. Kidney Int 2006;69:1124-1130.
29. A. Benigni, S. Tomasoni, L.A. Turka, L. Longaretti, L. Zentilin, M. Mister, A. Pezzotta, N. Azzollini, M. Noris, S. Conti, M. Abbate, M. Giacca, G. Remuzzi. Adeno-Associated Virus-mediated CTLA4Ig gene transfer protects MHC-mismatched renal allografts from chronic rejection. J Am Soc Nephrol 2006;17:1665-1672.
30. M. Abbate, C. Zoja, G. Remuzzi. How does proteinuria cause progressive renal damage? J Am Soc Nephrol 2006;17:2974-2984.
31. M. Abbate, C. Zoja, D. Corna, D. Rottoli, C. Zanchi, N. Azzollini, S. Tomasoni, S. Berlingeri, M. Noris, M. Morigi, G. Remuzzi. Complement-mediated dysfunction of glomerular filtration barrier accelerates progressive renal injury. J Am Soc Nephrol 2008;19:1158-1167.
32. M. Morigi, M. Introna, B. Imberti, D. Corna, M. Abbate, C. Rota, D. Rottoli, A. Benigni, N. Perico, C. Zoja, A. Rambaldi, A. Remuzzi, G. Remuzzi. Human bone marrow mesenchymal stem cells accelerate recovery of acute renal injury and prolong survival in mice. Stem Cells 2008;26:2075-2082.
33. F. Casiraghi, N. Azzollini, P. Cassis, B. Imberti, M. Morigi, D. Cugini, R.A. Cavinato, M. Todeschini, S. Solini, A. Sonzogni, N. Perico, G. Remuzzi, M. Noris. Pretransplant infusion of mesenchymal stem cells prolongs the survival of a semiallogeneic heart transplant through the generation of regulatory T cells. J Immunol 2008;181:3933-3946.
34. A. Benigni, D. Corna, C. Zoja, A. Sonzogni, R. Latini, M. Salio, S. Conti, D. Rottoli, L. Longaretti, P. Cassis, M. Morigi, T.M. Coffman, G. Remuzzi. Disruption of the Ang II type 1 receptor promotes longevity in mice. J Clin Invest 2009;119:524-530.
35. C. Zoja, D. Corna, E. Gagliardini, S. Conti, L. Arnaboldi, A. Benigni, G. Remuzzi. Adding a statin to a combination of ACE inhibitor and ARB normalizes proteinuria in experimental diabetes, which translates into full renoprotection. Am J Physiol Renal Physiol. 2010;299:F1203-1211.
36. C. Zoja, P. Bautista Garcia, C. Rota, S. Conti, E. Gagliardini, D. Corna, C. Zanchi, P. Bigini, A. Benigni, G. Remuzzi, M. Morigi. Mesenchymal stem cell therapy promotes renal repair by limiting glomerular podocyte and progenitor cell dysfunction in adriamycin-induced nephropathy. Am J Physiol Renal Physiol 2012;303:F1370-F1381.
37. C. Xinaris, V. Benedetti, P. Rizzo, M. Abbate, D. Corna, N. Azzollini, S. Conti, M. Unbekandt, J.A. Devies, M. Morigi, A. Benigni, G. Remuzzi. *In vivo* maturation of functional renal organoids formed from embryonic cell suspensions. J Am Soc Nephrol 2012;23:1857-1868.

38. M. Locatelli, S. Buelli, A. Pezzotta, D. Corna, L. Perico, S. Tomasoni, D. Rottoli, P. Rizzo, D. Conti, J.M. Thurman, G. Remuzzi, C. Zoja, M. Morigi. Shiga-toxin promotes podocyte injury in experimental hemolytic uremic syndrome via activation of the alternative pathway of complement. *J Am Soc Nephrol* 2014;25:1786-1798.
39. A. Remuzzi, F. Sangalli, D. Macconi, S. Tomasoni, I. Cattaneo, P. Rizzo, B. Bonandrini, E. Bresciani, L. Longaretti, E. Gagliardini, S. Conti, A. Benigni, G. Remuzzi. Regression of renal disease by angiotensin II antagonism is caused by re generation of kidney vasculature. *J Am Soc Nephrol* 2016;27:699-705.
40. C. Zanchi, D. Macconi, P. Trionfini, S. Tomasoni, D. Rottoli, M. Locatelli, M. Rudnicki, J. Vandesompele, P. Mestdagh, G. Remuzzi, A. Benigni, C. Zoja. MicroRNA-184 is a downstream effector of albuminuria driving renal fibrosis in rats with diabetic nephropathy. *Diabetologia* 2017;60:1114-1125.
41. L. Perico, M. Morigi, C. Rota, M. Breno, C. Mele, M. Noris, M. Intronà, C. Capelli, L. Longaretti, D. Rottoli, S. Conti, D. Corna, G. Remuzzi, A. Benigni. Human mesenchymal stromal cells transplanted into mice stimulate renal tubular cells and enhance mitochondrial function. *Nat Commun* 2017;8:983.
42. S. Conti, N. Perico, R. Novelli, C. Carrara, A. Benigni, G. Remuzzi. Early and late scanning electron microscopy findings in diabetic kidney disease. *Sci Rep* 2018;8:4909.
43. C. Rota, M. Morigi, D. Cerullo, M. Intronà, O. Colpani, D. Corna, C. Capelli, T.J. Rabelink, D.G. Leuning, D. Rottoli, A. Benigni, C. Zoja, G. Remuzzi. Therapeutic potential of stromal cells of non-renal or renal origin in experimental chronic kidney disease. *Stem Cell Res Ther* 2018;9:220.
44. P. Cassis, M. Locatelli, D. Cerullo, D. Corna, S. Buelli, C. Zanchi, S. Villa, M. Morigi, G. Remuzzi, A. Benigni, C. Zoja. SGLT2 inhibitor dapagliflozin limits podocyte damage in proteinuric nondiabetic nephropathy. *JCI Insight* 2018;3:98720.
45. P. Trionfini, O. Ciampi, M. Todeschini, C. Ascanelli, L. Longaretti, L. Perico, G. Remuzzi, A. Benigni, S. Tomasoni. CRISPR-Cas9-mediated correction of the G189R-PAX2 mutation in induced pluripotent stem cells from a patient with focal segmental glomerulosclerosis. *CRISPR J* 2019;2:108-120.
46. O. Ciampi, B. Bonandrini, M. Derosas, S. Conti, P. Rizzo, V. Benedetti, M. Figliuzzi, A. Remuzzi, A. Benigni, G. Remuzzi, S. Tomasoni. Engineering the vasculature of decellularized rat kidney scaffolds using human induced pluripotent stem cell-derived endothelial cells. *Sci Rep* 2019;9:8001.
47. M. Galbusera, M. Noris, S. Gastoldi, E. Bresin, C. Mele, M. Breno, P. Cuccarolo, M. Alberti, E. Valoti, R. Piras, R. Donadelli, M. Vivarelli, L. Murer, C. Pecoraro, E. Ferrari, A. Perna, A. Benigni, V. Portalupi, G. Remuzzi. An ex vivo test of complement activation on endothelium for individualized eculizumab therapy in hemolytic uremic syndrome. *Am J Kidney Dis* 2019; 74: 56-72.
48. V. Benedetti, A.M. Lavecchia, M. Locatelli, V. Brizi, D. Corna, M. Todeschini, R. Novelli, A. Benigni, C. Zoja, G. Remuzzi, C. Xinaris. Alteration of thyroid hormone signaling triggers the diabetes-induced pathological growth, remodeling, and dedifferentiation of podocytes. *JCI Insight* 2019; 4: 130249.

49. A. Benigni, P. Cassis, S. Conti, L. Perico, D. Corna, D. Cerullo, L. Zentilin, C. Zoja, A. Perna, V. Lionetti, M. Giacca, P. Trionfini, S. Tomasoni, G. Remuzzi. Sirt3 deficiency shortens lifespan and impairs cardiac mitochondrial function rescued by Opa1 gene transfer. *Antioxid Redox Signal* 2019; 31: 1255-1271.
50. A. Remuzzi, S. Conti, B. Ene-lordache, S. Tomasoni, P. Rizzo, A. Benigni, G. Remuzzi. Role of ultrastructural determinants of glomerular permeability in ultrafiltration function loss. *JCI Insight* 2020; 5: 137249.
51. M. Noris, A. Benigni, G. Remuzzi. The case of complement activation in CODIV-19 multiorgan impact. *Kidney Int* 2020; 98: 314-322.
52. L. Perico, S. Tomasoni, T. Peracchi, A. Perna, A. Pezzotta, G. Remuzzi, A. Benigni. COVID-19 and Lombardy: TESTing the impact of the first wave of the pandemic. *EBioMedicine* 2020; 61: 103069.
53. D. Cerullo, D. Rottoli, D. Corna, P. Rizzo, M. Abbate, D. Macconi, A. Benigni, G. Remuzzi, C. Zoja. Characterization of a rat model of myeloperoxidase anti-neutrophil cytoplasmic antibody associated crescentic glomerulonephritis. *Nephron* 2021; 145: 428-444.
54. M. Locatelli, C. Zoja, S. Conti, D. Cerullo, D. Corna, D. Rottoli, C. Zanchi, S. Tomasoni, G. Remuzzi, A. Benigni. Empagliflozin protects glomerular endothelial cell architecture in experimental diabetes through the VEGF-A/caveolin-1/PV-1 signaling pathway. *J Pathol* 2022; 256: 468-479.
55. L. Perico, M. Morigi, M. Galbusera, A. Pezzotta, S. Gastoldi, B. Imberti, A. Perna, P. Ruggenenti, R. Donadelli, A. Benigni, G. Remuzzi. SARS-CoV-2 spike protein 1 activates microvascular endothelial cells and complement system leading to platelet aggregation. *Front Immunol* 2022; 13: 827146.
56. D. Cerullo, D. Rottoli, D. Corna, M. Abbate, A. Benigni, G. Remuzzi, C. Zoja. Add-On cyclic angiotensin-(1-7) with cyclophosphamide arrests progressive kidney disease in rats with ANCA Associated Glomerulonephritis. *Cells* 2022; 11: 2434.
57. C. Zanchi, M. Locatelli, D. Corna, D. Cerullo, E. Fishilevich, D. Desai, D. Rottoli, R. Donadelli, M. Noris, C. Zoja, G. Remuzzi, A. Benigni. Liver Factor B silencing to cure C3 glomerulopathy: evidence from a mouse model of complement dysregulation. *Mol Immunol* 2023; 161: 25-32.
58. M. Locatelli, D. Rottoli, R. M. A. Mahmoud, M. Abbate, D. Corna, D. Cerullo, S. Tomasoni, G. Remuzzi, C. Zoja, A. Benigni, D. Macconi. Endothelial glycocalyx of peritubular capillaries in experimental diabetic nephropathy: a target of ACE inhibitor-induced kidney microvascular protection. *Int J Mol Sci* 2023; 24: 16543.
59. L. Perico, F. Casiraghi, F. Sonego, M. Todeschini, D. Corna, D. Cerullo, A. Pezzotta, P. Isnard-Petit, S. Faravelli, F. Forneris, K. Thiam, A. Benigni, G. Remuzzi. Bi-specific autoantigen-T cell engagers as targeted immunotherapy for autoreactive B cell depletion in autoimmune diseases. *Front Immunol* 2024; 15: 1335998.

