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Recellularization of vascular and tubular compartments of porcine kidney scaffolds with embryonic stem cells

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Chronic kidney disease (CKD) is a progressive condition marked by deteriorating kidney function over time. The therapeutic strategies for CKD are currently directed at limiting renal functional decline or at renal replacement therapies with either dialysis or transplantation. Novel alternative tools help to address this shortcoming by regeneration of damaged kidney using natural occurring scaffolds seeded with stem cells. The aims of the present study were to produce porcine whole-kidney scaffolds by a decellularization process and to test the efficacy of scaffold recellularization using physiological perfusion condition. The efficacy of cellular removal and biocompatibility of the preserved porcine matrices, as well as scaffold reproducibility, are critical to the success of this approach. To this aim, we designed and custom built a chamber to allocate large organs for decellularization and subsequent cell seeding. Complete decellularization of porcine kidneys can be achieved after 48 hr perfusion with sodium dodecyl sulfate 0.5%, as documented by histologic and immunofluorescence findings confirming complete cell removal without loss of structural components. The whole-kidney scaffolds preserved the 3D architecture of vessels, glomeruli and tubuli as shown by SEM analysis. To regenerate functional tissue, we repopulated acellular porcine kidneys with mouse embryonic stem (mES) cells through the renal artery and through the ureter. To obtain cell seeding within the tubular compartment a negative pressure of -70 mmHg was applied to the perfusion chamber. H&E staining and immunofluorescence demonstrated that mES cells infused through the renal artery were uniformly distributed in the vasculature and in glomerular capillaries while cells infused through the collecting system reached tubular compartments. Our findings indicate that porcine kidney can be successfully decellularized to produce intact renal extracellular matrix scaffolds. We also demonstrate the ability of the perfusion protocol to obtain cell engraftment in vascular and tubular structures. Because porcine scaffolds have similar morphology and function as their human counterparts, they certainly represented a platform for clinically applicable renal bioengineering investigations.

Biography

Marina Figliuzzi graduated in Biological Sciences at the University of Milano (Milano, Italy) in 1991 and got specialization in Pharmacological Research at the Mario Negri Institute, Bergamo, Italy in 1994. From 1994-2000 she was a research investigator at the Mario Negri Institute for Pharmacological Research, Bergamo, Italy. From the 2000-2014 she is the Head of the Unit of Tissue Engineering, Department of Biomedical Engineering. From the 2014 she is the Head of the Laboratory of Tissue Engineering for Regenerative Medicine, Department of Biomedical Engineering. Main areas of interest are: Pancreatic cell transplantation in experimental models of insulin dependent diabetes; Immunoisolation devices for pancreatic islets; Differentiation of progenitor pancreatic cells in insulin containing cells; Immunhistochemistry; Cell culture; Organ decellularization.

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