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Perfusion Decellularization of Discarded Human Kidneys: A Valuable Platform for Organ Regeneration

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In this issue of *Transplantation* Andrea Peloso and colleagues report on the successful application of perfusion decellularization in discarded human kidneys to generate scaffolds for organ regeneration. (1) The authors provide important insight into mechanical integrity and morphological features of the native vascular tree and examine matrix bound growth factors after perfusion decellularization of human kidneys. Both of these are fundamental scaffold properties that enable cell engraftment, tissue formation, and perfusion during culture and after transplantation.

The enthusiasm to build functional, transplantable kidney grafts from patient derived cells, is fueled by recent progress in the fields of kidney stem cell and developmental biology.[2] Through directed differentiation, human pluripotent stem cells have been successfully guided through key developmental milestones to generate cellular constituents of metanephric mesoderm, and ureteric bud.[3–5] Once generated in sufficient numbers and purity, these cells could be a nearly inexhaustible source of building blocks to regenerate autologous kidney tissue and possibly transplantable grafts.[6] As we begin to decifer pathways of both kidney development and adult kidney repair and regeneration, we will hopefully learn to control the process of tissue formation and eventually achieve graft homeostasis in regenerated or bioartificial constructs.[7–9]

One possible approach to organ engineering follows the principle of tissue engineering, in which an extracellular matrix scaffold provides the three dimensional foundation of structural boundaries, architecture, vasculature, and the cell specific niches for different endothelial, mesenchymal, and epithelial cell phenotypes.[10] Despite recent advances in additive manufacturing and other techniques, deriving scaffolds of comparable composition, scale, and complexity of mature human organs has been a challenge. Since the first report of detergent based perfusion decellularization of mammalian organs, and it's use to engineer functional tissue in 2008,[11] this technology has been successfully applied to multiple organ systems including the heart,[12] lung,[13–19] kidney,[20–25] liver,[26] and pancreas.[27, 28] Detailed matrix analysis of some organ systems has been performed,[19, 29] but kidney scaffolds of human origin have yet to be fully examined. The present article provides valuable data points on composition and physical properties, and further underlines the translational value of this platform for kidney bioengineering. Future work comparing

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composition, growth factor levels, and mechanical properties to native developing and adult kidneys similar will be helpful to even better understand which components are preserved, and which are lost during decellularization. This will guide us in developing strategies to optimize kidney scaffolds to accommodate the myriad of different cell types required for mature organ function.

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