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Renal Fibrosis: Common Enemy of Many Origins

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This special issue of the *Journal of Histochemistry & Cytochemistry* highlights the role of fibrosis in the pathophysiology of kidney. The presence of a structural framework for the organization of an organ may not always be obvious; however, it is essential. The arterial supply depends on additional structure to withstand the pulsatile nature of blood flow. The extracellular matrix of basement membranes is equally essential for maintaining the complex juxtaposition of cells to maintain the individual elements of the nephron. Other structural elements of the framework of organs are less obvious but equally important.

Fibrosis is a common but not ubiquitous response to injury. Furthermore, even in those organs that respond to injury, it is commonly but not ubiquitously permanent. Injury to the adrenal gland is not characterized by fibrosis. In contrast, fibrosis is a common element of injury to the liver, yet it is reversible when the inciting injury is removed. And last are organs such as the heart, lungs, pancreas, and kidney for which fibrosis is not reversible. In the heart, the fibrosis of ischemia is functionally identical to the fibrosis of wound healing commonly encountered in the epidermis—self-limited and lacking in the inflammatory response that can render the process progressive.

As the articles highlight, fibrosis in the kidney is a complex, dynamic, and destructive process that, once started, will progress at variable rates. Ultimately, fibrosis will result in diminished renal function, but only when the renal reserve is depleted, resulting in chronic kidney disease and variably progressing to end-stage renal disease/renal failure. As these papers highlight, there is no one mechanism, there is no one method of diagnosis, there is *no* treatment for kidney fibrosis, but there is an active research community. There is also hope.

Biomolecular studies continue to highlight the role of myeloid-derived cells, in concert with B cells and T cells as the *bad actors* in many forms of fibrosis. Recent studies in immuno-oncology and autoimmune disorders are unwinding the complexity of cell signaling within the hematopoietic system that sets off these injurious cascades. The role of vascular endothelial growth factor (VEGF) and its receptors, as well as other factors associated with angiogenesis, provides insights into the actions of these myeloid-derived cells. And more recently, inhibitors of the JAK/STAT pathway are demonstrating the modulation of these myeloid cells to modify the extracellular milieu associated with this fibrosis.

The extracellular milieu and the cells that contribute to its physiological functions in patterning organs and immune surveillance are now the subject of intense research across organ systems and disease processes. The special issue highlights one segment of this research.

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