Fibrosis is a common response of tissues to chronic injury. Following acute injury, tissue repair is promoted by an intricate inflammatory reaction and matrix remodeling process. In contrast, chronic inflammatory injury results in exaggerated and dysregulated wound healing, characterized by an imbalance between excessive synthesis of extracellular matrix (ECM, comprising collagens and other proteins) and decreased degradation of ECM. Scar formation is typically—but not always—self-limited. The accrual of ECM produced by activated fibroblasts, also known as myofibroblasts, can continue unabated and produce excessive scarring with associated tissue remodeling and loss of functional parenchyma. The latter scenario defines tissue fibrosis.

Knowledge regarding the cell physiology of tissue fibrosis has advanced considerably in recent years. Major areas of study have included the production and regulation of myofibroblasts, the formation and turnover of extracellular matrix, the role of inflammation in fibrotic tissues, and the interplay of pro- and antifibrotic factors and mechanisms (extracellular, intracellular, genetic, and epigenetic). A major impetus for such efforts is the realization that fibrosis can be reversible, at least in some tissues and prior to the “end-stage” with large accumulation of acellular ECM. A major challenge is to identify and define common mechanisms underlying fibrosis in different organs and ones that differ (or are specialized) in particular tissues. The former are particularly important because they may provide general ways to treat (blunt or perhaps reverse) tissue fibrosis.

We have thus invited several leading experts to write review articles for a Theme series on tissue fibrosis and its cell physiology so as to provide readers with current insights and to identify major unresolved questions. The series begins in this issue with an introductory article by Michael Zeisberg and Raghu Kalluri (“Common and organ-specific mechanisms associated with tissue fibrosis”) that highlights and expands on some of the ideas noted above. Subsequent articles will explore cardiac fibrosis (Francis Spinale), renal fibrosis (Jeremy Dufield), pulmonary fibrosis (Paul Noble), and hepatic fibrosis (Sophie Lotersztajn).

We believe that readers will find the review articles in this Theme of interest. In addition, though, we hope that the ideas and results provided in the articles will stimulate experiments that address unanswered, important questions regarding cellular mechanisms that contribute to tissue fibrosis. We look forward to receiving manuscripts that provide such results for publication in AJP-Cell.

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