Molecular Medicine

EDITORIAL

Molecular Medicine Commemorates the Achievements of the First 20 Years

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To celebrate the 20th anniversary of *Molecular Medicine*, this special issue showcases the fields of science influenced by the most cited scientific contributions to the journal over the past two decades. The authors of these reviews are leaders in the fields of immunology, cancer, atherosclerosis, Alzheimer's disease and diabetes. We asked them to provide updates that highlight the progress made in the selected fields of research to which their highly cited *Molecular Medicine* publication contributed.

Two reviews discuss key elements in the immune response to tissue injury: one focuses on the fibrocyte, which acts during the earliest phase of the innate immune response, and the other focuses on HMGB1, which acts as a later mediator of inflammation. Richard Bucala reports on the advances made on the "fibrocyte," the unique collagen-producing leukocyte that he discovered in the 1990s and its role beyond the original context of wound repair. The contribution of this cell type to the pathogenesis of different fibrosing disorders has led to fibrocyte-directed therapies that are currently being tested in the clinic. Huan Yang and colleagues provide an overview of HMGB1, a later mediator of infection and tissue injury. The authors review its multiple functions and complex regulation. They conclude with a discussion on the first two HMGB1-specific antagonists that are paving the way toward future therapeutic applications.

A third review by Antonino Nicoletti and colleagues looks at the adaptive immune response in the context of atherosclerosis. The authors discuss the roles that proatherogenic and athero-protective T and B cells play in this disease. They also highlight the different strategies used in preclinical studies with an outlook to clinical applications.

Jason A Chesney and Robert A Mitchell follow the saga of macrophage migration inhibitory factor (MIF) from its discovery through the many studies that implicate this cytokine in several aspects of cancer biology. They focus in particular on the role of MIF in tumor neovascularization, which likely participates in primary and metastatic disease progression. The advances made in this field are underscored by the first clinical trial that has been initiated to test anti-MIF therapies.

Jennifer Hardingham and colleagues cover the circulating tumor cells (CTCs), another interesting aspect of cancer biology with great implications for clinical applications. Their discussion of various technical efforts that have been made to capture these cells from the patients' blood, the advances made and the challenges that still remain offer a clear picture of the state of the art of this new approach. These advances will certainly augment the battery of cancer diagnostic tools in the clinic in the not too distant future.

Sho-ichi Yamagishi and colleagues tackle the role of advanced glycation end products (AGEs) in diabetes. They describe how the products of reactions occurring between sugars and proteins, lipids and nucleic acids lead to altered function and metabolism of these macromolecules with severe consequences in diabetes and aging-associated disorders. The authors also discuss the potential

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value of measuring serum levels of AGEs to evaluate organ damage in diabetes.

Finally, Jochen Walter summarizes the incredible progress made over the past two decades in understanding the role of presenilins in the onset of Alzheimer's disease. From the discovery of the gene mutations in inherited familial forms of early onset of Alzheimer's disease, Walter follows the path of discoveries that leads to the identification of their functions as components of a protease complex responsible for the cleavage of the amyloid precursor protein, an important determinant of the pathophysiology of the disease. He also discusses the hopes associated with the development of several inhibitors of presenilins and the disappointing results of their use in the clinic. Dr. Walter concludes with a positive outlook on development of more selective inhibitors of presenilins that could provide future therapies for Alzheimer's disease.

We are pleased to offer these engaging and interesting historical perspectives of fields that were introduced to the scientific public in our journal and hope that our readers will enjoy them, too.

DISCLOSURE

The author declares that she has no competing interests as defined by *Molecular Medicine*, or other interests that might be perceived to influence the results and discussion reported in this paper.

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