CELLULAR MECHANOTRANSDUCTION

"Mechanotransduction" is the term for the ability, first described by nineteenth-century anatomist Julius Wolff, of living tissues to sense mechanical stress and respond by tissue remodeling. More recently, the scope of mechanotransduction has been expanded to include the sensation of stress, its translation into a biochemical signal, and the sequence of biological responses it produces. This book looks at mechanotransduction in a more restricted sense, focusing on the process of stress sensing and transducing a mechanical force into a cascade of biochemical signals. This stress has become increasingly recognized as one of the primary and essential factors controlling biological functions, ultimately affecting the function of the cells, tissues, and organs. A primary goal of this broad book is also to help define the new field of mechanomics, which attempts to describe the complete mechanical state of a biological system.

Dr. Mohammad R. K. Mofrad is currently Assistant Professor of Bioengineering at the University of California, Berkeley, where he is also an affiliated faculty member of graduate programs in applied science and technology and biophysics. Dr. Mofrad received his B.A.Sc. degree from Sharif University of Technology. After earning M.A.Sc. and Ph.D. degrees from the Universities of Waterloo and Toronto, respectively, he spent two years at MIT and Harvard Medical School/Massachusetts General Hospital as a post-doctoral Fellow. Before joining the faculty at Berkeley, Dr. Mofrad was a Principal Research Scientist at MIT for nearly two years. At Berkeley, he has developed and taught several courses, including Cell Mechanics and Mechanotransduction and Molecular Cell Biomechanics. He is the founder of the Mechanotransduction Knowledgebase Web site, mechanotransduction.org.

Dr. Roger D. Kamm has long been interested in biomechanics, beginning with his work in vascular and pulmonary physiology and leading to his more recent work in cell and molecular mechanics in the context of cellular responses to mechanical stress. Dr. Kamm has been on the faculty at MIT since receiving his Ph.D. in 1977 and now holds a joint appointment in the Biological Engineering and Mechanical Engineering Departments. He is currently the Chair of the U.S. National Committee on Biomechanics and the World Council on Biomechanics, and he is Director of the Global Enterprise for MicroMechanics and Molecular Medicine. Kamm has a long-standing interest in bioengineering education, directs a National Institute of Health–funded biomechanics training program; co-chaired the committee to form MIT's new undergraduate major in biological engineering; and helped to develop MIT's course on molecular, cellular, and tissue biomechanics.

Cellular Mechanotransduction

DIVERSE PERSPECTIVES FROM MOLECULES TO TISSUES

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Preface

Many studies during the past two decades have shed light on a wide range of cellular responses to mechanical stimulation. It is now widely accepted that stresses experienced *in vivo* are instrumental in numerous pathologies. One of the first diseases found to be linked to cellular stress was atherosclerosis, where it was demonstrated that hemodynamic shear stress influences endothelial function, and that conditions of low or oscillatory shear stress are conducive to the formation and growth of atherosclerotic lesions. Even before then, the role of mechanical stress on bone growth and healing was widely recognized, and since then, many other stress-influenced cell functions have been identified.

Many have investigated the signaling cascades that become activated as a consequence of mechanical stress, and these are generally well characterized. The initiating process, however, by which cells convert the applied force into a biochemical signal, termed ''mechanotransduction,'' is much more poorly understood, and only recently have researchers begun to unravel some of these fundamental mechanisms. Various processes and theories have been proposed to explain this phenomenon. The objective of this book is to bring together these different viewpoints to cellular mechanotransduction, ranging from the molecular basis of mechanotransduction phenomena to the tissue-specific events that lead to such processes. Our intent is to present in a single text the many and varied ways in which cellular mechanotransduction is viewed and, in doing so, spur on new experiments to test the theories, or the development of new theories themselves. We view this as an ongoing debate, where one of the leading proponents of each viewpoint could present his or her most compelling arguments in support of the model, so that members of the larger scientific community could form their own opinions. As such, this was intended to be a monograph that captured the current state of a rapidly evolving field. Since we began this project, however, it has been suggested that this book might meet the growing need for a text for courses taught specifically on cellular mechanotransduction. More broadly, it could be used to introduce concepts at the intersection of mechanics and biology, a field of study that has come to be termed ''mechanobiology.'' Or, even more broadly, this collection

might be useful as supplemental readings for a course that covers a range of topics in molecular, cellular, and tissue biomechanics. In any event, our hope is that this presentation might prove stimulating and educational to engineers, physicists, and biologists wishing to expand their understanding of the critical importance of mechanotransduction in cell function, and the various ways in which it might be understood.

In the end, we would like to extend our enormous thanks to all the contributing authors whose expert contributions made this text possible. Finally, we wish to express our deepest gratitude to Mr. Peter Gordon and his colleagues at Cambridge University Press, who provided us with the encouragement, technical assistance, and overall guidance that were essential to the ultimate success of this endeavor. In addition, we would like to acknowledge Ms. Elise Oranges, who steered us through the final stages of editing.

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