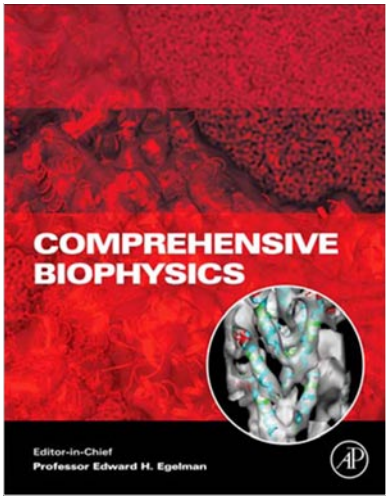

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7.1 Introduction

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The human body contains approximately 10 trillion human cells, enough cells to cover approximately 800 000 football fields and many more cells in each of us than there are human beings on Earth. Yet, each cell in a single individual contains the same genome. Not only undifferentiated stem cells, but also partially and terminally differentiated cells of the epithelial and endothelial layers, germ and nurse cells, brain cells, metabolic and storage cells, muscle cells, immune cells, and cells of connective tissues, all contain the exact same genes in the same individual. Hence this unbelievable cellular diversity within a single individual cannot be explained by genetic variations among cells. Indeed, one just has to observe the truly fascinating diversity of phenotypes displayed by clonal, 'normal' cells, stemming from the same single mother cell and plated on a uniform culture dish to immediately appreciate how incredibly heterogeneous cellular phenotypes can be. Within just a few generations, isogenic cells display multifold variations in not only cellular and nuclear size, but also in cellular and nuclear shape, cell motility parameters, the ability of cells to secrete soluble and insoluble factors and to adhere to each other and to their extracellular matrix, cytoskeletal organization, and in spatial and temporal distribution of organelles.

Further complicating this picture is the fact that cells during development grow extremely rapidly and migrate to their exact proper location with exquisite regularity. During each step of development, cells selectively, directly and indirectly interact with a myriad of other cells of the same or different type in a highly orchestrated ballet. How cells 'know' where to go, how do they get there and, most intriguingly, how do they stay in that organ and tissue all remain unclear.

While inherited genetic mutations can largely explain the induction of a large number of human diseases, including auto-immune diseases, patterns of genetic mutations, particularly in cancer, seem to only partially correlate with clinical outcomes. Hence genetic heterogeneity may not be entirely responsible for different clinical outcomes, limiting the impact of current purely genetic strategies to cancer therapy and diagnostic. The differential responses and adaptations of cells in different individuals to the same mutations and therapies may be partially explained by differences in cellular microenvironments and, in particular, differences in their biophysical properties. As they grow, developing cells create and continuously modify the biochemical and physical properties of microenvironment and, in a healthy individual, eventually enter a phase of much lower rate of growth. Hence subtle and not-so-subtle differences in cellular microenvironments may be caused by the extraordinary range of phenotypes shown by otherwise genetically identical cells, themselves presumably caused by epigenetic variations and variations in patterns of protein expression.

In this volume, experts in the field of cell biophysics review in thirteen chapters our current knowledge of the fundamental molecular and biophysical principles underlying the diversity of highly regulated cellular functions that drive normal development and, when these functions become misregulated, contribute to disease phenotypes. These functions include cell growth and development, cell division, cell motility in diverse microenvironments including flat substrates and three-dimensional matrices and blood vessels, nuclear and cellular mechanics, cell–matrix adhesion, and cell–cell adhesion via cell–surface molecules cadherin and selectin. These chapters also describe how the biophysical properties of the microenvironment – stiffness, topology, and microstructure – as well as cell-induced mechanical forces and the physical properties of cells all greatly regulate and contribute to cellular function, diversity, and identity.

In addition to his/her cellular building blocks, each human contains a staggering number of hyper specialized bacterial cells, which are symbiotically essential to human life. There are an average of approximately 100 trillion bacterial cells per person (i.e., 10 bacteria per human cell) in an individual. The number and diversity of bacteria specifically localized and contained to each subsection of the human skin best illustrate the number and extent of diversity of types of bacteria, just associated with humans: A square inch of human skin contains approximately 32 million bacteria. The diversity of shape and organization of bacterial cells is even more impressive than those of human cells. Two chapters describe the biophysical underpinnings of variations in bacterial cell shape and temporal and spatial variations in the organization of cytoplasmic molecules.

Common to these chapters are the quantitative aspects brought upon through predictive theories and highly quantitative measurements at single-molecule and/or single-cell levels. In particular, the development of novel types of microscopy, spectroscopic techniques, as well as nano- and microscale manipulating tools have had tremendous impact on our understanding of cell functions.

We hope that you will enjoy reading these reviews and will be using their contents and insights for a long time to come.