PREFACE

One of the most exciting scientific advances with great potential clinical impact over the past two decades is in the field of tissue engineering and cell-based therapy. If this promising scientific endeavor proves to be clinically successful, it will completely change the paradigm of medical management in many otherwise untreatable diseases. More importantly, it will completely change the traditional concept that terminally differentiated organs cannot regenerate or restore function effectively following surgical resection or tissue loss as a result of disease process. In fact, numerous observations have suggested the regenerative capacities of various biological organisms and the puzzles may indeed be at our fingertips.

Through observations of various vertebrates, scientists have reported that adult salamanders could regenerate a lost arm or leg over and over again throughout its life time; no matter how many times the limbs were amputated. Frogs could also re-grow a limb during tadpole stages when their limbs were first growing out, but they lost this ability in adulthood. Even mammalian embryos have some ability to regenerate developing limb buds, but that capacity also disappears well before birth. This trend towards declining regenerative capacity over the course of an organism's development in higher animal forms, and how the salamanders pull off this feat, have puzzled scientists and fueled the search for understanding how the regeneration process works in nature. Discovery suggests that the regenerative process in salamanders is very similar to the embryological development of limb bud that involves pluripotent progenitor cells.

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A similar genetic program also occurs at some point during the development of human limbs. More interestingly, the early cellular responses of tissues at the amputation site are not that different in salamanders and in humans. Yet, human tissues eventually form a scar and fail a regeneration response, whereas the salamanders re-activate the embryonic process to regenerate an intact limb. An important implication of this finding is that we probably have the same programming necessary to regenerate a lost limb or organ, and all scientists have to do is to re-activate this latent process or simulate this embryologic process by supplying the tissue organ with the proper signals and substrates.

In fact, over the past few decades, tremendous efforts have been invested in the characterization and understanding of the pathophysiology of many disease processes as well as the role of various mediators, growth factors, and cytokines etc. in the biological system. The mechanistic discoveries in the disease process have provided the foundation in regenerative research since tissue organ functions are mediated by a pool of biologically active proteins, and peptides that modulate cell function through direct physical interactions with extra-cellular domain of transmembrane receptors. A diverse aspect of sub-cellular activities and biological responses to their environments are therefore transduced through these signals mediated at a sub-cellular level. The pool of protein mediators and their biological activities, therefore, regulate the mechanisms and pathways that govern wound healing and tissue regeneration. Determining the spatio-temporal roles that these cellular molecules and mediators interact in the biological system will play as important a role as designing, developing, and properly applying the current technologies in tissue engineering and regeneration to the clinical arena. In other words, providing the injured tissues the necessary biological signals is crucial for the functional recovery or regenerative process of a diseased organ.

Understanding the micro-environment of tissue development and injury will, therefore, provide valuable insight into the mechanisms that guide progenitor cells to differentiate into specific phenotypes in a particular organism. Learning to control the human wound micro-environment will probably redirect the divergent healing strategies in different vertebrates, and help to trigger a salamander-like wound healing even in human

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beings. The ideal substrate for this regenerative process, on the other hand, should have the capacity to renew itself while being able to differentiate to various phenotypes. Various types of stem cells that exist in the organism at different stages of their lifespan are naturally the ideal candidate to fulfill this role. It is, therefore, not surprising that stem cell therapy and bio-engineering is currently one of the most intensively investigated topics in the research arena, both in the basic science and clinical setting from all over the world. The objective of this monograph is in an attempt to summarize the current state of stem cell bio-engineering and tissue engineering micro-environment contributed by some of the experts worldwide in the field, both from the bench and bed sides. The general contents are divided into three main themes. In part I, it will include topics that involve investigation and manipulation of the micro-environment of tissue regeneration. Part II will present various bio-engineering updates, involving stem cell therapy. In part III, application of stem cell therapy in various experimental models, and finally in clinical settings will be described by experts in the field. The editors believe that this comprehensive review of the current state of stem cell bio-engineering and tissue engineering micro-environment will provide a unique perspective of the field as it merges two separate and yet closely related platforms between basic scientists and clinicians, which is the ultimate goal of all clinically related research.

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