

PREFACE

During the past several years, significant advances have been made in understanding control of proliferation at the cellular, biochemical, and molecular levels. As the complexity and interdependency of parameters mediating growth control become increasingly apparent, the demarcations between regulated and regulatory components of mechanisms that promote or inhibit proliferation are eroding. There is recognition of both cause and effect relationships between the activities of factors that modulate the cell division cycle reflecting multidirectional signaling between segments of regulatory cascades that are selectively operative in specific cells and tissues. The necessity of accommodating the integration of positive and negative growth regulatory signals is now appreciated in a broad spectrum of biological contexts. These include but are not restricted to (1) repeated traverse of the cell cycle for cleavage divisions during the initial stages of embryogenesis and continued renewal of stem cell populations, (2) stimulation of quiescent cells to proliferate for tissue remodeling and wound healing, and (3) exit from the cell cycle with the option to subsequently proliferate or terminally differentiate. Equally important is an appreciation of the cell cycle regulatory mechanisms that have been compromised in transformed and tumor cells and in nonmalignant disorders where abnormalities in cell cycle and/or growth control are operative. These insights into regulatory mechanisms operative in cell cycle and growth control are rapidly being translated to clinical diagnosis and therapeutics.

Proliferation is explored in this volume from the perspectives of conceptual and experimental approaches to fundamental principles as well as biomedical applications. The biological problem of cell cycle control is introduced within the historical context of contributions from a broad spectrum of model systems that have provided the foundation for our current understanding of growth control in mammalian cells. The identification of checkpoints and restriction points as well as the factors responsible for proliferation competency and cell cycle progression are presented. The chapters focus on DNA replication and S phase; mitosis and meiosis; regulation of gene expression; growth factors and growth factor receptor-mediated pathways; signal transduction and integration of regulatory information; differentiation; development and programmed cell death; and cellular senescence and immortalization. The concluding chapter addresses cancer and other disorders that are linked to perturbations in control of proliferation. Each chapter was developed with a balance between presentation of biological parameters and gene regulatory mechanisms that mediate growth control and cell cycle progression. A concerted effort has been made to provide a comprehensive bibliography and illustrations that assimilate components of the increasing complexity associated with proliferation.

THE EDITORS