

VIEWPOINTS

Growth and Differentiation: Fulfilling the Dream

Deciphering the genetic code in the 1960s, discovery of cytokines in the 1970s, and the current decade of oncogene and now suppressor gene discovery have elevated the expectation that we will soon comprehend the intricate process of embryogenesis and development as the cellular biochemical pathways of signal reception and transduction and nuclear–cytoplasmic and intercellular communication are defined. Many of the *Prospects* and articles in the *Journal of Cellular Biochemistry* will deal with growth and differentiation at the molecular, descriptive, or some intermediate level of biological action.

The functional relationship between cell proliferation and development has intrigued investigators for more than a century, as J.B. Lian, G.S. Stein, R. Bortell, and T.A. Owen point out in this issue in their *Prospect*, “Phenotype Suppression: A Postulated Molecular Mechanism for Mediating the Relationship of Proliferation and Differentiation by *Fos/Jun* Interactions at AP-1 Sites in Steroid Responsive Promoter Elements of Tissue-Specific Genes.” Elsewhere in this issue, F.D. Coffin, K.L. Fresa, and S. Cohen in their *Prospect*, “The Initiation of Lymphocyte DNA Synthesis,” discuss the intracellular regulation of proliferation in terms of a balance between activation and inhibitory pathways as illustrated by their investigations of the activating ADR protease and ADR inhibitory protein in human and murine lymphoid cells. In a related yet different approach, D. Michalovitz, O. Harelvi, and M. Oren in their *Prospect*, “p53 Mutations: Gains or Losses?,” reflect upon the complex interrelationships between normal negative regulatory factors and mutations within the genes of the control elements to produce positive proliferation signals.

Turning to the level of molecular events underlying progression of the cell cycle, S.R. Mallery, H.B. Laufman, O.W. Solt, and R.E. Stephens in their article, “Association of Cellular Thiol Redox Status With Mitogen-Induced Calcium Mo-

bilization and Cell Cycle Progression in Human Fibroblasts,” relate how the thio redox state of human gingival fibroblasts and its potential association with compromised Ca^{2+} sequestration and/or mobilization is important in the transition out of the G1 phase of cell growth. Exploring the complexity of proliferation and differentiation resulting from oncogene product interactions, J.B. Lian et al. in their *Prospect* indicate how *fos/jun*-mediated suppression of osteocalcin gene expression may occur as a result of *fos/jun* interactions at the transcription element AP-1 sites, which then prevent steroid receptor complex gene activation in the cells. The role of intercellular signaling resulting from increased cellular density in differentiation is explored by J.J. Egan, G. Gronowicz, and G.A. Rodan in their article, “Cell Density-Dependent Decrease in Cytoskeletal Actin and Myosin in Cultured Osteoblastic Cells: Correlation With Cyclic AMP Changes,” in which they demonstrate that the density-dependent increase in cAMP is associated with a decrease in crosslinked actin and myosin accompanying the change from fibroblast-like to cuboidal morphology of osteoblastic cells. In the forthcoming February 1991 issue of the journal, E.A. Grimm and L. Owen-Schaub discuss the sequential interactions of multiple cytokines in the signal reception and transduction control of MHC un-restricted lymphocyte growth and differentiation in their *Prospect*, “The IL-2 Mediated Amplification of Cellular Cytotoxicity.”

These are some of the *Prospects* and research articles in the *Journal of Cellular Biochemistry* you will want to read in increasing your understanding of the biochemical pathways underlying the fundamental biological basis of intra- and intercellular communication controlling growth and development. The role of cytokines, in particular in growth and differentiation is of increasing importance. No stage of development or any disease classification or treatment modality is discussed today without reference to one or

more of the cytokines. The pivotal questions, however, are what are the links between the basic molecular biology and the biochemical pathways being elucidated and the resulting biological action. The interconnections between these areas are essential to our understanding of fundamental biology and the ability to de-

velop more effective diagnosis, prevention, and therapy of disease.

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