Eur J Cancer, Vol. 29A, No. 3, p. 471, 1993.
Printed in Great Britain
0964-1947/93 $6.00 + 0.00

Book Review

Oncogenes in the Development of Leukaemia

Series Editor L. M. Franks, Guest Editor O. W. Witte. Cold Spring Harbor, Cold Spring Harbor Laboratory Press. Cancer Surveys, 1992, Vol. 15.

THE COLLECTION of essays in this volume of Cancer Surveys covers a broad range of concepts that we should consider in the study of leukaemia.

When a patient or experimental animal succumbs to a leukaemia or lymphoma the pathological consequences of an overabundance of a specific blood cell type filling the marrow, peripheral blood or lymph nodes are easy to discern. Normal blood forming capacity of the bone marrow may be blocked, and infiltration of solid organs with leukaemic cells may lead to secondary problems, including infections and bleeding. The end result of hundreds of cell divisions by the leukaemic clone is the global breakdown of the homoeostasis that keeps the bone marrow's production of specific blood cells in balance with the needs of the peripheral organs. What is not obvious is the pathway on which the leukaemic clone travelled. Deciphering the mechanisms that upset the normal equilibrium to initiate the disease can be difficult to separate from the effects of secondary oncogenic changes that accumulate as the disease progresses.

The special properties of the pluripotent stem cell are described by Ihor Lemischka. The remarkable ability of stem cells to rest in a G_0 state, and later display a vast replicative capacity that enables them to repopulate a damaged marrow quickly with differentiated progeny, must involve special control mechanisms that are potential targets for leukaemogenic events. The use of retroviral marking experiments has now permitted a detailed analysis of the behaviour of stem cells that can be used as a basis for comparison with the growth properties of leukaemias and lymphomas.

It is clear that normal haematopoietic development depends on a balance of extracellular factors and cell–cell contacts that regulate autonomous cellular events and the differentiated phenotype. Perturbation anywhere along the signal transmission pathways from extracellular growth factor to nuclear controls on transcription and cell cycle regulators can initiate leukaemic progression. Alan D'Andrea describes the remarkable story of molecular mimicry of erythropoietin by the glycoprotein gene of the spleen focus forming virus (SFFV) component of the Friend strain of murine leukaemia virus. Although this event may seem very specific to this animal virus model, the implications for the role of receptor stimulation in leukaemia in general are important.

Growth deregulation by members of the tyrosine kinase family of oncogenes is a common event in human and animal models of leukaemogenesis. Charles Sawyers describes how the *bcr–abl* oncogene plays a critical part in the genesis of chronic myelogenous and acute lymphocytic leukaemia in man. The intriguing problem of how two different genetic elements fused into a single chimaeric protein can lead to deregulation of their intrinsic biochemical activities is considered. The important model of the avian erythroblastosis virus is discussed by Mike Hayman and Harmut Beug to exemplify the critical synergy between a growth stimulating tyrosine kinase receptor gene and a nuclear regulator of differentiation phenotype.

Signals sent from the cell surface or cytoplasm must eventually reach the nucleus and affect transcriptional regulation and cell cycle events. Tom Gilmore covers the *rel* family of oncogenes and transcriptional regulators. He points out their complex modes of regulation which include the action of specific inhibitors and cytoplasmic to nuclear relocalisation. Changes in the *rel* proteins themselves, as well as their regulators, can be associated with leukaemia. A large number of transcription factor related oncogenes have now been defined. Mike Cleary discusses how they can augment growth through positive or dominant negative mechanisms.

Most oncogenes involved in leukaemogenesis are grouped into the positive acting or growth stimulating class or the tumour suppressor on negative oncogene class. Stan Korsmeyer describes a new type of oncogene that maintains cell viability by blocking programmed cell death. Failure to die can result in the accumulation of unwanted cells and the beginning of the leukaemic phenotype.

All leukaemias, and in fact all cancers, are likely to be the final product of sequential oncogene changes that accumulate and give greater advantage to specific clones of cells. Our understanding of the specific combinations and synergies that work in different types of leukaemia is reviewed by Jerry Adams and Suzanne Cory, who describe the use of transgene technology and related approaches to establish tumour prone animal models for such studies.

The impact of new genetic technologies in the molecular analysis of chromosomal alterations in human haematopoietic disease is exemplified by Michelle LeBeau in her discussion of the role of chromosome 5 deletions in malignant myeloid disorders which includes the complex myelodysplastic syndromes that often precede frank leukaemia.

Progress in understanding human leukaemia has often been limited by our inability to culture or maintain leukaemic cells in the laboratory. John Dick covers the dramatic improvements in the use of immunodeficient rodent models for the propagation of normal and leukaemic cells. Such techniques are likely to have a major impact on the study of leukaemogenesis as well as other cancers.

Professor O.N. Witte
Howard Hughes Medical Institute
Research Laboratories
University of California
10833 Le Conte Avenue
Los Angeles
California 90024-1662
U.S.A.

News

Towards Professional Training of (Local) Data Managers, an Objective of the EORTC Study Group on Data Management (SGDM)

We would like to introduce the objectives and programme of the EORTC Study Group on Data Management (SGDM) and inform EORTC investigators of the possibilities of support