

ENHANCERS AND OTHER REGULATORS OF EUKARYOTIC GENE EXPRESSION: A FIRST ACCOUNT

Enhancers and Eukaryotic Gene Expression. Edited by Yakov Gluzman and Thomas Shenk. Pp. 218. ISBN 0-87969-161-1. (Current Communications in Molecular Biology, Cold Spring Harbor Laboratory: 1983) \$27.00.

In multicellular organisms, different sets of genes are switched on in different tissues. Therefore, regulation of the initiation of transcription is of paramount importance to an understanding of some basic biological functions, such as differentiation and growth (normal and malignant), adaptation to external stimuli, and viral infection. The recent discovery of a 72 bp repeat close to the origin of the small DNA tumor virus SV40, that has a stimulating effect on the transcription of nearby genes (J. Banerji et al., 1981, *Cell* 27:299), appears to be a breakthrough in this field. Similar sequences, "enhancers" or "activators," as they are called, were soon found in a variety of other systems. At a meeting held in Cold Spring Harbor on April 3-6, 1983, an audience of 44 invited participants heard presentations of 35 papers dealing with this new and rapidly expanding field. The book contains an introductory chapter by the editors, followed by the individual papers presented at the meeting.

Several general features of eukaryotic gene transcription are central to an understanding of enhancers and gene regulators. The site where transcription starts is called the cap-site, because a cap is usually attached to the 5'-terminus of mRNA. About 30 bases upstream there is an AT-rich sequence (the TATA or Goldberg-Hogness box) that serves as a promoter for the RNA polymerase. Further upstream, at a distance of about 100-200 bp from the cap-site, one finds stretches of 70-150 bp of enhancer sequences. Although few naturally occurring enhancers and their environments have been studied, the properties of these sequences became clear in a series of constructs in which they were placed in various orientations and positions relative to the promoter of a test gene—e.g. a thymidine kinase or a chloramphenicol acetyl transferase gene, whose gene products can be measured in enzyme assays. The remarkable outcome of

these experiments is that enhancers activate nearby promoters relatively independent of their position and orientation. Some experiments suggested that species- or tissue-specific factors play a role in the mechanisms by which enhancers function. This gave rise to the speculation that enhancers are "bidirectionally active 'super'-entry sites for components of the transcriptional machinery" (P. Moreau et al., 1981, *Nucleic Acids Research* 9:6047).

The presence of enhancers in a number of gene systems helps researchers to understand and sometimes manipulate their specific mechanism of action in each system. Thus, the presentations focused on the relationship between enhancers and the functions of the long terminal repeats of RNA tumor viruses, on the activation of oncogenes, on the expression of immunoglobulin genes, and on the regulation of the expression of early adenovirus genes. A few papers discussed more general effects, such as the enhancer-induced alterations in chromosome structure and Z-DNA formation.

Overlapping somewhat with the discussion on enhancers is the second main topic of the conference: inducible genes in eukaryotes. There is insufficient detail available at the molecular level on most inducible systems in eukaryotes. Although small in

number, they represent a range of functions including mouse mammary tumor virus (induced by hormones), herpes simplex virus α , β , and γ genes (whose products induce and repress each other in a complicated manner), metallothionein (induced by certain cations), β -interferon, and heat shock proteins of *Drosophila*.

The editors certainly rendered the scientific community a service by publishing these proceedings so soon after the conference. Naturally, there is a price to pay for the rapid publication: the considerable overlap in the text and in the lists of references of the papers. For example, the first page of most chapters contains historical background on the topic presented and a set of definitions that are nearly identical among chapters. This abundance and repetition do not stimulate the reader, especially when few contributors separated their introduction from their new results with subheadings.

The book is the first complete account of enhancers and other eukaryotic regulatory sequences. Of course, in such a rapidly growing field, the book will be outdated in a short time. For now, however, it is an efficient introduction to the topic.

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THE AGE OF GENETIC ENGINEERING

The Gene Age. By Edward J. Sylvester and Lynn C. Klotz. Pp. 208. ISBN 0-684-17950-4 (Charles Scribner's Sons, New York: 1983) \$14.95.

The Gene Age is an excellent one-stop review of the controversies and some of the promises brought on by the advent of genetic engineering. The text is written in a breezy, journalistic style applicable to a diverse audience. The real jewels of the book are three scientific chapters in which the authors sequentially explain genetic engineering. It is the clearest exposition of the science that I have read to date. This section provides a model of how to explain a complex scientific subject in easily understandable and non-threatening language.

Just to make sure the reader doesn't get too much education all at once, the authors disperse the scientific chapters among those dealing with lighter, more general topics.

The scientist should find the book useful for learning more about the extended impacts of genetic engineering. The businessman and investor should find it useful as an overview to understanding the field, enabling them to ask the right questions to hopefully make money in their area of interest. The layman should find it a useful primer to understanding current articles about cutting-edge developments in genetic engineering and related areas in health care, agriculture, and industry.

The basis for genetic engineering's