

Molecular Biology and Biochemistry of Differentiation

by Stephen E. Harris*

Recent work in the field of molecular biology and differentiation has been directed towards an assessment of the number of different genes involved in the development and differentiation process. By the techniques of RNA-DNA hybridization to single copy DNA, it appears that some 50,000-200,000 different RNA sequences are expressed during embryonic development in the mouse. The differentiating brain shows the highest degree RNA transcription diversity. The new technique of cDNA-poly(A)-containing RNA hybridization is described. The nuclear poly(A)-containing RNA appears to reflect the high complexity of sequences as determined in RNA-DNA experiments described above. The cytoplasmic poly(A)-containing RNA or messenger RNA appears to represent a subset of approximately 10-20% of the information in the nuclear poly(A)-RNA. Also, the major portion or frequency class of messenger RNA in different organs such as kidney, spleen, and liver are common to these different organs. However, brain, although containing many of the cytoplasmic messenger RNA sequences found in liver, kidney, and spleen, has a large class of messenger RNA sequences which are specific to the nervous system.

At the heart of understanding the mechanisms involved in cellular differentiation in eukaryotic organism is an assessment of the genomic output, both qualitative and quantitative, during embryonic development and in the final differentiated organ systems. Since each somatic cell contains the same genome in terms of DNA content and sequence information, the mechanisms underlying cellular differentiation must be reflected in differential gene activation and repression of specific DNA sequences at various times during development. There must be control mechanisms capable of activating and selecting part of the total genetic potential while repressing other regions at different developmental stages or in different cell types. It is assumed that specific cellular products produced by one cell can and do influence the fate of gene expression patterns of other cell types in the surrounding environment of the differentiating system. There must be

many genes, both structural and regulatory, involved in cellular processes of differentiating cells as well as in the final differentiated adult organ. We assume that many of these expressed genes will be both common to different cell types as well as genes which will be specific and characteristic of a given cell or organ.

Recent work in the field of the molecular biology of differentiation in eukaryotes, and in particular in the mouse system, has concerned itself with analysis of the informational content of RNA transcripts during development. With this information one can obtain a feel for the number of potential genes that are involved in the stabilization of the final differentiated state. The techniques of nucleic acid hybridization have provided us with useful information about genomic output in normal and abnormal development, and this tool could in the future be very useful for assessing the effect of various toxic and teratogenic compounds on various organ systems during embryonic development.

Although much information has accumulated on biochemical and genetic aspects of the pre-

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