Evolution of genetic regulatory mechanisms

The number, morphology or chemistry of chromosomes alone do not provide clues for understanding the various stages of evolution. They only help to understand the basis of the unity and diversity of living forms. If evolution has to be studied at the level of the gene, the best mode of attack could be the unravelling the various methods of gene function. Since in multicellular organisms, all the cells arise from a single initial cell (zygote), it is clear that all cells contain identical chromosome sets and genetic factors. Under such conditions, the cell should have the potency to express all the characters of the organism. That this is indeed the case has been demonstrated by Prof. F.C. Steward and his colleagues in the United States who produced in artificial cultures entire carrot plants from individual cells of the carrot roots. Similarly, Prof. E. Hadorn of Zurich has shown that cells of the imaginal disc of the fruit fly Drosophila melanogaster form wings, antennae, legs or genital organs in culture tubes. While the cell is thus totipotent, the differentiation of cells into tissues and organs demands that not all genes can be active in all cells. There has to exist a system of selective activation (derepression) and inactivation (repression) of genes in different cells. Probably only a small portion of genes are active at any one time. The processes which regulate genes are currently one of the most fascinating areas of research.

There appears to be at least two levels of gene control. One of these involves a very selective control of individual structural genes. The other involves the inactivation of whole chromosomes. The genetic systems that control gene action are best understood in bacteria

and the system proposed by the French scientists Jacob and Monod serves as the basis for studies in this field. The bacterial control systems are composed of two genetic elements, each distinct from the structural gene. One of them, designated the 'Operator', is located adjacent to the structural gene (or sequence of structural genes) and controls its activation. The structural gene, when activated, is responsible for the production of a particular sequence of amino-acids and thus for the specificity of a protein. The second element of this system, termed the 'regulator', may be located close to the structural gene or it may be located elsewhere in the bacterial chromosome. The regulator is responsible for the production of a repressor substance that appears in the cytoplasm. The operator element responds to changes in degree of effective action of the repressor substance by 'turning on' or 'turning off' the action of the structural gene in accordance with such changes. Each operator - regulator system is specific in that an operator will respond only to the specific product of the regulator of its system. Cytoplasmic feed-back is though to occur through influences on stability of the repressor-operator complex. Control of this process is assumed to occur at the level of messenger RNA synthesis.

Precise knowledge of regulatory genes is still largely restricted to micro-organisms. Operon systems of control are, however, suspected in several higher organisms including man. At the level of the chromosome, uncoiling and dissociation of the DNA from the histone are believed to play an important part in gene activation. Gene action is usually repressed in a tightly coiled chromosome segment (i.e., heterochromatin). The potentiation of the nucleotide sequence, within a gene for the formation of a RNA copy requires that the histone component be separated from the nucleic acid. Frenster of the United

Sta[illegible]postulated that the polyanions
the chromosomes such as RNA, phosphoproteins,
phospolipids and non-histone residual proteins may
displace histones from DNA and thus help in genetic
de-repression. There is evidence from several other
studies that the repressor may be a protein. Mechanisms
of this kind help in differential gene action.

The other major category of selective repression
of gene activity involves the inactivation of whole
chromosomes of the type demonstrated by Mary Lyon in the
case of the X-chromosome in the female of mouse. The
inactive - X theory postulates that the normal method
of dosage compensation in mammals is inactivation of
one X-chromosome of females early in embryonic development.
This form of heterochromatinization of entire chromosome
may be operative in autosomes also and needs criti
study. The evolution of the operon system of regul
of gene action is significant in this context, si
this would involve grouping together on the same ch
of genes controlling analogous functions. Heterochrom
tion as a trigger in differentiation may henc
in two ways, which I would like to describe as
or "facultative", depending upon whether the en
is irreversible or reversible. The heterochromat
which have traditionally served as morphological
in karyotype studies in maize, rye and other pla
all represent a permanent state of gene repression.
Hence, genes are seldom located in such regions and this
led to the now-discarded view that such regions provide
the location for polygenes.

Thanks to the work of Prof. G.L. Stebbins and
his co-workers, morphological traits in higher plants are
also now being used in studying the complete chain of

events from primary gene activity to final expression of morphological differences. They have studied intensively those events at the cellular and submicroscopic level which might provide a link between gene controlled processes and the form-determining activity of individual cells and groups of cells. Such studies would help in throwing light on problems of differentiation in plants.

As mentioned earlier, the operon system of control of gene action is well established in micro-organisms and is indicated in some higher organisms as well. The question can however be asked whether such a system is necessary in higher organisms, since it can be argued that a mechanism of genetic regulation would be most efficient if the control is exercised at the level of the gene itself. This is because only one molecule would be sufficient to block the activity of a single gene at the level of the genetic material, while a regulation at the level of the ultimate gene product may require thousands of molecules. In view of the high efficiency of the process, it is reasonable to assume that the operon type of regulations has been retained and perhaps new dimensions of control added to it. The need for further sophistication in genetic regulatory mechanisms in higher organisms, as compared to bacteria on viruses, is clear from the fact that while differentiation in unicellular forms reversible, the process of differentiation in higher organisms is both reversible and irreversible. Although there is sufficient evidence in support of the theory that in most cases, cellular differentiation in higher plants does not involve any irreversible nuclear change, permanent changes in the nucleus concomitant with development