Meetings

Genetic Control of Differentiation

Differentiation is a central phenomenon in biology which poses something of a paradox. Most evidence from cytology and genetics supports the conclusion that each cell of multicellular plants, and probably of animals, normally carries the full amount of genetic information; yet the cells follow a regulated and coordinated program to become different in structure and function during the development of an individual. Anticipation of a "breakthrough" in solving key problems of the genetic control of differentiation has led to an increasing volume of research directed toward this goal in areas that associate the disciplines of cytogenetics, biochemistry, microbiology, embryology, and morphology. The 18th annual Brookhaven Symposium in Biology, held on 7–9 June 1965 at Brookhaven National Laboratory, Upton, New York, brought together investigators who are using widely different approaches to study the genetic control of differentiation in a variety of biological materials at different levels of organization.

The main address was given by E. Hadorn (University of Zürich) who described results of a new method for investigating cellular determination in *Drosophila* by culturing cells of the imaginal disc. These cells have been determined to form wings, antennae, legs, or genital organs; but differentiation, that is, the evident expression of determination, is more delayed than elsewhere in the body. In 50 sublines, derived from a single imaginal disc and cultured through 72 transfer generations, Hadorn has shown that cells which normally would form male genitalia can undergo surprising "transdeterminations" in time to give rise eventually to transplanted parts of head, legs, wings, and thorax.

Cellular differentiation is now generally regarded as a consequence of differential gene activity. In the more restricted biochemical sense it is considered to apply to the differential synthesis of immediate gene products, transcription to RNA, and the production of different arrays of proteins (enzymes) in different cell lineages. One example of this phenomenon given by H. Ursprung and K. D. Smith (Johns Hopkins University) is the development of lactate dehydrogenase isozyme pattern in tissues. This reflects the relative abundance of two basic subunits, which in turn indicates the occurrence of changes during development in the relative activity of two genes controlling formation of these subunits. Mechanisms which regulate gene activity may involve hormones, histone proteins acting as nonspecific repressors, and nonhistone proteins acting as more specific derepressors.

H. E. Umbarger (Purdue University) described patterns of "feedback" mechanisms in bacteria that are known to regulate enzyme activities. He pointed out that, since these can exert only transient changes, they may have limited applicability to processes of differentiation in higher organisms. However, he suggested that enzymes, catalyzing the same reaction but distinguishable by the compounds regulating their activity, would serve as useful "markers" in monitoring the emergence of different cell types in multicellular forms.

In the ciliated protozoan, *Tetrahymena*, there is a macronuclear basis for intraclonal variation in certain stable isozyme types. S. L. Allen (University of Michigan) found that the best hypothesis to fit the data is (i) that the macronuclear units involved are diploid subnuclei, and (ii) that variations in heterozygotes result because subnuclei are differentiated following interallelic action in each subnucleus and because there is a physical segregation of the differentiated subnuclei during division. Interallelic interaction may afford a type of regulation that is unique for all diploid forms. In the related protozoan, *Paramecium bursaria*, R. W. Siegel (University of California at Los Angeles) described the inheritance of factors controlling the differentiation of cells of exconjugant clones into three distinct mating types. Their expression depends on the sequential production of two mating-type proteins, each of which is governed by an independent gene locus. Regulatory genes determine which of the two loci will be expressed first, and, once this is accomplished, other regulators control the switching on of the second locus.

The regulatory program of the enzyme uridine-diphosphate-galactose polysaccharide transferase during cellular development of a slime mold was described by M. Sussman (Brandeis University). The enzyme appears at a specific stage, accumulates rapidly to a peak of specific activity, is preferentially released by the cells, and is destroyed. The periods of specific RNA synthesis and of actual enzyme accumulation and destruction were shown to be genetically governed in that these processes are altered in a mutant whose overall temporal controls are deranged. K. Paigen and R. Ganschow (Roswell Park Memorial Institute) use the term "enzyme realization" to refer to the total cumulative pattern of appearance of factors that affect the physiological role of a specific protein in a cell. These include the cell types in which it appears, when and how much of the protein is produced, the site (or sites) within the cell into which it may become integrated, and the regulatory systems that control it. At least four classes of genetic factors—structural, regulatory, architectural and temporal—may be involved in the realization of any protein.

The initial processes of animal development depend on a reservoir of preformed components in the egg cytoplasm which are synthesized during oögenesis. E. H. Davidson and A. E. Mirsky (Rockefeller University) reported analyses of the gene products formed during amphibian oögenesis when the "lampbrush" chromosomes are in a state of intense gene activity. RNA synthesis occurs at practically all extended sites along the lampbrush chromosome, though at a remarkably low rate compared with nucleolar ribosomal RNA synthesis. The latter appears to occur on thousands of separate replications of the ribosomal RNA locus, contained in thousands of nucleoli in each oöocyte nucleus, and accounts for 97 to 99.5 percent of RNA synthesis per unit time. The relation between differential nucleic acid metabolism in polytene chromosomes of *Diptera*, as shown by puffing, and patterns of differentiation was discussed in independent papers by C. Pavan (University of São Paulo) and U. Clever (Purdue University). An enhanced synthesis of RNA, resulting from greater gene activity, is associated with the puffed chromosomal region. Some of the most convincing evidence that puffing is related to developmental processes is afforded by experiments with the hormone ecdysone which induces molting and also causes puffing at specific loci.

One session of the symposium was devoted to discussions on the genetic control of differentiation in plant development. The present status of research on species of the genus *Acetabularia* was presented by G. Werz (Max Planck Institut für Meeresbiologie, Wilhelmshaven). Morphogenesis in these unicellular and uninucleate green algae is governed by the activity of "morphogenetic substances," probably messenger RNA. Under the influence of "regulators," located within the cytoplasm, the potentialities of the morphogenetic substances are realized, that is, expressed in morphological development. Realization depends, therefore, not only on temporary activations of nuclear genes, but also on activations of certain gene products already transferred and stored in the cytoplasm.

B. McClintock (Carnegie Institution of Washington) summarized evidence in maize for identifiable controlling elements that govern the action of genes during development. Three systems were discussed in some detail: the *Ac* system, the *Spm* system, and the *Dt* system. The elements of all three systems share many properties in common, which suggests a basic relationship among them with regard to origin and composition. Furthermore, elements with the same properties are present in some strains of maize derived from different geographic regions, so that there is little reason to doubt that they are common components of the maize genome. A basic difference between differentiation in plants and animals is that meristems of plants remain in an embryonic condition throughout the life of the individual, whereas most animals have only one early embryonic stage. G. L. Stebbins (University of California) pointed out that, as a consequence, the most significant genetic changes in the evolution of higher plants are those that affect the structure of, and cell behavior in, the primary meristem from which the various organs are differentiated. Shifts between a condition that is basically determined by cellular elongation to one that is determined mostly by mitotic divisions without cell enlargement can be demonstrated to be under gene control in barley. Furthermore, morphogenetic effects in meristematic regions and where a symmetrical mitoses occur are shown to be related to changes in nucleic acid synthesis and mitotic rhythm.

This symposium will be published in a volume entitled *Genetic Control of Differentiation*, which is expected to be available around the first of the year from the Clearinghouse of Federal Scientific and Technical Information, National Bureau of Standards, Springfield, Virginia. The volume represents, then, a judicious sampling of present research activity on the genetic control of differentiation where, at some future time, a new synthesis in biology may emerge.

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Forthcoming Events

January

11–12. Man's Extension into the **Sea**, symp. on SEALAB II, Washington, D.C. (T. Evans, Conference Management Organizer, Colonial Bldg., 105 N. Virginia Ave., Falls Church, Va. 22046)

12–14. **Medicinal and Aromatic Plants in India**, symp., Central Indian Medicinal Plants Organization, Lucknow, India. (S. C. Datta, CIMPO, 4 Sapru Marg, Lucknow)

12–20. International **Fertility** Assoc., Latin American mtg., Acapulco, Mexico. (M. Roland, 109-23 71st St., Forest Hills, N.Y. 11375)

13–14. **Body Fuel Utilization**, conf., Boston, Mass. (F. D. Moore, Dept. of Surgery, Harvard Medical School, 25 Shattuck St., Boston, Mass. 02115)

13–14. Institute of **Mathematical Sciences**, 4th Mathscience anniversary symp., Madras, India. (C. P. Ramaswami Aiyer, Inst. of Mathematical Sciences, Madras)

13–16. Indian Institute of **Metals**, 19th annual mtg., Hyderabad. (The Institute, 31 Chowringhee Road, Calcutta 16)

16–21. American **Chemical** Soc., winter mtg., Phoenix, Ariz. (ACS, 1155 16th St., NW, Washington, D.C. 20036)

17–19. **Labelled Proteins in Tracer Studies**, conf., Pisa, Italy. (Euratom, Labelled Compounds Div., 51-53, rue Belliard, Brussels, Belgium)

19–21. **Instrumentation** for the Process