GENES, CHROMOSOMES AND DEVELOPMENT *

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Geneticists presently use to state that nobody ever affirmed the genes were physical, independent corpuscles. Then, come the arguments to prove that a given gene, in order to perform its genetical activities, needs the cooperation of all the others.

In fact, when somebody speaks about gene independence he is not willing to attribute to this particle the faculty of producing the character ascribed to it independently of the rest. The genetical property of the gene "vermilion" certainly is not *to dye* the eyes, but to cooperate with all the other genes for the developing organism having vermilion eyes. However, even on the light of this evidence one cannot deny that the gene is an independent entity as stated in the definition, for the independence recognized in it is a completly distinct one.

The gene has been considered as an independent biological entity in the sense that it can vary in composition or in function without affecting any other member of the individual genotype. Thus, a gene may mutate or simply alter the expressivity of the character due to its specifical activity, without influencing any one of the rest, not even those which are in the same chromosome. Crossing-over and fragment translocations show that genes may pass from chromosome to chromosome without changing its own activity, as well as the activity of the genes to which it was linked or of those with which it becomes associated. It is this kind of independence ascribed to the genes that constitutes one of their most important characteristics and at the same time serves to demonstrate the constancy of their attributes and therefore to warrant the individuality and specificity recognized in them since the beginnings of Mendelism.

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Genetics does not obtain to get rid of the idea of individual particles endowed with specifical activity not even when it recognizes that the character depends upon the interaction of many genes. Even following DOBZHANSKY (1955) when he states that "the development of the organism is due to all the genes acting together in concert" one cannot abandon the concept of corpuscular gene which prevails in the modern heredity, simply because the genes, by definition, must differ from one another. Though cooperating with all the others for producing the character, each gene is a different gene, since there is in the developing organism at least one peculiarity which depends specifically upon a particular gene. It is this particular stroke which serves to denominate the gene and at the same time do distinguish it individually from all the others.

Suffering of no modifying influence from their like, each gene presents itself as a constant entity, that means, as an entity which always has the same attributes anywhere in the body.

In fact, as we know, the cells in the body of the developing animal originate from preceding ones through mitoses. Mitoses, thus, bring to all parts of the organism the same chromosomes (exact copies of those which were assembled in the egg), and therefore the same genes. But, if all the cells have the same gene collection and genes are constant entities, it is clear that neither differentiation nor characterization of the organism can be ascribed to genes. The same genes working in the same way in all the cells cannot, evidently, be responsible for the regional differences noted in the individual. Thus, if all the genes work in the same manner in the imaginal disc from which an eye or a wing develops, I cannot understand how the characters shown by these organs of the adult insect are attributed to the genes.

I cannot understand, but the geneticists can and do it with great simplicity. They use to say, for instance, that the genes really are the same everywhere, but do not work at the same place. In the embryonic area determined to form eye enter into activity eye-genes, while in that determined to form wing, wing-genes. This means that genes for wings, legs, antennae, genitalia, bristles, body colour, etc., have nothing to do in the tissue destined to form eyes. Really, have nothing to do, because, being, specific, an eye-gene, for instance, cannot work in an area determined for producing any other organ. Therefore, they keep rest. And, since the number of genes which have to work specifically in a given area is much lesser than the number of the other genes also present in this area, or, in other words, there having in an eye-disc much less eye-genes than genes for other structures, it follows that in the developing organism there is much more rest than biological activities, what sounds inconsistent.

Moreover, this question of active and inactive particles together in the organism, Genetics inherited from former theories and has done it without considering that such assumption, not resisting criticism, caused the ruin of those theories. It was exactly what happened to DARWIN's (1868) theorie of the pangenesis of the gemmules: inactive gemmules circulate through the organism until predestinated cells appear, into which they enter for becoming active; it was what occurred with DE VRIES (1889) intracellular pangenesis theorie, in conformity to which inactive pangenes contained in the nucleus pass from cell to cell until they reach unities in which they leave the nucleus for getting active in the cytoplasm; it was what took place with WEISMANN's (1892) monumental theory of the biophors: as mere passengers embarked in the chromosomes, dorment biophors travel throughout the organism for attaining the station they are destined to, where they get off and pass to the cytoplasm for developing their specific activity. (See DELAGE 1903 and PIZA 1951).

Not a single theory based upon the rest of fundamental elements could endure. Recognizing this fact some geneticists more ingeneous began to admit that all the genes work at the same time, but differently as MORGAN (1934) suggested many years ago (WADDINGTON 1950, 1956, 1957). It means that in the cells of the eye-discs of a Dipteran larva all the genes cooperate in making an adult with eyes exhibiting the characters expected. But, if all the genes in the ocular discs contribute to the production of eyes typical of the race at tissue, and in the alar discs these same genes work in consonance for the formation of typical wings, one may ask what has been done of the gene constancy.

The answer to this question is as follows: genes have no constancy, working differently in different parts of the body. Indeed, when MORGAN (1943), under the pressure of the facts, first accepted this situation, DUNN (1934) judiciously noted : "The chief proponent of the stability and integrity of the gene in transmission, appears from this statement to be prepared to abandon the keystone of the theory of the gene when applying it to development". Therefore, if every gene individually considered changes its function as many times as are the unitary characters to the elaboration of which it cooperates with all the others, then the gene has no specificity. And if it has no specificity it does not correspond to the definition. A gene in such a condition can no longer be a gene. On the other hand, if all the genes of a given chromosome work jointly to produce each character, what actually works at each time is the whole chromosome.

Really, the chromosome is a whole and as a whole it functions. In every cell of the organism the chromosomes work with their entire body, never entering into rest.

The micromerists have some difficulty for understanding how can a chromosome perform, say hundred different genetical activities, working as a whole at the distinct places its copies take in the body. However, the Biology offers some informations which make the situation fairly conceivable.

From embryology we know that the cells in the walls of the gastrula stage are of epithelial type and generally equipotent relatively to what they should be at the end of the development. This means that, depending on the circumstances, anyone of them may give origin to muscular, nervous, glandular, sanguineous, or reproductive elements. But later, the embryonic cells still epithelial in nature and morphologically indistinguishable from each other, become determined, that is, specialized for the production of distinct lineages, some giving rise to muscles, some to glands, to nerves, or to reproduction organs. After determination the cells at any circumstace will produce only the elements corresponding to the determination. For instance, a cell determined to produce myocites, will originate these structural elements anywhere in the body of the embryo.

Determination gives origin in the organism of a Dipteran larva to the so called imaginal discs. These are pairs of undif ferentiated bodies specifically destined to form distinct organs of the adult, as eyes, antennae, wings, legs, etc . An eye-disc transplanted into the abdominal cavity of a larva of the same age will give there origin to an eye.

Now, the chromosomes, as integrating parts of the cellu lar system, do not scape the determination process that affects the whole cell. When an indifferent cell is determined to produce muscular fibers, its chromosomes, in consonance to the other el ements of the system, are correspondingly modified. In this way, a given chromosome charged with genetical functions to develop in the wings, the eyes, the legs, or the antennae, as soon as it gets determined as for instance eye-chromosome, it loses all the other faculties, to develop, at the right time, only that activities concerning the formation of an eye. Another copy of this same chromosome - since all the cells in the body get one - now in the alar, antennal, or podal discs, becomes there special ized to perform the respective function. Therefore, by means of distinct copies, each chromosome develops, one by one, all the functions ascribed to it, working "eye" in the eyes, "wing" in the wings, "leg" in the legs, and so on, functioning always as a whole.

BRIGGS (1953, 1955), BRIGGS and KING (1952), KING (1954, 1955), KING and BRIGGS (1953) have shown experimentally that the nucleus of embryonic cells are modified during development, losing the pluripotency it had before, to restrain more and more its faculties, that is, as an integrative part of a transforming system, the nucleus cannot keep unaltered the composition and the potenciality it had when in the egg. The nucleus, then , are determined and differentiated in correspondence to the modifica tions processing in the cytoplasm. Otherwise, an experimental modification of the nucleus following cell differentiation seems unnecessary, since histologists always know how to distinguish dif ferent types of nuclei in the cells of the organism (see fig. 7-4 in WILLMER, 1960, p. 125). It is not even needed to be much clever for recognizing the differences separating from one another the nuclei of eggs, spermatozoa, muscle fibers, secretory cells, several leucocyte types, etc .

It is clear that the chromosomes, as fundamental parts of the nucleus, are also attained by the differentiation process . From a physiological point of view they surely are different. Morphologically, however, it is difficult to discover the peculiarities which make them different in different cell types. Fortunately, there are some favorable cases to demonstrate the thesis. It suffices to compare salivary and cerebral chromosomes of the *Drosophila* larva to visualize the effect of the differenciation process on the chromosomes. Otherwise, as shown by several papers, the chemical composition of the chromosomes is different in different tissues. (Review and literature in Bloch 1958).

The imaginal discs are formed as ectodermal diverticles and appear as corpuscles of different sizes bound to several larval organs (brain, tracheae, etc.) by means of thin peduncles and are destined to form distinct parts of the adult body. In what concerns the structure they cannot be distinguished, since they all are formed by the same type of cells. Not withstanding that, as early as they can be manipulated in still very young larvae, they show to be already potencially distinct, since each one gives origin only to the structures corresponding to the determination it has previously received. Transplantation experiments carried out with *Drosophila* have shown that to whatever place it is brought to develop, the imaginal disc gives rise to the organ it should form if it had developed in its normal site.

Imaginal discs therefore are potential adult organs. Thus, a wing-disc represents a wing, an eye-disc an eye. Consequently, they are true embryomeres, that is, embryos of parts, waiting for the stimulation coming from the metamorphosis hormone elaborated in the ring-gland in order to develop itself epigenetically and give rise to the corresponding organs.

We arrive by this way at a situation wherefrom the problem can be fairly appreciated. In fact, in the course of the development of an Amphibian egg one can see that the embryo, prior to the organogenesis, is already divided into areas of different prospective value. These areas, called also morphogenetic fields , are constituted by cells determined to form distinct organs (eyes, anterior and posterior legs, ears, gills, tail, etc), each area forming only the expected organ **even when transplanted to any other** place of the embryo body. The determined cells may also be considered as differentiated cells. But, being not histological or even morphological the differentiation in this phase (neurula stage), the cells beloging to different areas cannot be distinguished. One thing, however, seems to be fairly alighted: the natural processes which divide the embryo into a mosaic of potencially distinct fields affect every parts of the cells there having no scientif reasons for admitting that only the cytoplasm is attained and consequently the chromosomes are exactly the same every where in the body. Otherwise, it is not known in the whole Biology an unique case of modification in one of the organs of a two-organs system (cytoplasm and nucleus), without introducing corresponding modification into the other.

Now we reach the theory of the chromosome-unity. Iniciating his career in the developing egg as an indifferent entity endowed with the faculty of developing many distinct genetical activities, the chromosome finishes by being differentiated for the fulfilment of only one, which depends on the place it gets in the body of the embryo.

We are not yet prepared for understanding the nature of the transformations experienced by different copies of the same chromosome in different parts of the body. For the time being it suffices to admit that these transformations really occur and constitute the basis of the phenomenon referred to before as "functional independence of the genes" .

RESUMO

Procura-se mostrar, no presente artigo, que nenhuma teoria micromerista consegue explicar os fenômenos genéticos, por não ser possível conferir a partículas a independência funcional relacionada com o trabalho que devem exercer de maneira específica no organismo.

O fato dos gens se encontrarem em tôdas as células do organismo em desenvolvimento, mostra que essas entidades desenvolvem distintas atividades em diferentes tecidos. Mas acontece, que nem a microscopia eletrônica, nem a bioquímica, consegue descobrir nos cormossômios algo que possa corresponder ao conceito de gen-conta-de rosário da genética clássica. Entretanto, o cromossômio considerado como um todo pode com vantagem substituir os gens no seu papel de determinar os caracteres do organismo. Admitindo-se que os cromossômios se determinam com as células de que fazem parte, uns para trabalhar nos esboços de asas, outros nos de olhos, patas ou outras estruturas, compreende-se fàcilmente, que, por intermédio de distintos membros do clone que se inicia com a primeira divisão do ôvo, uma dada sorte de cromossômio, funcionando como um todo especializado, pode exercer as atividades específicas que lhe são atribuídas. E isso, de pleno acôrdo com a embriologia experimental.

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