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Genome and stresses: reactions against aggressions, behavior of transposable elements

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Abstract

The action of stresses on the genome can be considered as responses of cells or organisms to external aggressions. Stress factors are of environmental origin (climatic or trophic) or of genomic nature (introduction of foreign genetic material, for example). In both cases, important perturbations can occur and modify hereditary potentialities, creating new combinations compatible with survival; such a situation may increase the variability of the genome, and allow evolutive processes to take place. The behavior of transposable elements under stress conditions is thus of particular interest, since these sequences are sources of mutations and therefore of genetic variability; they may play an important role in population adaptation. The survey of the available experimental results suggests that, although some examples of mutations and transposable elements movements induced by external factors are clearly described, environmental injuries or introduction of foreign material into a genome are not systematically followed by drastic genomic changes.

Introduction

The fluidity of the genome allows one to imagine evolutive mechanisms, since it makes possible long-term and rapid changes, and creates new variability, which is the source of adaptation. The short-term changes show that genomes have the capacity to reorganize rapidly within the lifetime of an organism. These changes have not always a clearly determined origin, but they can be submitted to experimentation. When they occur in absence of known reason, the results are called 'spontaneous changes'. Assays of application of factors capable of modifying the hereditary characteristics in cells or organisms provide a very large field of investigations; the results constitute a patchwork from which a picture of genomic susceptibility may emerge. The effects of stresses on the genome, resulting from action of various aggressive agents with consequences on the evolution of organisms, populations and species, have been discussed in many cases to establish theories based on observations or on experimental results (Parsons, 1973, 1993). Stresses are supposed to induce resistance or to select the best adapted genetic combinations. In many cases mutagenic consequences of aggressive factors with effects on genomes have been demonstrated (see Walbot & Cullis, 1985, for a review). The mutagenic action was mainly known as DNA breakages or base-composition changes, resulting in chromosomal aberrations as well as punctual mutations. After the discovery of transposable elements, however, most of the mutations affecting laboratory strains were found as resulting from insertions of such elements into structural genes (Inoue & Yamamoto, 1987). The capacity of these elements to move was compatible with their mutagenic effect, and thus with the possibiblity of transposition induction by mutagenic agents. Now it is clear that insertions of mobile sequences concord with mutagenic effects (Sankaranarayanan, 1986; McDonald, 1990). What is more difficult to demonstrate, especially in higher organisms, is the possible connection between stresses and mobilization of the repeated sequences, because of the permanent question of the 'directed mutation controversy' (Lenski & Mittler, 1993): if movements

are observed, are they the causes or the consequences of genetic changes in germ cells? Are these changes induced by external factors, or are we observing only the result of selective processes on a preexisting variability?

Investigations to detect the genomic effects of aggressive factors have been performed in many examples, from unicellulars to highly-integrated organisms, with various methods used to detect the changes, according to the biological material. Among the experimental results, it is necessary to distinguish between different kinds of effects: 1) effects on somatic or germinal cells (DNA damage, chromosome aberrations) compatible with individual survival and hereditary transmission; 2) effects on transcription level (regulation of specific RNAs consecutive to stress, with consequences on increase or inhibition of protein synthesis). These effects can be observed on 'classic' genes as well as on transposable elements. The action and role of these elements are not yet completely understood; since they are candidates for mobilization by external factors, and to take place in evolutive mechanisms, we will consider them apart from classic genes. Under stress conditions, changes in transposable element copy numbers have been shown in very specific cases, including bacteria, yeast, cultured cells and protoplasts. Such a genomic answer is much less evident in organisms of a higher integrated level, where the germ cells do not often seem to be modified in their genomic content by external factors, as will be discussed below.

Stress factors and biological materials

Environmental factors. Factors used as aggressive agents in the studies of stress consequences (Parsons, 1973) can be of a physical (temperature, radiations) or chemical nature (gas, drugs, hormones). In recent experiments, factors already known for their action on DNA and protein synthesis mechanisms are often used, since they are the best candidates to generate hereditary effects (Hoffmann & Parsons, 1991). This category of environmental stresses can also include the process of *in vitro* culture initiation (cell or tissue cultures, protoplasts) where the medium could be a determinant factor of perturbations, even if this effect is relatively uncontrolled.

Genetic factors. The association between two incompatible genomes can also lead to a modification of the genetic characters of the hybrids. For instance, in crosses between particular strains (within and between species), such phenomena as increases of mutation rate, replication errors, chromosomal aberrations, and transpositions of mobile elements, can occur and may be associated with sterility of interspecific hybrids. The introduction of foreign DNA into an organism or cells may also correspond to a genetic stress. This situation can be due to viral infection, bacterial symbiosis, ingestion of molecules with food; it may be experimentally obtained by injection of DNA sequences from an individual to another belonging to the same or an unrelated species, and creating transgenic individuals.

Biological materials. Experimental models for the studies of stress effects are widely representative of the living organisms. Among microorganisms and fungi, *Bacillus subtilis*, *Escherichia coli*, *Dictyostelium discoïdeum*, *Streptomyces*, and *Saccharomyces cerevisiae* have been used experimentally. On plants (maize, tobacco, flax, soya, sugar beet, snapdragon), stresses were applied either on whole organs or on tissue cultures and protoplasts. Among invertebrates, insects (*Drosophila*, *Calliphora*, *Culex*, *Rhynchosciara*) and the nematode *Caenorhabditis elegans* were mostly studied. In vertebrates, studies are made on mice (embryos, post-natal stages, cell cultures), and on human cells in culture.

Effects of stress on the genome

Description of stress effects on the genome is closely related to the evolution of the methods: the level of detection has historically changed with the improvement of the techniques, from macroscopic observations to molecular analyses.

Genetic consequences of stress: detection at the organismic level

The macroscopic effects of stress were first established by their action on fitness in individuals and populations: increase in mortality rates at different developmental stages, induction of resistance to high temperatures or to drugs like antibiotics or insecticides, and physiological changes.

In *Drosophila melanogaster*, Zuitin (1938) had already demonstrated that temperature fluctuations were able to increase the mutation rate, and Ushakov *et al.* (1977) showed the possibility of acclimation to high temperature. Cold has no effect in *Drosophila*