Jumping genes have essential biological functions

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"Alu" sequences are small repetitive elements representing about 10% of our genome. Because of their ability to move around the genome, these "jumping genes" are considered as real motors of evolution. However, they were considered for a long time as "junk" DNA, because, although they are transcribed into RNA, they encode no proteins and do not seem to participate actively in the cell's functions. Now, the group of Katharina Strub, professor at the Faculty of Science of the University of Geneva (UNIGE), Switzerland, has uncovered two key functions of Alu RNAs in human cells, which are the subject of two different articles published in *Nucleic Acids Research*.

Alu RNA can bind to specific proteins forming a complex called Alu RNP. On the one hand, this complex allows the cells to adapt to stress caused for example by chemical poisoning or viral infection. On the other hand, the same complex plays a role in protein synthesis by regulating the number of active ribosomes, suggesting that it could be part of the innate system of cellular defense against certain viruses.

Having emerged within mammals from a common ancestor, the genomic "Alu" elements multiplied during evolution to the point of representing about 10% of the primate and human genomes, whereas they are about ten-fold less abundant in rodents. These small repetitive elements are an important source of genetic variations, due to their ability to move freely around the genome, and they are therefore considered as motors of evolution, Apart from this essential function, what could be the advantage for the human genome to tolerate such a large number of Alu elements, which encode no proteins?

Alu elements are transcribed into RNA molecules, which bind specific proteins to form a complex called Alu RNP. "Alu RNP levels increases strongly in response to stress caused for example by poisoning or viral infections. The function of the Alu RNP is not known and we wished to determine whether these complexes play an active role in the stress response", explains Katharina Strub, professor at the Department of Cell Biology of the UNIGE.

A protection against toxics

Cells experiencing a stress react by temporarily forming numerous "stress granules", whose function is to sequester cell signaling proteins to prevent cell death. In addition, these granules accumulate various factors necessary for the synthesis of new proteins, while waiting for the situation to normalize. "When we treat human cells with arsenic, the Alu RNP complexes dissociate from their proteins called SRP9/14. The released proteins then bind key components of the protein synthesis machinery and participate in the formation of stress granules", says Audrey Berger, researcher and first author of the first article.

How does Alu RNA help cells to return to normality? "Following stress, cells actively produce a lot of Alu RNA, which will associate with the SRP9/14 proteins to form Alu RNPs. This will release components sequestered in stress granules and allows protein synthesis to resume", indicates the biologist. Thus, Alu RNAs actively participate in stress granule formation and dissolution.

Against viruses too

When viruses such as HIV and hepatitis C infect cells, they shut down cellular protein synthesis to hijack the protein synthesis machinery to their own profit. Many viral RNAs indeed possess specific sequences called IRES, which allow the direct recruitment of ribosomes to produce viral proteins instead of cellular proteins.

Based on the second study of the research group, Alu RNP complexes also play a protective role in case of infection. "They interfere with the formation of viral proteins, by inactivating the ribosomes before they are recruited to the viral RNA via the IRES", explains Elena Ivanova, researcher and first author of the second article. The cells in which Alu RNA expression increases following certain types of infection would thus produce a lot fewer viral particles.

As suggested by the authors, Alu RNP complexes could therefore be a component of the innate system of cellular defense against certain viruses. These complexes are also used by cells to adapt to conditions of stress and they play a role in the process of protein synthesis, by regulating the number of active ribosomes.

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