Cell nuclei harbor factories that transcribe genes

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Our genetic heritage is contained—and protected—in the nucleus of the cells that compose us. Copies of the DNA exit the nucleus to be read and translated into proteins in the cell cytoplasm. The transit between the nucleus and the cytoplasm takes place through the nuclear pores, genuine "customs agents" that monitor the import-export between these two compartments. Françoise Stutz, professor in the Faculty of Science at the University of Geneva (UNIGE), Switzerland, and her team have just discovered how nuclear pores also regulate the production speed of these DNA copies. This work, published in the journal *Molecular Cell*, reveals a new role for each nucleus' several hundred pores, which constitute as many microscopic factories of gene transcription.

Gene activity is not only determined by the sequence of the DNA, but also by the dynamic three-dimensional structure of the genome. The spatial distribution of genes inside the cell nucleus and their movement towards specific compartments influence their expression as well as chromosome stability and repair. One of these compartments is none other than the nuclear pore, present in the hundreds or thousands, depending on the type of nucleus.

If the gene does not go to the pore…

Pores, composed of many different proteins, the nucleoporins, cross the nuclear envelope and monitor the heavy traffic of the molecules, which takes place between the nucleus and the cytoplasm of the cell.

"Moreover, we know that, once activated, many genes attach to the pores to be transcribed there," notes Françoise Stutz, professor in the department of Cell Biology at UNIGE, Switzerland. To try to understand why, the researcher carried out experiments with baker's yeast. This unicellular fungus is often used as a model organism, because it works as a mammalian cell, though it is easier to handle.

When yeast ingests galactose, it will transform this sugar into energy thanks to an enzyme called GAL1. However, the gene encoding this enzyme is normally repressed by various proteins that mask its activation domain. "The whole complex is maintained in this state, blocked by the attachment of a tiny protein called SUMO," explains Lorane Texari, team member and first author of the article.

… the pore comes to it

After the yeast absorbs the sugar, the GAL1 gene is relocated to the nuclear pore. "We have discovered that the gene anchors itself with the help of an enzyme called Ulp1, which will remove the mini-protein SUMO. This will enable an array of factors to position themselves on the activated gene and to initiate its transcription," says the PhD student. The many copies thereby produced will then be exported directly into the cytoplasm. Once they are decoded, the instructions that they contain will enable the production of the enzyme GAL1, so that the yeast can use the galactose as fuel.

The nuclear pores thus create an environment conducive to the efficient production of gene copies. "For that matter, these microscopic transcription factories seem to have their equivalent in mammalian cells. We also find various enzymes anchored to the nucleoporins, including the enzyme responsible for removing the SUMO protein. However, given the size of their nucleus, much larger than yeast's, it is the nucleoporins that move towards the activated genes and not vice versa,"

explains Françoise Stutz. These mobile nucleoporins result, once again, from the infinite ingenuity demonstrated by the cells for adapting to new conditions of life.

Provided by University of Geneva