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Epigenetic treatments: New allies for chemotherapies?

- Tumour cells are able to adapt to anti-cancer treatments
- A research team has found that some epigenetic marks determine how well tumour cells tolerate chemotherapy
- Using epigenetic medicines in conjunction with chemotherapies would enhance their long-term effectiveness

Though chemotherapies are effective in some patients, tumour cells may acquire tolerance to these treatments. In other words, cells adapt to chemotherapy so they can survive. In a new study published in *Nature Genetics* on April 11, 2022, the team of Celine Vallot, CNRS Research Director at the Institut Curie, delivers promising results from their study of epigenetic mechanisms that regulate gene expression.

If genetics is interested in gene sequencing, epigenetics studies how genes are going to be used, or not used, by a cell. The epigenome of a cell represents the set of chemical modifications of the DNA or associated proteins that will determine the expression of the genes and thus the cell's identity. This information, which is central from the development of the embryo onwards, leads to changes in how our genes are expressed without affecting their sequence. By modifying its epigenome, the cell can adapt quickly to its environment. Genetics and epigenetics work together to enable cells to perform their function.

A research team[1] led by Celine Vallot, CNRS Research Director in the Laboratoire Dynamique de l'information Génétique: Bases Fondamentales et Cancer (CNRS/Institut Curie/Sorbonne Université), and the Département de Recherche Translationnelle de l'Institut Curie (CNRS/Institut Curie/Sorbonne University), analysed cell by cell the epigenetic variations acquired by tumour cells during chemotherapy treatment. In collaboration with the team of Léila Périé, a CNRS researcher at the Physico-chimie Curie (CNRS/Institut Curie/Sorbonne Université), the scientists identified the genes whose expression allowed cells to tolerate[2] treatment, as well as the epigenomic modifications that regulate them. Scientists have found that epigenomic marks "lock" the expression of these genes in the absence of treatment, and that this lock jumps under chemotherapy in rare cells. If this lock is prevented from jumping, all cancer cells remain sensitive to treatment. Scientists have demonstrated this by using chemical compounds called epi-drugs[3] on animal models of breast cancer that inhibit the removal of epigenetic marks. These molecules still need to be adapted for human use.

These results clearly demonstrate the epigenome's involvement in resistance to cancer treatment. The scientists are now actively seeking how to apply this concept to humans from a therapeutic perspective. If future clinical trials are convincing, scientists imagine that these epi-treatments could be used in conjunction with chemotherapies to prolong their effectiveness in patients.

Notes

[1] Scientists also participated from laboratories Physico-chimie Curie (CNRS/Institut Curie/Sorbonne Université), Génétique et Biologie du Développement (CNRS/Institut Curie/INSERM), Plateforme de Séquençage Haut-débit (ICGEX) du Centre de Recherche at the Institut Curie, Chimie Biologie Innovation (CNRS/ESPCI Paris - PSL) and from company HiFiBio Therapeutics.

[2] Tolerance is the ability of some cancer cells to survive a drug (in this case, chemotherapy), the first step before the actual acquisition of resistance capabilities. In the state of resistance cells are able to ignore the treatment and multiply normally.

[3] Drugs acting on the epigenome

Bibliography

H3K27me3 conditions chemotolerance in triple-negative breast cancer. Justine Marsolier, Pacôme Prompsy, Adeline Durand, Anne-Marie Lyne, Camille Landragin, Amandine Trouchet, Sabrina Tenreira Bento, Almut Eisele, Sophie Foulon, Léa Baudre, Kevin Grosselin, Mylène Bohec, Sylvain Baulande, Ahmed Dahmani, Laura Sourd, Eric Letouzé, Anne-Vincent Salomon, Elisabetta Marangoni, Leïla Perié and Céline Vallot. *Nature Genetics*, 11 April 2022. DOI: 10.1038/s41588-022-01047-6

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