Discovering cancers of epigenetic origin without DNA mutation

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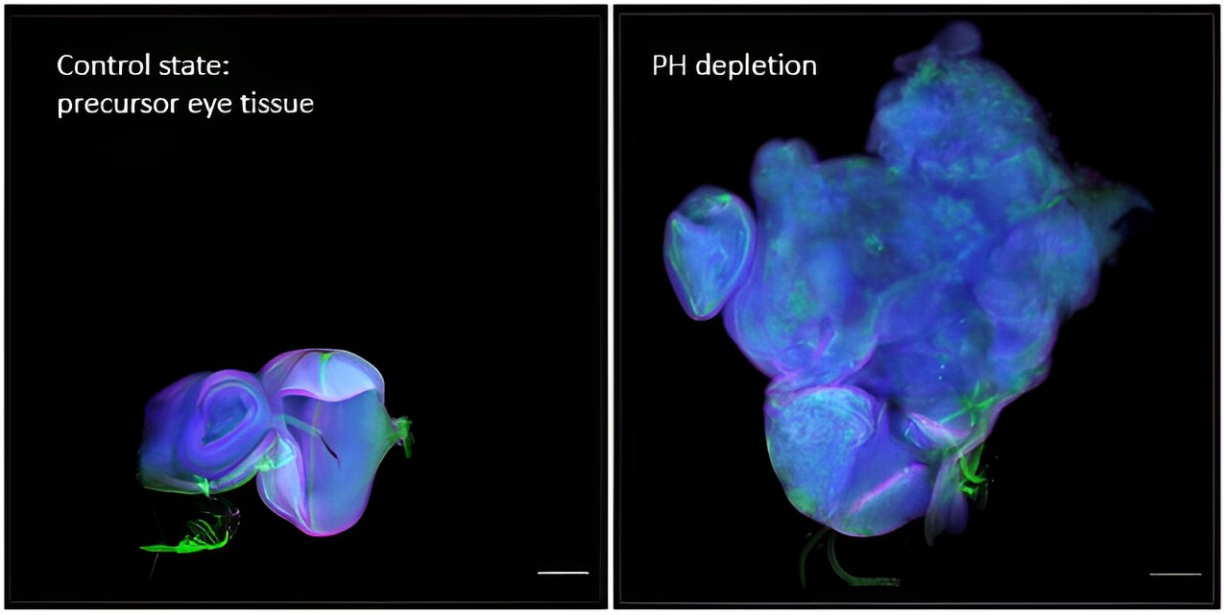

Example of a tumor obtained by reducing the expression levels of a Polycomb protein. On the left is an example of precursor tissue of the eye during normal development. On the right, a tumor has been initiated by reducing the level of a Polycomb protein. DNA is stained blue. In green, a protein located at the end of the cells is labeled to visualize how cells organize in the tissue. Normal organization is lost in the tumor. Scale: 100 micrometers. Credit: Giacomo Cavalli

A research team including scientists from the CNRS has discovered that cancer, one of the leading causes of death worldwide, can be caused

entirely by epigenetic changes, in other words, changes that contribute to how gene expression is regulated, and partly explain why, despite an identical genome, an individual develops very different cells (neurons, skin cells, etc.). The study is published in the journal *Nature*.

While studies have already described the influence of these processes in the development of cancer, this is the first time that scientists have demonstrated that genetic mutations are not essential for the onset of the disease.

This discovery forces us to reconsider the theory that, for more than 30 years, has assumed that cancers are predominantly genetic diseases caused necessarily by DNA mutations that accumulate at the genome level.

To show this, the research team focused on epigenetic factors that can alter gene activity. By causing epigenetic dysregulation in Drosophila, and then restoring the cells to their normal state, scientists have found that part of the genome remains dysfunctional.

This phenomenon induces a tumor state that is maintained autonomously and continues to progress, keeping in memory the cancerous status of these cells even though the signal that caused it has been restored. These conclusions open up new therapeutic avenues in oncology.

More information: Transient loss of Polycomb components induces an epigenetic cancer fate, *Nature* (2024). 10.1038/s41586-024-07328-w. www.nature.com/articles/s41586-024-07328-w

Provided by CNRS