Position of the cell nucleus affects epigenetics and therefore gene activity and cell function

Depending on whether the cell nucleus of an epithelial cell is located on the outer or inner side of the tissue, the genome is more or less acetylated - genes can therefore be translated easier or harder. Scientists from the German Cancer Research Center (DKFZ) have demonstrated this for the first time in the development of the Drosophila wing. The results have now been published in the journal Nature.

Histone acetylation is an important epigenetic mechanism. If acetyl groups are attached to the DNA-binding protein histone, the genetic material is less condensed and can therefore be read more easily. Histone acetylation therefore influences which genes are active and thus also cell function and cell fate. Proper histone acetylation is required for normal tissue development, and impaired histone acetylation is associated with cancer.

Proper histone acetylation depends on several factors. Phillip Willnow and Aurelio Teleman from the DKFZ have now studies the developing wing of the fruit fly Drosophila to show that the position of the cell nucleus in epithelial cells also influences the epigenetic status and thus the properties of the cells. Epithelia are the boundary tissues that line and delimit the inner and outer surfaces of the body. Epithelial cells therefore have two sides: one facing outwards and one facing the tissue.

Willnow and Teleman examined the cell nuclei in the so-called "imaginal disc", the developmental center of the Drosophila wing. These nuclei always exhibit high histone acetylation when they are positioned close to the outside. These surface nuclei also contain large amounts of the enzyme acetyl-CoA synthase, which is required for histone acetylation.

The carbon source for histone acetylation is fatty acid β-oxidation, which is enhanced in the outer region of the imaginal disc. If this fatty acid degradation is blocked, histone acetylation weakens in the vicinity of genes involved in wing development.

"The metabolism in the developing Drosophila wing is not homogeneous. In the outer region, near the blood-like hemolymph, fatty acids are metabolized. The cell uses the resulting acetyl CoA to acetylate histones," summarizes study leader Teleman and adds: "We now want to investigate whether similar phenomena occur in other organisms or in tumors that have an irregular tissue structure and abnormal histone acetylation."

Many of the common types of cancer, such as breast cancer, colon cancer and many forms of lung cancer, arise from epithelial tissue.

Publication:

Willnow, Phillip et al. "Nuclear position and local Acetyl-CoA production regulate chromatin state." Nature (2024), DOI: 10.1038/s41586-024-07471-4

Press release

13-Jun-2024
Source: German Cancer Research Center (DKFZ)

Further information

- German Cancer Research Center