Website address:
https://www.gesundheitsindustrie-bw.de/en/article/press-release/molecular-arms-race-how-genome-defends-itself-against-internal-enemies

Molecular arms race: How the genome defends itself against internal enemies

An international research team has deciphered a mechanism of evolutionary arms race in human cells. The findings provide insights into how mobile elements in DNA hijack cellular functions – and how cells can defend themselves against this in order to prevent conditions such as tumour formation or chronic inflammation.

An international research team led by Freiburg biologists Dr. Wenjing Qi and Prof. Ralf Baumeister has discovered how the LINE1 retrotransposon exploits a cell protein to become active itself, as occurs in tumours. At the same time, the researchers have also deciphered the cell's appropriate countermeasure to prevent conditions such as tumour formation or chronic inflammation. The results have been published in the journal *Nature Communications*.

Cellular sleepers

"Sleepers" are the name the Secret Service gives agents who live inconspicuously in a society for years before being activated by their employers. The human genome contains thousands of such sleepers, known as retrotransposons. These – probably left over from virus attacks millions of years ago – are equipped with only minimal information to jump out of the genome and multiply when the opportunity arises. To do this, they misuse the enzyme machinery of human cells.

LINE1 is the name of the most common of these elements, accounting for almost 20 percent of the entire genome. When LINE1 becomes active, it copies itself and reintegrates itself into the genetic material at a different location, thereby disrupting the cell's blueprint. This may sometimes be beneficial in terms of introducing diversity into the genome, but it can easily become uncontrollable, especially in progressive tumours. In addition, active LINE1 can alert the cell's immune system, which can lead to chronic inflammation. Over the course of evolution, human cells have therefore developed many mechanisms to prevent precisely this activation. How LINE1 itself is mobilised has been largely misunderstood until now.

Competition between proteins

The research team has unlocked the mechanisms on how this works: LINE1 recruits a non-working protein in the cells called NRBP1. This former kinase had lost its enzymatic functions through mutations in its gene over time. Since the uncontrolled reproduction of LINE1 is a major problem for the host cell, it also developed a counter-mechanism over time. A slightly modified copy of this protein, the paralog NRBP2, marks NRBP1 so that it is recognised as waste and thereby disposed of.

The competition between the two proteins must be won by NRBP2 in order to prevent damage. Until now, both factors had only been noticed in cancer biology due to their different involvement in tumours, without their functions being known. An analysis of the evolutionary history of this competition shows that the blocking function of NRBP2 was probably acquired later in evolution in order to escape the destructive influence of NRBP1 and LINE1.

Detailed insights

Wenjing Qi is a research group leader in the laboratory of Ralf Baumeister, Professor of Bioinformatics and Molecular Genetics at the University of Freiburg. Both were also supported by the CIBSS – Centre for Integrative Biological Signalling Studies, a cluster of excellence at the University of Freiburg. The first authors of the publication are her colleagues Dr. Wei Yang and Shaobo Cong. "Our findings not only show the involvement of NRBP1/2 in the development of human tumours," says Qi. "They also provide insight into the regulatory details that have emerged from gene duplication over the course of evolution."

Publication
Yang, Wei et. al. (2025): Opposing roles of pseudokinases NRBP1 and NRBP2 in regulating L1 retrotransposition. Nature Communications.
DOI: 10.1038/s41467-025-61626-z

Press release

11-Jul-2025
Source: Albert-Ludwigs-Universität Freiburg

Further information

- University of Freiburg