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Press information

Human “Jumping Genes” Caught in the Act!

Over the course of evolution, the genomes of most living organisms have grown more complex thanks to transposable elements, a.k.a. “jumping genes,” or DNA fragments that can move and copy themselves from one chromosome location to another. Researchers from Inserm, the CNRS, Université Côte d’Azur, and Université de Montpellier were able to capture these “jumping genes” just after they moved. The researchers compared their observations with existing databases. Their work, to be published in *Molecular Cell*, shows that the integration of “jumping genes” in humans is not random. Instead, it is thought to be influenced by specific genome properties. These results open up new perspectives for interpreting whole genome sequencing data.

Transposable elements, also known as “jumping genes,” are small DNA fragments that can multiply and move in the chromosomes of most living organisms. They have proliferated so intensely in mammals and primates that they make up more than half of our chromosomes! Of course, they don’t jump all at once in all of our cells. Of all the copies present in our DNA, only a small fraction remain active. All the rest are molecular remnants reflecting millions of years of evolution, during which harmful insertions were eliminated and beneficial ones retained.

In humans, the most active jumping genes are L1 retrotransposons. They can alter or destroy genes when they jump, triggering the manifestation of genetic diseases like hemophilia and muscular dystrophy. L1 retrotransposons are also particularly active in some forms of cancer, and could be involved in cellular aging or in some mental illnesses.

Do L1 retrotransposons target specific chromosome regions, or do they choose their positions at random? Teams led by Inserm head researchers Gaël Cristofari and Simona Saccani working at the Nice Institute for Research on Cancer and Aging (IRCAN, Inserm, CNRS, Université Côte d’Azur), along with their colleagues at Université de Montpellier, were able to use a “high-speed” genome sequencing technique to catch actively jumping genes right after they jumped to a new position.

After comparing their observations with genomic and epigenomic databanks, the researchers were able to identify which genome characteristics influenced the integration of the L1 retrotransposons. The most notable characteristic was DNA replication, and natural selection phenomena after integration played a preponderant role.

“We already knew that L1 retrotransposons tend to accumulate in specific areas of our chromosomes, especially heterochromatin. But we didn’t know whether that reflected a particular attraction to those regions, or if they are simply tolerated in those regions and eliminated elsewhere through natural selection. When we know where they jump to and which copies are retained over the course of evolution, we can discover – by deduction – the regions where they can do damage,” explains Cristofari.

Their results make it easier to understand how jumping genes can trigger mutations in humans, and how they contribute to the evolution of our genetic heritage. In the future, this research could be used to interpret whole genome sequencing data, particularly in personalized medicine and vast sequencing programs.

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Sources

The Landscape of L1 Retrotransposons in the Human Genome Is Shaped by Pre-insertion Sequence Biases and Post-insertion Selection

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