

Like an instruction manual, the genome groups genes together for convenience

September 16 2019



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Every living organism's cell has a complete copy of DNA, which is condensed tightly in chromosomes. Every time the cell needs to perform a function, it activates genes that open or close different regions in the DNA. Like following an instruction manual with consecutive pages, it's easier to activate two genes that are closer together to complete a function.



Until now, researchers knew little about how the genome of eukaryotic organisms organized groups of genes in accordance with their function, i.e., whether they were physically near or not. Previous efforts have studied the link between gene clusters and the secondary metabolism.

In a study published today in *Nature Microbiology*, researchers from the Centre of Genomic Regulation (CRG) in Barcelona, led by ICREA Professor Toni Gabaldón, shed light on this sorting process in primary metabolism. They chose to study fungi because they have smaller genomes and are easier to sequence than other eukaryote species like plants or animals.

"If genes for a specific biological process are placed near each other in the chromosome, they can co-regulate each other in a more coordinated and effective manner," says Gabaldón.

The scientists developed an algorithm capable of identifying genes near each other in genomes of different species according to their evolutionary history, i.e. looking for whether they were conserved clusters in different species of fungi, independently of the function they had. They predicted more than 11000 families of grouped genes in the genome. Of the 300 genomes analysed, they found that a third were part of a conserved group.

"Natural selection means some genes are near each other for functional relevance. The way they're organized isn't random chance—they have been selected because it makes regulating genes easier. We've found that it's pretty common, and that it affects an important proportion of the genome," says Gabaldón. "The selective forces favor the conformations of genes that allow a smaller investment in energy and improved regulatory processes," he adds.

Previous studies of gene groups linked to secondary metabolism



observed that they had a switch, a type of transcription factor, to turn them on and off. Other observations also found that these gene groups passed from one species to another in block, known as horizontal transfer, though no one knew why.

The CRG scientists have now provided evidence that horizontal transfer may be less common than previously thought, and their most recent findings don't represent what the <u>genome</u> does as a whole. They saw that a cluster made up of the same groups of genes appeared independently twice, in parallel distant lineages.

Surely, the groups of genes carry out a specific function. "When you need something at a precise moment, it's when you most need it to be co-regulated. A general function, which is active most of the time, doesn't need such precise regulation," says Marina Marcet-Houben, first author of the study.

"Now we have a list of functions to explore. Some might have a pharmaceutical or industrial use. The gene candidates we have found affect a lot of different species that until now hadn't been found. Many of them are interesting genes and it's likely they code a function with an applied potential," adds Gabaldón.

The study's findings were based on public databases. For this reason, the CRG has also publicized its results on primary genes. "We want to give this knowledge back to the scientific community thanks to the information and data we've gathered from the public domain."

More information: Evolutionary and functional patterns of shared gene neighbourhood in fungi, *Nature Microbiology* (2019). DOI: 10.1038/s41564-019-0552-0, nature.com/articles/s41564-019-0552-0



Provided by Center for Genomic Regulation

Citation: Like an instruction manual, the genome groups genes together for convenience (2019, September 16) retrieved 1 May 2024 from <u>https://phys.org/news/2019-09-manual-genome-groups-genes-convenience.html</u>

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