Research shows how RNA 'junk' controls our genes

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The tiny roundworm C.elegans is the focus of a new study examining 3'UTRs. These short segments of RNA play a critical role in the regulation of genes. The resulting map, the product of 20 years of research, is the most complete dataset of its kind for any animal, and will help advance basic understanding of mechanisms of gene regulation critical in human health and disease. Credit: Jason Drees, Arizona State University

Researchers at Arizona State University have made a significant advance

in understanding how genes are controlled in living organisms. The new study, published in the journal *Nucleic Acids Research*, focuses on critical snippets of RNA in the tiny, transparent roundworm Caenorhabditis elegans (C. elegans).

The study provides a detailed map of the 3'UTR regions of RNA in C. elegans. 3'UTRs (untranslated regions) are segments of RNA involved in gene regulation.

The new map is a valuable tool for scientists studying how DNA genes are switched on and off after they are transcribed into RNA. Using this data, scientists can make improved predictions of how small RNA molecules (miRNAs) interact with genes to control their activity. The researchers also explored crucial regions of the 3'UTRs that help in processing and regulating RNA molecules.

By studying the genetic material in this model organism, researchers are gaining deeper insights into the mysteries of gene behavior, shedding light on fundamental biological processes essential to human health and disease.

"This monumental work represents a culmination of 20 years of hard work. We finally have the complete picture of how genes are formed in higher organisms," says Marco Mangone, corresponding author of the new study.

"With this complete dataset, we can now pinpoint and study all the regulatory and processing elements within these gene sections. These elements determine the duration of gene expression, their specific locations within cells, and the level of expression required."

Mangone is a researcher in the Biodesign Virginia G. Piper Center for Personalized Diagnostics and a professor in the School of Life Sciences

at ASU.

Genes are only half the story

Genes are segments of DNA that contain the blueprints for an astonishing diversity of life on Earth. However, part of the secret to this versatility lies not in the genes themselves but in how their effects are delicately fine-tuned. Genes provide the instructions for making proteins, which play essential roles in building and repairing cells and tissues, speeding up chemical reactions and defending the body against pathogens.

To produce proteins, genes require an intermediary molecule called RNA. During this process, DNA is first copied into RNA, which acts as a bridge between the DNA template and the resulting proteins. Although our DNA genome is fixed from birth, RNA provides the body enormous flexibility by regulating how genes are expressed.

Once genetic instructions are transcribed from DNA into messenger RNA (mRNA), specialized segments of the mRNA—the 3'UTRs—can regulate how the proteins are produced.

3'UTRs are sections of RNA located at the end of a messenger RNA molecule. They help to govern how and when proteins are made by controlling the stability and efficiency of the mRNA. This regulation allows for dynamic responses to environmental changes and enables control over protein production, which is essential for adapting to various physiological needs.

3'UTRs reconsidered

Initially, noncoding RNAs like 3'UTRs were regarded as nonessential

genetic fragments because they themselves do not code for proteins. However, recent research reveals that they are crucial for modifying gene behavior and influencing mRNA stability, localization and translation efficiency. Translation refers to the process of converting RNA into proteins composed of sequences of amino acids.

3'UTRs are an integral part of a sophisticated and highly adaptable system of checks and balances on protein production. Additionally, these RNA regulatory elements often contain binding sites for other elements responsible for protein regulation, including microRNAs and RNA-binding proteins.

Despite their importance, scientists previously knew little about them. The new study addresses this gap by mapping out 3'UTRs for nearly all genes in C. elegans, providing the most complete map of its kind for any animal.

A window into gene function and disease

C. elegans is a small, transparent nematode that is one of the most extensively studied model organisms in biological research. Its significance lies in its simplicity, short life cycle and well-mapped genetic structure.

The organism shares many essential biological pathways with humans, making it invaluable for studying gene function, development and disease processes. Its transparent body allows researchers to observe cellular processes in real time, and its genetic composition enables the precise manipulation of genes.

These characteristics make C. elegans a powerful tool for uncovering fundamental mechanisms of biology that are often conserved across species, including humans.

The study found that the process of switching between different 3'UTRs is less common in C. elegans than previously thought. This challenges earlier beliefs and highlights the complexity of gene regulation. Using the new data, scientists updated predictions for how microRNAs interact with genes.

The insights gained from the new study have far-reaching implications for human health. Problems with gene control can lead to diseases like cancer, diabetes and neurological disorders. By providing a detailed map of 3'UTRs and their regulatory elements, the research offers new insights that could lead to better treatments and therapies.

The new dataset produced in the study will be a key resource for scientists studying genetics and human health. The ASU team plans to continue their research to further explore how these regulatory elements work and their critical influence on gene control.

More information: Emma Murari et al, A comprehensive analysis of 3′UTRs in Caenorhabditis elegans, *Nucleic Acids Research* (2024). DOI: 10.1093/nar/gkae543

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