redHUMAN: Deciphering links between genes and metabolism

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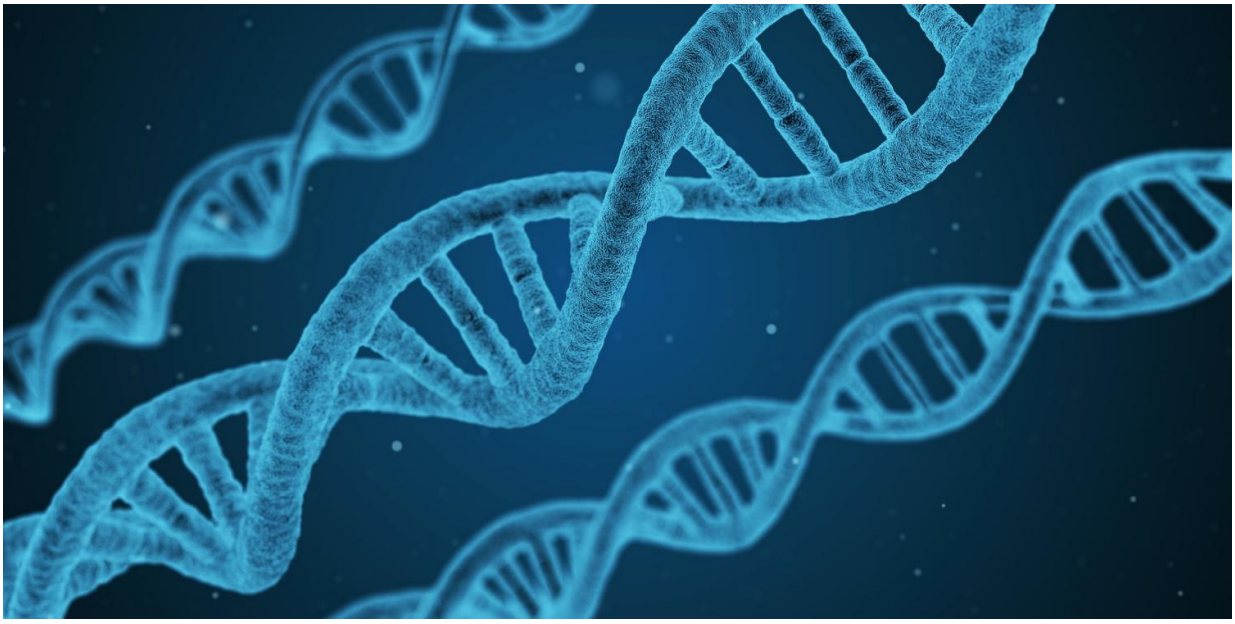

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In the last two decades, the life sciences have seen a growing partnership with information technology. The main drive behind this is the need to process and integrate enormous volumes of data from different fields including genetics, biochemistry, cell and molecular biology, and physiology in order to gain a deeper understanding of biological systems, processes, and even entire organisms.

The problem is that putting together data from numerous interconnected biological networks across different strata of biological analysis (e.g. genetic vs biochemical) has proven too complicated. The sheer volume and complexity of data across multiple fields is difficult to standardize and process, and has partly caused the proliferation of different "omics" fields (e.g. genomics, transcriptomics, proteomics, metabolomics, etc), which try to characterize and quantify pools of biological molecules in a way that relates to their structure and function in an organism.

One way that scientists have addressed the issue in the context of genes and metabolism analysis is by developing genome-scale metabolic models, or GEMs. These are computer models built from genetic and biochemical data, and associate genes with metabolic pathways in the cell.

GEMs are rapidly becoming a common tool for researchers. "They are powerful tools for integrating experimental data for a specific physiology and building context-specific models that can identify changes in the metabolism of diseased cells, such as cancer cells," says Maria Masid, a Ph.D. student from the lab of Vassily Hatzimanikatis at EPFL.

Working to further simplify the GEMs, Masid and her colleagues have now published a paper in *Nature Communications* that introduces a new mathematical method to analyze human metabolism by reducing the complexity of the human genome-scale GEMs by simply focusing on certain parts of metabolism while minimizing the information loss from the other pathways.

The study of cell metabolism is highly relevant because metabolic alterations have been recognized as a sign of several human diseases, including cancer, diabetes, obesity, Alzheimer's, and cardiovascular diseases. Therefore, understanding the relationships between metabolic

mechanisms and genes can guide drug discovery and the design of new therapies.

The researchers named their method redHUMAN, and describe it as "a workflow for reconstructing reduced models that focus on parts of the metabolism relevant to a specific physiology". redHUMAN generates reduced size metabolic models that contain the pathways of interest and the metabolic routes required to study nutrient metabolism and biomass synthesis, all this taking into account bioenergetics of the cell. By doing this, the redHUMAN model guarantees the consistency of its predictions, overcoming a major hurdle of the current GEMs.

"By combining these metabolic models with gene-expression data, we can identify functional changes that cannot be extracted directly from the data," says Masid, and "we can also formulate hypotheses to guide experimental design."

More information: Maria Masid et al. Analysis of human metabolism by reducing the complexity of the genome-scale models using redHUMAN, *Nature Communications* (2020). DOI: 10.1038/s41467-020-16549-2

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