Analysis suggests people with more copies of ribosomal DNA have higher risks of developing disease

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Ribosomal DNA (rDNA) is present in hundreds of copies in the genome, but has not previously been part of genetic analyses. A new study of

500,000 individuals indicates that people who have more copies of rDNA are more likely to develop inflammation and diseases during their lifetimes.

Standard genetic analysis techniques have not studied areas of the human genome that are repetitive, such as ribosomal DNA (rDNA), a fundamental part of the molecular mechanism which makes proteins in cells.

A new study, led by Vardhman Rakyan and Francisco Rodriguez-Algarra from Queen Mary University of London's Blizard Institute in collaboration with David Evans from the University of Queensland's Institute for Molecular Bioscience, has discovered that genetic disposition to disease can be found in these previously understudied areas of the genome.

The results, published in *Cell Genomics*, suggest that wider genome analysis could bring opportunities for preventative diagnostics, novel therapeutics, and greater insight into the mechanism of different human diseases.

In this study, samples from 500,000 individuals in the UK Biobank project were analyzed. Researchers used new whole genome sequencing (WGS) techniques to identify differences in numbers of copies of rDNA in each sample, and compared them with other health metrics and medical records.

The researchers found that the number of copies of rDNA in an individual showed strong statistical association with well-established markers of systemic inflammation—such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII). These statistically significant associations were seen in the genomes of individuals of different ethnicities, suggesting a

common indicator for risks of future disease.

rDNA copy number was also linked with an individual's kidney function within the sample of individuals of European ancestry. A similar effect was seen in samples from other ancestries, but further research using larger sample sizes will be needed to confirm this connection.

Professor Vardhman Rakyan, from the Genomics and Child Health in the Blizard Institute at Queen Mary, said, "Our research highlights the importance of analyzing the whole genome to better understand the factors impacting on our health. This study is also an example of how having access to large biobanks allows us to make unexpected discoveries, and provides new avenues for harnessing the power of genetics to understand human diseases."

Professor David Evans, from the University of Queensland's Institute for Molecular Bioscience, said, "Geneticists have long struggled to fully explain the genetic basis of many common complex traits and diseases. Our work suggests that at least part of this missing heritability resides in difficult to sequence regions of the genome such as those encoding ribosomal copy number variation."

More information: Ribosomal DNA Copy Number Variation Associates with Hematological Profiles and Renal Function in the UK Biobank, *Cell Genomics* (2024). DOI: 10.1016/j.xgen.2024.100562. www.cell.com/cell-genomics/ful … 2666-979X(24)00128-9

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