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Repeated sequences (also known as repetitive elements, repeating units or repeats) are patterns of nucleic acids (DNA or RNA) that occur in multiple copies throughout the genome. Repetitive DNA was first detected because of its rapid re-association kinetics. In many organisms, a significant fraction of the genomic DNA is highly repetitive, with over two-thirds of the sequence consisting of repetitive elements in humans.[1] Repetitive elements found in genomes fall into different classes, depending on their structure and/or the mode of multiplication. The disposition of repetitive elements consists either in arrays of tandemly repeated sequences, or in repeats dispersed throughout the genome (see below). Functions Debates regarding the potential functions of these elements have been long standing. Controversial references to 'junk' or 'selfish' DNA were put forward early on, implying that repetitive DNA segments are remainders from past evolution or autonomous self-replicating sequences hacking the cell machinery to proliferate.[2][3] Originally discovered by Barbara McClintock,[4] dispersed repeats have been increasingly recognized as a potential source of genetic variation and regulation. Together with these regulatory roles, a structural role of repeated DNA in shaping the 3D folding of genomes has also been proposed.[5] This hypothesis is only supported by a limited set of experimental evidence. For instance in human, mouse and fly, several classes of repetitive elements present a high tendency for co-localization within the nuclear space, suggesting that DNA repeats positions can be used by the cell as a genome folding map.[6] Tandem repeats in human disease Tandem repeat sequences, particularly trinucleotide repeats, underlie several human disease conditions. Trinucleotide repeats may expand in the germline over successive generations leading to increasingly severe manifestations of the disease. The disease conditions in which expansion occurs include Huntington's disease, fragile X syndrome, several spinocerebellar ataxias, myotonic dystrophy and Friedrich ataxia.[7] Trinucleotide repeat expansions may occur through strand slippage during DNA replication or during DNA repair synthesis.[7] Hexanucleotide GGGGCC repeat sequences in the C9orf72 gene are a common cause of amyotrophic lateral sclerosis and frontotemporal dementia.[8] CAG trinucleotide repeat sequences underlie several spinocerebellar ataxias (SCAs-SCA1; SCA2; SCA3; SCA6; SCA7; SCA12; SCA17).[8] Huntington's disease results from an unstable expansion of repeated CAG sequences in exon 1 of the huntingtin gene (HTT). HTT encodes a scaffold protein that directly participates in repair of oxidative DNA damage.[9] It has been noted that genes containing pathogenic CAG repeats often encode proteins that themselves have a role in the DNA damage response and that repeat expansions may impair specific DNA repair pathways.[10] Faulty repair of DNA damages in repeat sequences may cause further expansion of these sequences, thus setting up a vicious cycle of pathology.[10] Types This section is in list format but may read better as prose. You can help by converting this section, if appropriate. Editing help is available. (December 2018) Main types Major categories of repeated sequence or repeats: Tandem repeats: are copies which lie adjacent to each other, either directly or inverted. Satellite DNA - typically found in centromeres and heterochromatin. Minisatellite - repeat units from about 10 to 60 base pairs, found in many places in the genome, including the centromeres. Microsatellite - repeat units of less than 10 base pairs; this includes telomeres, which typically have 6 to 8 base pair repeat units. Interspersed repeats (aka. interspersed nuclear elements): Transposable elements. DNA transposons.retrotransposons.LTR-retrotransposons (HERVs).non LTR-retrotransposons.SINEs (Short Interspersed Nuclear Elements)LINEs (Long Interspersed Nuclear Elements).SVAs In primates, the majority of LINEs are LINE-1 and the majority of SINEs are Alu's. SVAs are hominoid specific. In prokaryotes, CRISPR are arrays of alternating repeats and spacers. Repeated sequences evolutionary derived from viral infection events.[11] Other types Note: The following are covered in detail in "Computing for Comparative Microbial Genomics"[12] Direct repeats Global direct repeat Local direct simple repeats Local direct repeats Local direct repeats with spacer Inverted repeats Global inverted repeat Local inverted repeat Inverted repeat with spacer Palindromic repeat Mirror and everted repeats Biotechnology Main article: Microsatellite § Analysis Repetitive DNA is hard to sequence using next-generation sequencing techniques: sequence assembly from short reads simply cannot determine the length of a repetitive part. This issue is particularly serious for microsatellites, which are made of tiny 1-6bp repeat units.[13] Many researchers have historically left out repetitive parts when analyzing and publishing whole genome data.[14] See also FREP Genome Eukaryotic chromosome fine structure Genetic marker Intergenic region Noncoding DNA Polymorphic simple sequence repeats database Regulator gene Satellite DNA References ^ de Koning AP, Gu W, Castoe TA, Batzer MA, Pollock DD (December 2011). "Repetitive elements may comprise over two-thirds of the human genome". *PLOS Genetics*. **7** (12): e1002384. doi:10.1371/journal.pgen.1002384. PMC 3228813. PMID 22144907. ^ Ohno S (1972). "So much "junk" DNA in our genome". *Brookhaven Symposia in Biology*. **23**: 366–70. PMID 5065367. ^ Orgel LE, Crick FH, Sapienza C (December 1980). "Selfish DNA". *Nature*. **288** (5792): 645–6. doi:10.1038/288645a0. PMID 7453798. S2CID 4370178. ^ McClintock B (1 January 1956). 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"Word Frequencies and Repeats". *Computing for Comparative Microbial Genomics. Computational Biology*. Vol. 8. pp. 137–150. doi:10.1007/978-1-84800-255-5\_8. ISBN 978-1-84800-254-8. ^ De Bustos A, Cuadrado A, Jouve N (November 2016). "Sequencing of long stretches of repetitive DNA". *Scientific Reports*. **6** (1): 36665. doi:10.1038/srep36665. PMC 5098217. PMID 27819354. ^ Slotkin RK (1 May 2018). "The case for not masking away repetitive DNA". *Mobile DNA*. **9** (1): 15. doi:10.1186/s13100-018-0120-9. PMC 5930866. PMID 29743957. External links Function of Repetitive DNA DNA+Repetitious+Region at the US National Library of Medicine Medical Subject Headings (MeSH) Retrieved from " When the Human Genome Project announced that they had completed the first human genome in 2003, it was a momentous accomplishment - for the first time, the DNA blueprint of human life was unlocked. But it came with a catch - they weren't actually able to put together all the genetic information in the genome. There were gaps: unfilled, often repetitive regions that were too confusing to piece together. With advancements in technology that could handle these repetitive sequences, scientists finally filled those gaps in May 2021, and the first end-to-end human genome was officially published on Mar. 31, 2022. I am a genome biologist who studies repetitive DNA sequences and how they shape genomes throughout evolutionary history. I was part of the team that helped characterize the repeat sequences missing from the genome. And now, with a truly complete human genome, these uncovered repetitive regions are finally being explored in full for the first time. German botanist Hans Winkler coined the word "genome" in 1920, combining the word "gene" with the suffix "-ome," meaning "complete set," to describe the full DNA sequence contained within each cell. Researchers still use this word a century later to refer to the genetic material that makes up an organism. One way to describe what a genome looks like is to compare it to a reference book. In this analogy, a genome is an anthology containing the DNA instructions for life. It's composed of a vast array of nucleotides (letters) that are packaged into chromosomes (chapters). Each chromosome contains genes (paragraphs) that are regions of DNA which code for the specific proteins that allow an organism to function. Genetic material is made of DNA tightly packaged into chromosomes. Only select regions of the DNA in a genome contain genes coding for proteins. VectorMine/iStock via Getty Images Plus While every living organism has a genome, the size of that genome varies from species to species. An elephant uses the same form of genetic information as the grass it eats and the bacteria in its gut. But no two genomes look exactly alike. Some are short, like the genome of the insect-dwelling bacteria *Nasuia deltocephalinicola* with just 137 genes across 112,000 nucleotides. Some, like the 149 billion nucleotides of the flowering plant *Paris japonica*, are so long that it's difficult to get a sense of how many genes are contained within. But genes as they've traditionally been understood – as stretches of DNA that code for proteins – are just a small part of an organism's genome. In fact, they make up less than 2% of human DNA. The human genome contains roughly 3 billion nucleotides and just under 20,000 protein-coding genes - an estimated 1% of the genome's total length. The remaining 99% is non-coding DNA sequences that don't produce proteins. Some are regulatory components that work as a switchboard to control how other genes work. Others are pseudogenes, or genomic relics that have lost their ability to function. And over half of the human genome is repetitive, with multiple copies of near-identical sequences. What is repetitive DNA? The simplest form of repetitive DNA are blocks of DNA repeated over and over in tandem called satellites. While how much satellite DNA a given genome has varies from person to person, they often cluster toward the ends of chromosomes in regions called telomeres. These regions protect chromosomes from degrading during DNA replication. They're also found in the centromeres of chromosomes, a region that helps keep genetic information intact when cells divide. Researchers still lack a clear understanding of all the functions of satellite DNA. But because satellite DNA forms unique patterns in each person, forensic biologists and genealogists use this genomic "fingerprint" to match crime scene samples and track ancestry. Over 50 genetic disorders are linked to variations in satellite DNA, including Huntington's disease. Satellite DNA tends to cluster toward the ends of chromosomes in their telomeres. Here, 46 human chromosomes are colored blue, with white telomeres. NIH Image Gallery/flickr, CC BY-NC Another abundant type of repetitive DNA are transposable elements, or sequences that can move around the genome. Some scientists have described them as selfish DNA because they can insert themselves anywhere in the genome, regardless of the consequences. As the human genome evolved, many transposable sequences collected mutations repressing their ability to move to avoid harmful interruptions. But some can likely still move about. For example, transposable element insertions are linked to a number of cases of hemophilia A, a genetic bleeding disorder. Transposable DNA may be the reason why humans have a tailbone but no tail. But transposable elements aren't just disruptive. They can have regulatory functions that help control the expression of other DNA sequences. When they're concentrated in centromeres, they may also help maintain the integrity of the genes fundamental to cell survival. They can also contribute to evolution. Researchers recently found that the insertion of a transposable element into a gene important to development might be why some primates, including humans, no longer have tails. Chromosome rearrangements due to transposable elements are even linked to the genesis of new species like the gibbons of southeast Asia and the wallabies of Australia. Completing the genomic puzzle Until recently, many of these complex regions could be compared to the far side of the moon: known to exist, but unseen. When the Human Genome Project first launched in 1990, technological limitations made it impossible to fully uncover repetitive regions in the genome. Available sequencing technology could only read about 500 nucleotides at a time, and these short fragments had to overlap one another in order to recreate the full sequence. Researchers used these overlapping segments to identify the next nucleotides in the sequence, incrementally extending the genome assembly one fragment at a time. These repetitive gap regions were like putting together a 1,000-piece puzzle of an overcast sky: When every piece looks the same, how do you know where one cloud starts and another ends? With near-identical overlapping stretches in many spots, fully sequencing the genome by piecemeal became unfeasible. Millions of nucleotides remained hidden in the the first iteration of the human genome. Since then, sequence patches have gradually filled in gaps of the human genome bit by bit. And in 2021, the Telomere-to-Telomere (T2T) Consortium, an international consortium of scientists working to complete a human genome assembly from end to end, announced that all remaining gaps were finally filled. With the completion of the first human genome, researchers are now looking toward capturing the full diversity of humanity. This was made possible by improved sequencing technology capable of reading longer sequences thousands of nucleotides in length. With more information to situate repetitive sequences within a larger picture, it became easier to identify their proper place in the genome. Like simplifying a 1,000-piece puzzle to a 100-piece puzzle, long-read sequences made it possible to assemble large repetitive regions for the first time. With the increasing power of long-read DNA sequencing technology, geneticists are positioned to explore a new era of genomics, untangling complex repetitive sequences across populations and species for the first time. And a complete, gap-free human genome provides an invaluable resource for researchers to investigate repetitive regions that shape genetic structure and variation, species evolution and human health. But one complete genome doesn't capture it all. Efforts continue to create diverse genomic references that fully represent the human population and life on Earth. With more complete, "telomere-to-telomere" genome references, scientists' understanding of the repetitive dark matter of DNA will become more clear. [Get fascinating science, health and technology news. Sign up for The Conversation's weekly science newsletter.]





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