APPLICATIONS

Copy Number Variation

For years, single nucleotide polymorphisms (SNPs) were thought to be responsible for the majority of human variation. Until recently, larger scale changes (1,000+ nucleotides in length), known as copy number variants (CNV), were thought to be relatively rare. However, scientists have discovered that CNVs occur much more frequently than was suspected. These structural changes alter the number of copies of a specific DNA segment.

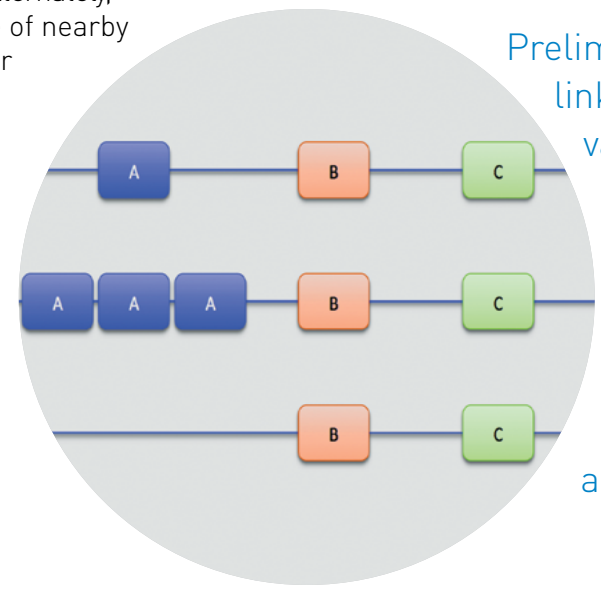
It came as a surprise to many scientists just how much DNA variation is due to copy number changes. Previous studies based primarily on SNPs suggested that any two randomly selected human genomes would differ by 0.1%. CNVs revise that estimate: the two genomes differ by at least 1.0%. While this may not seem like a major increase, remember that the human genome is composed of approximately three billion nucleotides, so the estimated number of nucleotides that vary between two random individuals has increased from three million to 30 million. Humans are still nearly 99% identical at the DNA sequence level, but the CNV research has broadened our understanding of how and where we differ.

It has been suggested that CNV regions influence gene activity by directly increasing or decreasing the number of copies of that gene, leading to a concurrent change in the amount of protein. Alternately, CNVs may alter the performance of nearby regulatory signals that activate or silence genes without directly impacting the copy number of the gene itself.

Relating genetic variation to human disease and inheritance is identified in the Biology COS in standard 3 and 12a. Genetic variation is also highlighted under standard 3b, which explores the ongoing impacts from the Human Genome Project and subsequent large-scale research projects. The impact of copy number variation intersects AP Biology in Enduring Understanding 3.B with discussions of gene regulation. Career/Tech Intro to Biotechnology should include discussion of copy number variation (COS objective 8).

Scientists are just beginning to understand the impact of structural genomic variation on plant, animal and human phenotypes. HudsonAlpha has created Aluminum Tolerant Corn™ an activity designed to introduce students to genome analysis and copy number variation. Students analyze a section of the corn genome, using the bioinformatics website DNA Subway (developed by the DNA Learning Center). Students use NCBI's BLAST program to identify and explore the genes that are located within this region. Throughout the process, students link an aluminum-tolerant growth phenotype to structural variants that alter the copy number of key genes. This kit is currently undergoing pilot testing. For more information, contact **edoutreach@hudsonalpha.org.**

Preliminary studies have linked CNVs to lupus, Crohn's disease, autism spectrum disorders, Alzheimer disease, HIV-1/AIDS susceptibility, rheumatoid arthritis and Parkinson disease. In some cases the associated CNV is rare, but in other diseases, the identified risk variant is quite common. It is also likely that CNVs may influence individual drug response and susceptibility to infection or cancer.



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