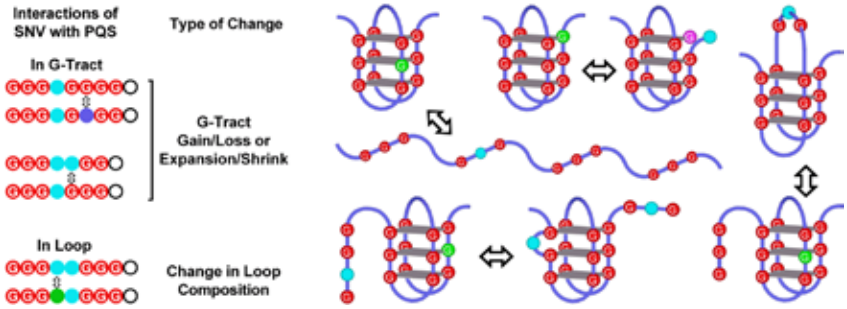
Researchers Unravel Genome-wide Variations in the Secondary Structure of Human Genomic DNA

Everyone's genome varies. Among the variations, single nucleotide variation (SNV) represents a difference in a single nucleotide in the human genome. As the most studied genetic variations, SNVs are associated with some important traits of an individual, such as susceptibility to disease, drug response and medical outcome, and other health-related phenotypes.



Potential G-quadruplex structure changes that can be induced by single nucleotide variations (SNVs). (Image by Dr. TAN Zheng's Lab)

Former studies of SNVs have mostly focused on the consequence of the change in an individual nucleotide along with the "central dogma". For example, a swap of a single nucleotide within a gene's coding region may allow an alternative amino acid to be introduced into the final protein, which may malfunction the protein.

A recent study, led by Dr. TAN Zheng from the CAS Institute of Zoology, reveals that SNVs in the human genome interact with DNA motifs that can form into four-stranded secondary structures called G-quadruplexes. By doing so, they result in millions of potential changes in the secondary structures of human genomic DNA. Most of these changes are within genes, preferentially enriched near transcription start sites, implying their roles in gene regulation. As suspected, they found that these SNVs-caused changes in the secondary structure of the genomic DNA can indeed alter the activity of host genes where they dwell.

"Genomic DNA provides a blueprint for all metabolic activities of a cell. The new findings made on the genome-wide structural variation in the human genomes provide an important addition to the mechanisms of how an SNV would influence the function of DNA. They will help us understand genetic variation and physiological consequences from a structural perspective. The structural variations should also represent a unique class of drug targets for individualized medicine, health assessment, and drug development," says Dr. TAN Zheng, one of the corresponding authors of this study.

This study, entitled "G-quadruplex structural variations in human genome associated with single-nucleotide variations and their impact on gene activity," appeared in the journal of *Proceedings of the National Academy of Sciences* on May 18, 2021.

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Reference

J. Y. Gong, C. J. Wen, M. L. Tang, R. F. Duan, J. N. Chen, J. Y. Zhang, . . . Z. Tan, (2021) G-quadruplex structural variations in human genome associated with single-nucleotide variations and their impact on gene activity. *Proc Natl Acad Sci U S A* 118. doi: 10.1073/pnas.2013230118.