Novel mutational process targeting gene regulatory elements discovered

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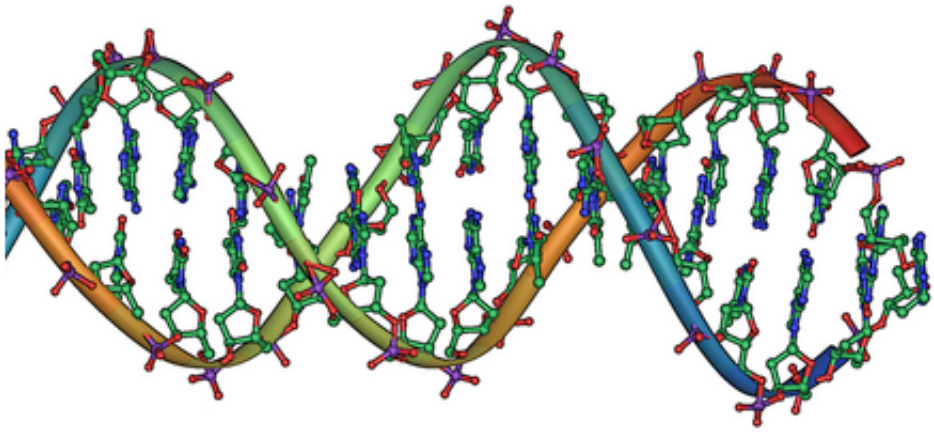

DNA double helix. Credit: public domain

Researchers at University of Helsinki, Finland, and Karolinska Institutet, Sweden, discovered previously uncharacterized mutational patterns in the human regulatory genome, especially in gastrointestinal tract cancers.

The research, published in *Nature Genetics* and led by Academy Professor Lauri Aaltonen, University of Helsinki, and Professor Jussi Taipale, Karolinska Institutet, was based on study of more than two hundred whole genomes of colorectal cancer samples. The scientists

detected a distinct accumulation of mutations specifically at sites where the proteins CTCF and cohesin bind the DNA.

Both CTCF and cohesin are transcription factors carrying out essential functions in the genome, including regulation of gene expression and chromatin structure. In hypermutated tumors, the CTCF/cohesin sites appear to be protected from mutations while in a distinct set of tumors, CTCF/cohesin sites are mutated with frequency higher than previously known protein coding cancer genes. Tumors with high CTCF site mutation load tend to have greater frequency of certain type of mutations distributed throughout their genome. The process producing these mutations is not fully understood and needs further investigation.

Until now the mutational patterns of the regulatory genome are poorly characterized. Unraveling the underlying mechanisms of regulatory mutations in cancer remains a great challenge. The novel findings from this study are significant and an important step towards understanding the cause and consequences of cancer-associated mutations.

"The findings of this study were totally unexpected; they uncover the second face of the cancer genome. However, we have a lot of work to do for understanding about the reasons and consequences of these changes", Professor Aaltonen states.

The result is totally unexpected; the control areas that have been found in the study are as often as subjects of genetic mutations like the actual known cancer genes. The finding is extremely significant and the work uncovers the second face of the cancer genome on the researchers, however, - is still enough in the understanding of the reasons and consequences for the changes, Aaltonen says

More information: CTCF/cohesin-binding sites are frequently mutated in cancer, DOI: 10.1038/ng.3335

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