Looking at the role epigenetics plays in the ways cancer behaves

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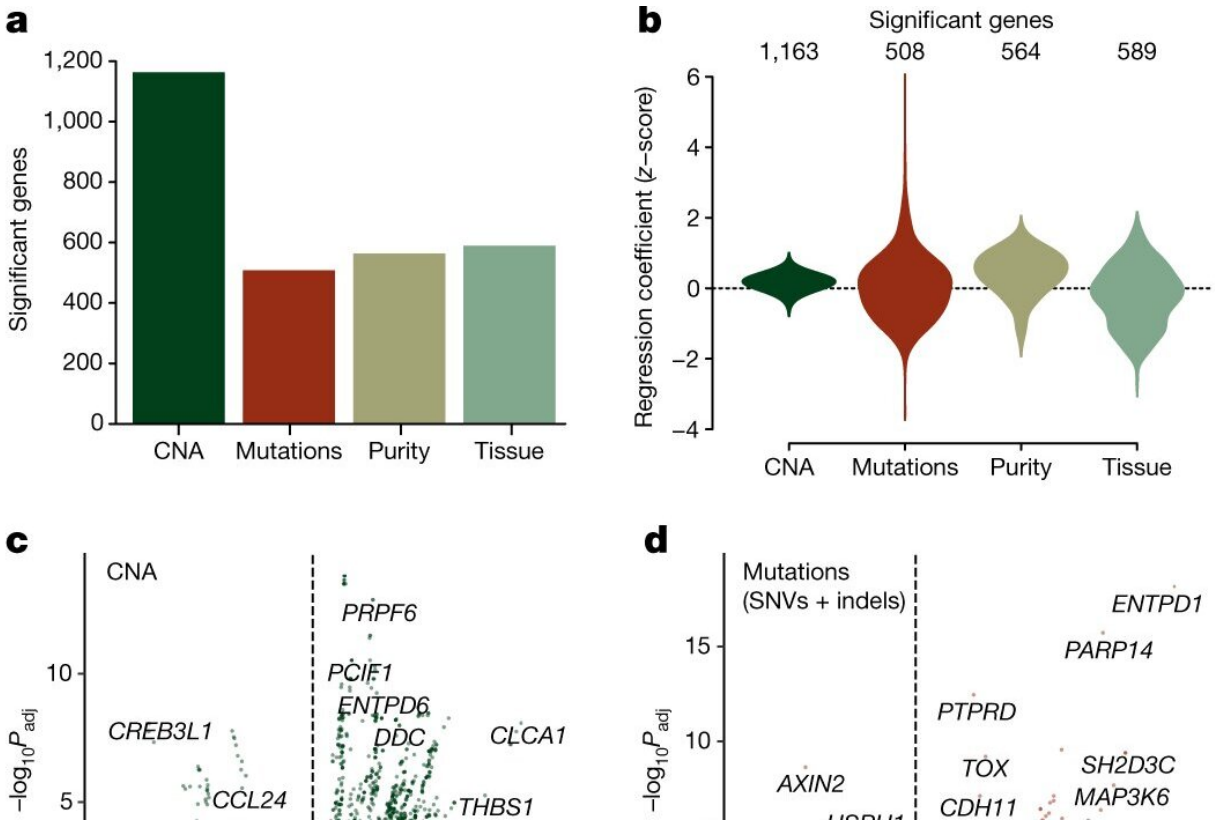

Genetic control of expression with eQTL. a, The number of genes with significant models for each data type. b, Distribution of regression coefficients (effect sizes) for each data type. c,d, Volcano plots highlighting selected genes significant for SCNA (c) and Mut eQTLs (d) (linear regression two-sided t-tests; P_{adj}, FDR-adjusted P values). e, In comparison with non-synonymous mutations (NS), enhancer (Enh) mutations tended to have large effect sizes and a higher proportion of positive effect sizes. f, The proportion of subclonal mutations associated with detectable changes in cis gene expression was significantly lower

than for clonal eQTL mutations. g, Visualization of Fisher's exact tests showing that gene–mutation combinations were more likely to be eQTLs if they were associated with recurrent phylogenetic genes (genes found to have evidence of phylogenetic signal in at least three tumors) for subclonal mutations, and that this was not significant for clonal mutations. Phylo and Non-phylo indicate whether a gene had evidence of phylogenetic signal in the tumor in which the mutation was present. Two-sided Fisher's exact tests, P values not corrected for multiple testing. Credit: *Nature* (2022). DOI: 10.1038/s41586-022-05311-x

Two teams of researchers working independently from one another have conducted studies to learn more about the role that epigenetics plays in the behavior of cancerous tumors. The first group, a team at the Institute of Cancer Research in the U.K., working with colleagues from several other institutions in the U.K. analyzed thousands of samples of bowel cancers from different patients looking for instances of epigenetic changes.

The second team, with members from around the globe, focused on multiple samples taken from the same tumor—they also looked for changes due to epigenetics. Both teams have published papers outlining their work in the journal *Nature*.

For many years, medical scientists have believed that most, if not all, cancers develop due to mutations in DNA, leading to abnormal tissue growth in the form of tumors. In more recent years, researchers have found evidence showing that not all cancers have a simple genetic origin. Instead, evidence has shown that some have an epigenetic factor. Through epigenetics, age or environment exert an influence on the way that DNA code in cancer cells is expressed. In this new effort, both teams looked to better understand the role of epigenetics in the development and progression of cancerous tumors.

In the first study, the researchers collected and studied tissue from various types of bowel cancer collected from 30 different patients. In all, they looked at 1,370 samples. Each was subjected to both whole-transcript RNA-seq and whole genome sequencing. They were able to track down which tumors were purely DNA based and which were not. They found that only 166 of them could be traced to underlying genetics.

In the second study, the researchers used spatially resolved, paired whole-genome and transcriptome sequencing on multiple tissue samples taken from the same tumor. They found evidence showing that the majority of variations they identified could not be blamed on underlying genetics.

Both teams acknowledge that their work did not prove that epigenetics leads directly to changes in the behavior of cancers, but both found evidence that suggests that is the case. They also both note that much more work is required to better understand the role that epigenetics plays in cancer development and progression.

More information: Jacob Househam et al, Phenotypic plasticity and genetic control in colorectal cancer evolution, *Nature* (2022). DOI: 10.1038/s41586-022-05311-x

Timon Heide et al, The co-evolution of the genome and epigenome in colorectal cancer, *Nature* (2022). DOI: 10.1038/s41586-022-05202-1