New classification system for tumors can guide diagnosis and treatment options for cancer

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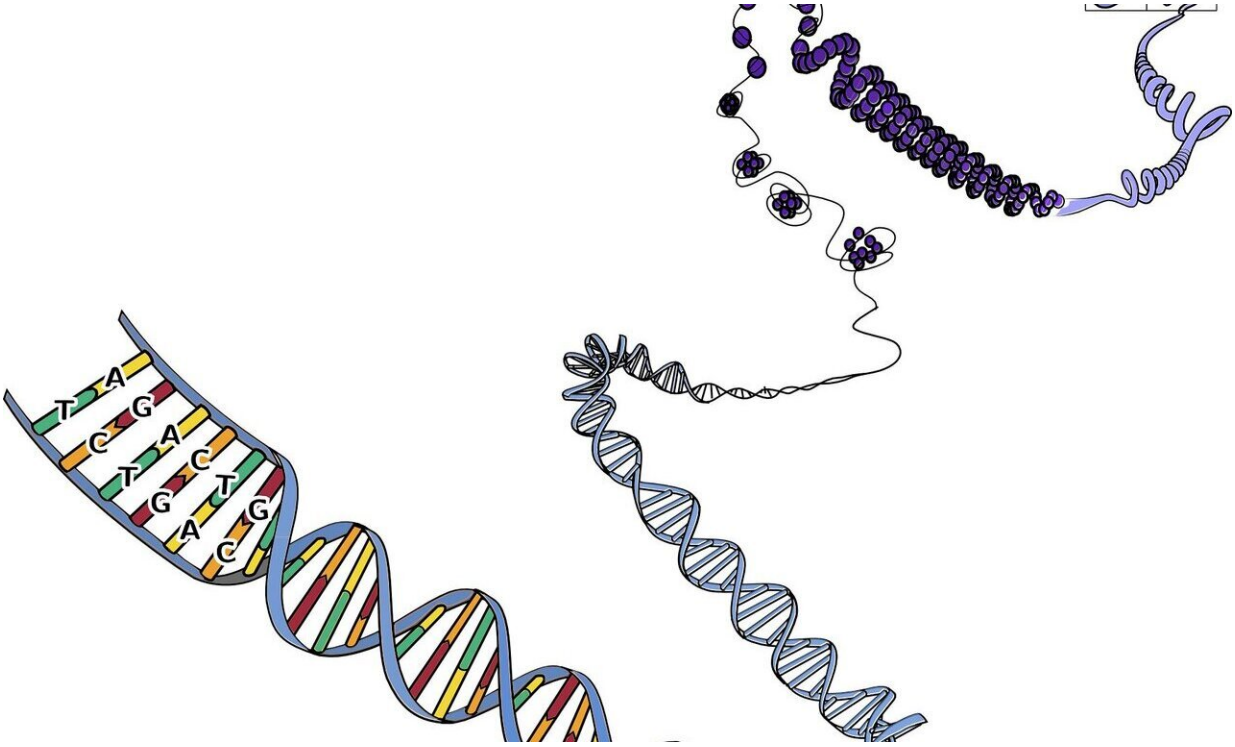

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Based on the largest study of cancer patients of its kind, scientists have created a new way of classifying tumours. Clinicians can use genome sequencing to assign their patients' tumours to one of sixteen groups in

the new classification system, ten of which provide important information for the diagnosis and treatment of the disease, like whether an individual will respond to immunotherapy.

Researchers at the Centre Nacional d'Anàlisi Genòmica, part of the Centre for Genomic Regulation in Barcelona, analysed the mutations found in 2,583 patients with 37 different types of cancer. They detected a total of 45 million mutations across all tumours, of which at least 1.2 million were non-unique mutations, meaning they were found in the same location for two or more cancer patients. With six billion potential sites in human DNA that can be mutated, the number of non-unique mutations is far higher than what's expected by chance alone. On average, 4% of the mutations in a tumour could also be found in one or more of the other tumours across the entire set of patients.

Further analyses showed these non-unique mutations were more likely to be found in certain types of primary tumours like skin cancer, oesophageal cancer and lymphoma. This suggests that causative agents of these cancers, such as UV light exposure or gastric reflux, damage DNA in a more predictable way than by chance alone. On the other end of the spectrum, researchers found very few non-unique mutations in lung cancer, liver cancer and kidney cancer, suggesting DNA damage by, for example, tobacco smoke exposure occurs more randomly compared to other groups.

Based on the number and type of non-unique mutations, researchers were able to classify the 2,583 primary tumours into one of sixteen groups, each of which have independent characteristics. Ten of these groups are clinically relevant, with the potential to help doctors make a more accurate diagnosis and select a more effective treatment course. For example, the number and type of non-unique mutations that define one group are linked to tumours unable to correct specific type of damage to their genetic code, resulting in their DNA becoming unstable.

These patients are likely to respond well to immunotherapy, which would in turn allow abstaining from conventional chemotherapy and its side effects.

"Cancer is a complex disease that requires a bespoke course of action to diagnose, manage and treat effectively," says Ivo Gut, senior author of the study. "Currently doctors look for individual mutations at specific locations in DNA, which has a limited view. Using whole genome sequencing provides a complete overview of the number of mutations in a tumour, allowing doctors to classify the cancer type and gain deeper understanding of disease, which can have important implications for the way they treat their patients."

The findings also highlight other benefits for whole genome sequencing. "In a small percentage of patients, the origin of the cancer is unknown and the biopsy taken turns out to be from a metastasis instead of the primary tumour," says Miranda Stobbe, lead author of the study. "If conventional analyses conclude that it is a metastatic tumour, but they cannot determine its origin, doctors will have to start scanning the rest of the patient to try to find the primary source. In some cases, the primary may already be gone, because of the response of the immune system, or the primary is too small to be detected. Our classification would get around that by assigning the tumour to one of 16 groups, providing important information on where the tumour originates from."

The study is published in *PLOS Computational Biology*.

More information: Miranda D. Stobbe et al, Recurrent somatic mutations reveal new insights into consequences of mutagenic processes in cancer, *PLOS Computational Biology* (2019). DOI: 10.1371/journal.pcbi.1007496

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