Genomic analysis of thousands of tumors supports new cancer classification

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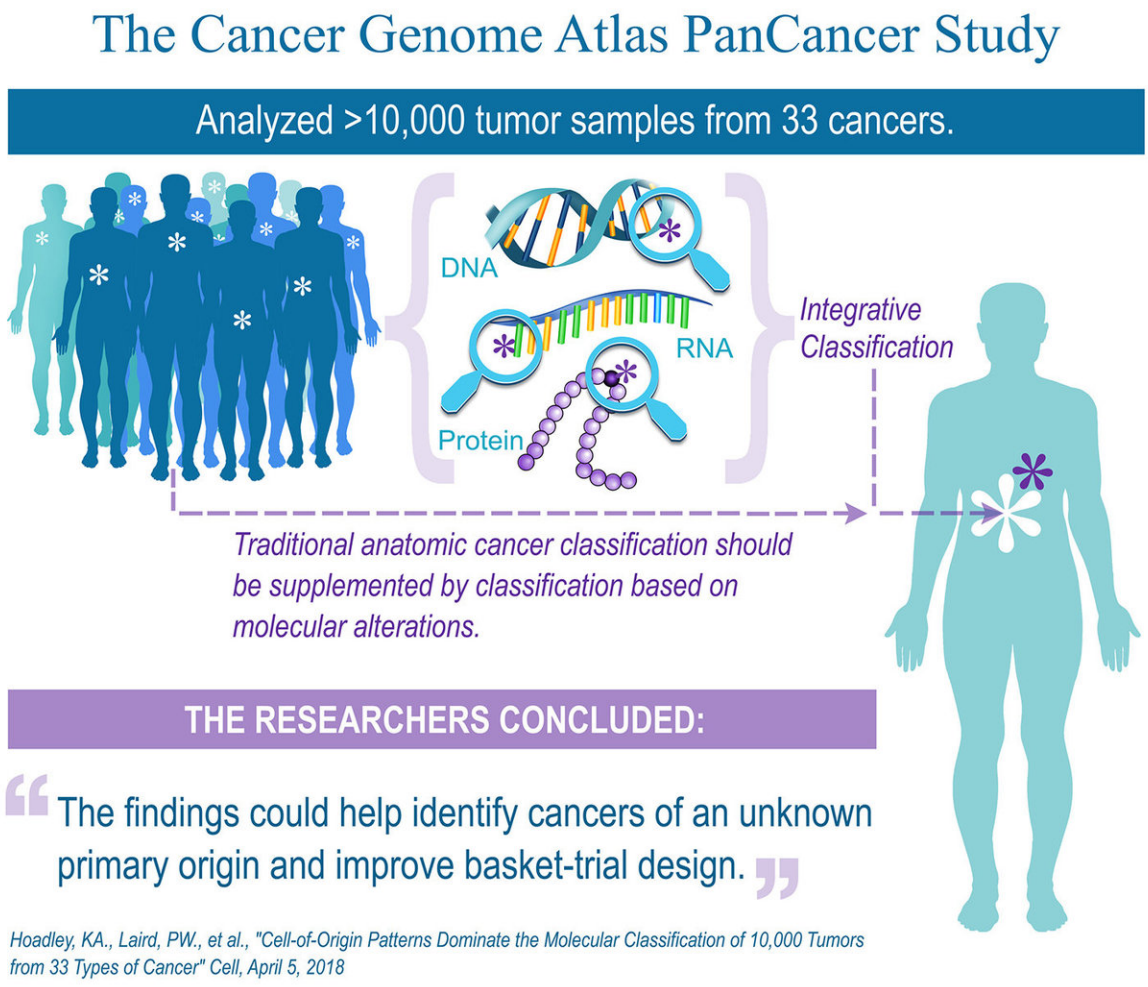

Researchers analyzed more than 10,000 tumor samples from 33 cancers to reveal a new molecular classification system. Credit: Hoadley, KA., Laird, PW., et al., "Cell-of-Origin Patterns Dominate the Molecular Classification of 10,000

Tumors from 33 Types of Cancer" *Cell*, April 5, 2018.

University of North Carolina Lineberger Comprehensive Cancer Center researchers are reporting the concluding findings from a major analysis of nearly 10,000 different tumor samples that focused on identifying similarities between cancers based on changes in their genes, and the way their genes are expressed. The study by researchers from The Cancer Genome Atlas (TCGA) Network, the largest of its kind to-date, supports an additional classification for human tumors.

Researchers determined more than a decade ago that cancer is not a single disease, but many, and different cancer subtypes can even occur within a single anatomic location, such as the breast, liver or colon. The new study, published in the journal *Cell*, shows that some cancers are very similar to others that originated from the same starting cell type - although these may have originated in a different organ.

"Tumor location has been the primary method for determining treatment for a given cancer patient," said UNC Lineberger's Katherine Hoadley, PhD, assistant professor in the UNC School of Medicine Department of Genetics, and the paper's first and co-corresponding author. "This study helps us get a better understanding of the relationship across and within different tumor types. If tumors are genetically diverse within an organ, we should rethink the way we treat them."

Led by the National Institutes of Health and the National Human Genome Research Institute, TCGA was launched to identify and develop a comprehensive understanding of genomic changes in cancer with the goal of improving cancer prevention, diagnosis and treatment. The effort tapped the expertise of approximately 150 different scientists at more than two dozen institutions across the United States and the world.

The project is now coming to a close.

As part of one of the final studies, Hoadley and a team of researchers analyzed genetic, epigenetic and proteomic changes in 33 different cancer types. They discovered that some cancers grouped together based on the cell type from which the tumor came from. For example, squamous cell cancers from the head and neck, lung, and bladder, cervix, and esophagus had strong molecular similarities and grouped together. Some types were defined by their anatomic location. Other cancers from the same organ system, such as gastric, colon and rectal cancers, also shared molecular similarities. Some organ sites had a broad diversity in molecular subtypes, such as the kidney.

"This new molecular-based classification system should greatly help in the clinic, where it is already explaining some of the similar clinical behavior of what we thought were different tumor types," said UNC Lineberger's Charles Perou, PhD, the May Goldman Shaw Distinguished Professor in Molecular Oncology, a professor of genetics, pathology and laboratory medicine, and another UNC Lineberger co-author on this paper. "These findings also provide many new therapeutic opportunities, which can and will be tested in the next phase of human clinical trials."

Hoadley said the findings have multiple implications. They demonstrated there can be many molecular alterations that occur in a cancer that contribute to its abnormal growth - ranging from repeats of genes, also known as copy number amplifications, or changes in the way genes are expressed. The findings could help researchers to identify cancers of an unknown primary origin. It could also have implications for treating cancers across tumor types.

"TCGA has created a catalogue of alterations that occur in a variety of cancer types," Hoadley said. "Having this catalogue of alterations is really important for us to look in future studies at why these alterations

are there, and to predict outcomes for patients."

Provided by UNC Lineberger Comprehensive Cancer Center