Cancer Health™

Tracing Tumor Evolution From a Single Cell

Understanding the evolutionary path that tumors follow is essential for designing effective clinical interventions.

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Like living species, cancer cell populations undergo evolution. They accumulate mutations and become heterogeneous, and the mutations that increase chances of survival become more common. In this way, a single genetic alteration can evolve into a tumor and eventually spread throughout the body. Understanding the evolutionary path that tumors follow, from a single-cell mutation to metastatic cancer, is essential for designing effective clinical interventions. However, environmental factors and other variables can confound efforts to trace a cancer's development from beginning to end.

But this month, Damon Runyon-Dale F. Frey Breakthrough Scientist Dian Yang, PhD, and colleagues at the Whitehead Institute for Biomedical Research unveiled a genetically engineered mouse model of lung cancer that they used to reconstruct the lifespan of a tumor at "unprecedented scale and resolution." The team used the gene editing tool CRISPR to induce Kras and Trp53 mutations in mouse lung cells and then employed a single-cell RNA-sequencing tool to monitor the ripple effect of those genetic changes as the cancer cell population grew from single-cell mutation to metastasis.

The researchers found that, once they induced the mutation, the lung cell population rapidly became heterogeneous, as seen in the adjacent illustration. This was due to an increase in cell plasticity, or the ability of cells to change their properties by turning genes "on" or "off" in response to environmental cues. Eventually, the cells best suited for survival and reproduction overtook the cell population in what is known as a "clonal sweep." From there, tumors developed and metastasized through predictable pathways; the researchers were able to identify the role of several genes and transcription factors along these paths.

With this model, Dr. Yang and his colleagues have provided the first report of the evolutionary history of a tumor from a single irregular cell to an aggressive cancer. Not only have they identified key steps in the development of lung cancer, but they have also shown that such attempts at tracing can be successful, paving the way for future models of other cancers and ultimately new therapeutic strategies.

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