Earlier Detection of Lung Cancer

Scientists develop a platform to study early-stage lung cancer and to identify potential new treatments.

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Lung cancer is often missed in its earlier stages and, as a result, is the leading cause of cancer deaths in the United States. To tackle this issue, Damon Runyon Fellow Aaron L. Moye, PhD, and colleagues at Harvard Medical School and Boston Children's Hospital have developed a platform to study early-stage lung cancer and to identify potential new treatments. They used lung cells to create organoids, or tiny, three-dimensional tissue cultures that replicate the complexity of the human lung. Inside the organoids, the researchers observed normal cells becoming cancerous over the course of seven days, a transformation that can take months to see in mice and years in patients.

Tracking the transformation

The researchers created four parallel models of adenocarcinoma, a common, hard-to-treat lung cancer, to track the molecular changes that occur from tumor onset to its advanced stages. They compared tumor samples from patients with early (stage 1A) lung cancer, genetically engineered mouse models, and lung organoids derived from either mouse lung stem cells or lung cells created from human induced pluripotent stem cells.

To initiate cancer in the organoid models, the researchers introduced the KRAS mutation into the precursors of the alveolar cells. They then used single-cell RNA sequencing to see which genes were turned on, or expressed, as a result. These studies revealed reduced expression of genes that are markers of mature lung alveolar cells and increased expression of genes involved in early lung development—known markers of cancer progression.

The samples from lung cancer patients confirmed that the organoids mimicked what happens in patients at the early stages of tumor progression. Understanding this process may lead to new therapeutic approaches to treat early-stage lung cancer, which currently has no targeted drugs.

Though this study looked at KRAS-driven lung cancer, the researchers believe that the organoid approach could facilitate the study of other kinds of cancer, including testing of candidate drugs.

Read more: As it unfolds

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