New genetic mutations found for non-Hodgkin lymphoma

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Scientists at the BC Cancer Agency in British Columbia, Canada and their U.S. collaborators have identified a number of new genetic mutations involved in non-Hodgkin lymphoma, or NHL.

This massive cancer-sequencing study, published online in the journal Nature, will open a floodgate for researchers around the world to explore the significant number of newly discovered gene mutations and their role in the growth and development of lymphoma cells.

The work was performed at the BC Cancer Agency Genome Sciences Centre, which has received major support from several governmental and private sources, including the U.S. National Institutes of Health in Bethesda, Md.

In an extensive undertaking, researchers sequenced the entire genome of lymphoma cancer cells from 14 NHL patient samples and the "active" genes from 117 NHL patients to search for genetic mutations specific to cancer cells.

Tumor samples were collected from British Columbia scientists as well as their U.S. collaborators, including the Arizona Lymphoma Repository housed at the University of Arizona's College of Medicine under the direction of Dr. Lisa Rimsza, a professor of pathology and Arizona Cancer Center member.

The magnitude of data revealed 109 genes with recurring mutations, from which 26 have been identified as contributors to NHL based on their mutation patterns. More than two-thirds of mutated genes had never been linked to lymphoma prior to this study.

Understanding tumors' genetic signatures "tells us what makes the tumors tick and what might be their vulnerable spots to aim for with treatment. This information should provide better diagnoses, more accurate prognostic information and help to identify unique targets of therapy for each tumor type, therefore advancing personalized medicine for our patients," Rimsza said.

"Based on the patterns of mutation in these 26 genes, we can see that these mutations enable tumor cells to grow and expand in non-Hodgkin lymphoma patients," said Ryan Morin, the study's lead author. "The mutated genes we've discovered, most of which were previously unknown to lymphoma or other cancers, should enable us to design new tests that allow us to recognize subtypes of lymphoma and may help us predict how each variation of this disease will react to different treatments."

Non-Hodgkin lymphoma is the fifth most common form of cancer in Canada, and the fourth most common cause of cancer in the U.S.

"This new abundance of genetic information is thrilling. Researchers and clinicians can now collaborate to eventually create new drugs, or identify existing drugs, that inhibit these mutated genes directly and prevent the growth of non-Hodgkin lymphoma," said Dr. Joseph Connors, a medical oncologist and distinguished scientist at the BC Cancer Agency and a clinical professor of medical oncology at the University of British Columbia.

The pattern of mutation observed in some of these genes is indicative of new tumor suppressors and oncogenes, the latter of which may be ideal targets for existing therapies.

Specifically, one of the novel lymphoma-related genes discovered in this study, MLL2, is mutated in 89 percent of Follicular lymphoma patients, suggesting it is the most commonly mutated gene in NHL. Mutation of MLL2, which appears to be a tumor suppressor, is suspected to provide cancer cells with the ability to grow rapidly in-spite of the body's regulatory mechanisms.

A second novel gene discovery, MEF2B, bears a so-called "hot spot" mutation pattern reminiscent of other known cancer genes.

Provided by University of Arizona