Genomic Marker Is Associated with Lynch Syndrome, a Hereditary Cancer Condition, Across Many Different Cancers

By Julie Grisham, **Saturday, June 2, 2018**

Zsofia Stadler says MSK has a “unique opportunity” to make connections to inherited genetic conditions that would otherwise be difficult to make. © ASCO/Brian Powers 2018.

Summary

MSK researchers have found that tumors with a particular genetic marker are likely to be associated with Lynch syndrome.

Memorial Sloan Kettering researchers have found that the genetic condition **Lynch syndrome** may be associated with more cancers than earlier thought. Lynch syndrome runs in families. It was previously known to increase the risk mainly of **colon cancer**, **rectal cancer**, and **endometrial (uterine) cancer**. The MSK team has now linked Lynch syndrome to cancers that are rarely or not already associated with the syndrome. These include **pancreatic cancer**, **prostate cancer**, **adrenocortical tumor**, **sarcoma**, and many others. Results of the study were reported today at the annual meeting of the American Society of Clinical Oncology (ASCO).

The study looked at people with advanced cancer whose tumors carried a genomic biomarker called high microsatellite instability (MSI). The data showed that these patients had a one in six chance of having Lynch syndrome — regardless of what type of cancer they had. Lynch syndrome is currently believed to occur in about 1 in 300 people in the general population.

The findings have wide-ranging implications. They suggest that people whose tumors demonstrate high MSI should be tested for Lynch syndrome mutations. Those who are found to have Lynch can undergo more frequent screening for certain cancers. Family members can also be tested to see if they have the condition.

"Our findings suggest that anyone with an advanced solid tumor who is found to have high MSI should be tested for Lynch mutations, regardless of the location of the tumor or family cancer history," says medical oncologist and clinical geneticist **Zsofia Stadler**, who led the study. The research was presented at the ASCO meeting by medical genetics fellow Alicia Latham Schwark.

"We expect that genetic testing of all people with high-MSI tumors will help identify additional individuals and families with Lynch syndrome," Dr. Stadler adds.

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Zsofia K. Stadler
medical oncologist and clinical geneticist

Expanding Tumor Testing

The study focused on more than 15,000 people with many different types of cancer who were tested at MSK for MSI in their tumors. MSI is a genetic defect that occurs in about 5% of advanced cancers. It leads to the accumulation of hundreds or even thousands of mutations in a single tumor. In the past, testing for this biomarker has been limited. But thanks to the **US Food and Drug Administration's approval of pembrolizumab** (Keytruda®) in May 2017 for any cancer that has a high level of MSI, many more people are now having their tumors analyzed for this defect.

In addition to tests for MSI, the people included in the study also had genomic testing with **MSK-IMPACT™**. This tool looks for mutations in 468 cancer-associated mutations in tumors as well as a number of cancer-linked hereditary mutations found in normal tissues. These inherited mutations include those linked to Lynch syndrome.

"At MSK, because we sequence the tumors of so many people, we have a unique opportunity to make these kinds of discoveries," says Dr. Stadler, who is clinic director of MSK's **Clinical Genetics Service** and a member of the **Robert and Kate Niehaus Center for Inherited Cancer Genomics**. "This kind of research helps people with cancer and, in this case, also helps us provide predictive genetic testing for at-risk family members, who may then benefit from increased cancer surveillance and cancer prevention measures."

A Cancer Syndrome That Runs in Families

Lynch syndrome is an inherited condition caused by a mutation in one of five genes known as mismatch repair (MMR) genes. When one of the MMR genes is mutated, cells are unable to repair errors that can occur when they divide — resulting in MSI.

Lynch syndrome has been known about for decades, but in the past, it has been largely associated with just a few cancers. MSK's Clinical Genetics Service offers testing for Lynch syndrome to people who have multiple relatives with related cancers. However, the findings from this study suggest that many cases of Lynch syndrome could be going undetected.

Genetic Testing & Counseling at Memorial Sloan Kettering

Memorial Sloan Kettering's Clinical Genetics Service offers hereditary cancer risk assessment, genetic counseling, and genetic testing by specially trained genetic counselors and physicians.

Learn more

Consequences for Future Research, and for Families

Knowing whether a cancer is due to Lynch syndrome has important implications for families. Lynch mutations are autosomal dominant, which means a person with Lynch has a 50% chance of passing it down to a child. MSK's genetic counselors recommend that when someone is found to have Lynch syndrome, their parents, siblings, and children get tested too.

Experts also recommend more frequent screening for certain cancers if a Lynch-associated mutation is found. In particular, people with Lynch mutations should get regular colonoscopies to look for colon and rectal cancer.

Focusing on families with inherited cancer genes is a major part of the **Precision Interception and Prevention (PIP) initiative**. This MSK effort concentrates not only on catching cancer very early but also on preventing it from developing in the first place.

PIP is led by **Luis Diaz**, Head of MSK's Division of Solid Tumor Oncology, and MSK Physician-in-Chief José Baselga. It was created to take advantage of all of the findings coming out of MSK-IMPACT.

"Dr. Baselga's initiative of genomic analysis of a very large number of patients through MSK-IMPACT has been instrumental to this project," Dr. Stadler concludes. "This test has been vital in making sure that people get the best treatments for their cancer and enabled us to do these kinds of important studies that can ultimately benefit whole families."

This research was funded in part through the Romeo Milio Lynch Syndrome Foundation, the Marie-Josée and Henry R. Kravis Center for Molecular Oncology, the Robert and Kate Niehaus Center for Inherited Cancer Genomics, the Fieldstone Family Fund, and a Stand Up To Cancer (SU2C) Colorectal Cancer Dream Team Translational Research Grant (number SU2C-AACR-DT22-17). Stand Up To Cancer is a program of the Entertainment Industry Foundation. Research grants are administered by the American Association for Cancer Research, a scientific partner of SU2C, and the National Institutes of Health and National Cancer Institute Cancer Center Support Grant P30 CA008748.

Comments

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Choya Davis

Jun 3, 2018 • 9:18 AM
I have Lynch Syndrome and I had my stomach removed in January because of stomach cancer.I am screened once a year for colon cancer and esophagus and stomach cancers thanks for all your people do to make others be aware of the dangers in these diseases.

Jennifer Gude

Jun 3, 2018 • 1:41 PM