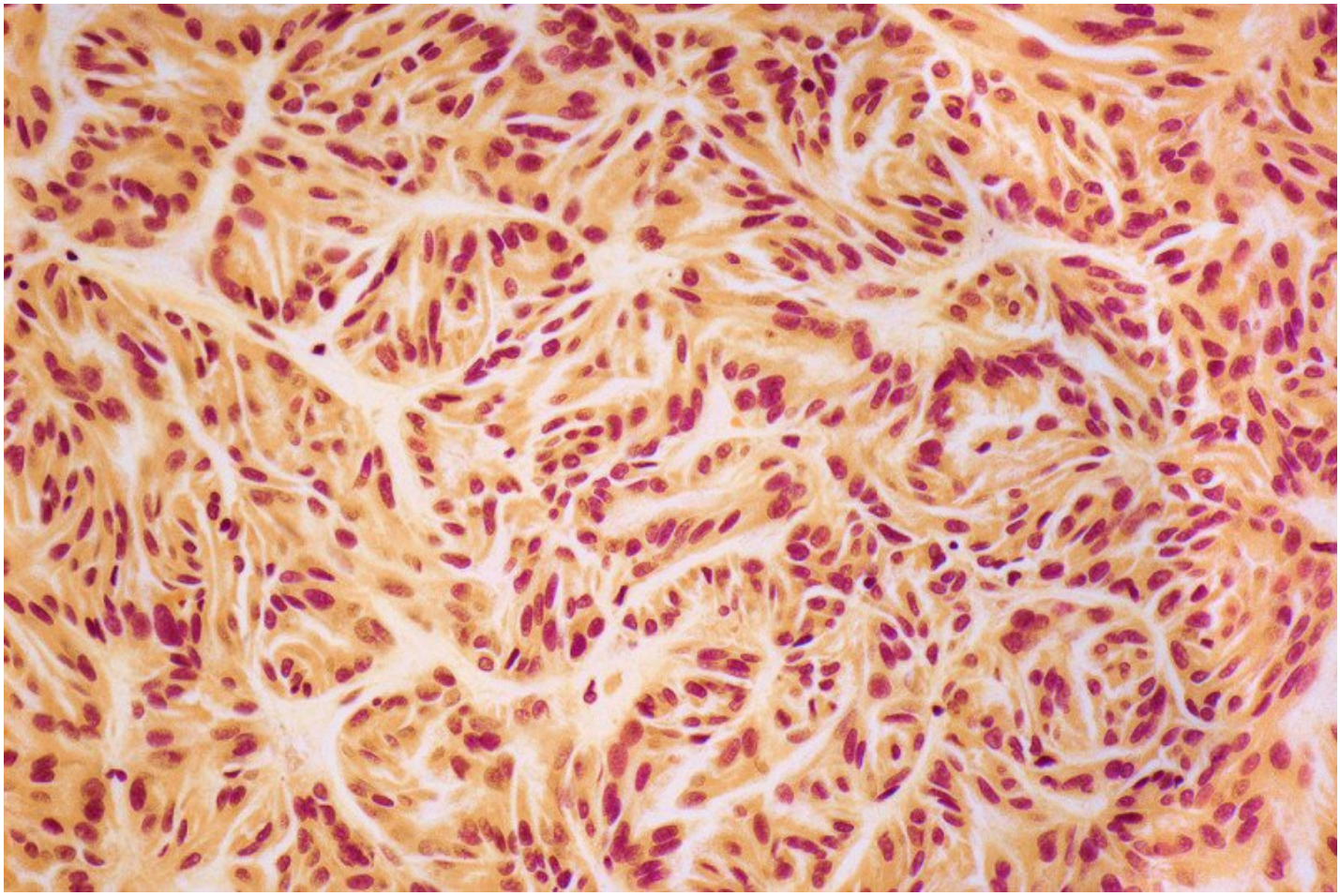
Study Suggests More People with Kidney Cancer Should Be Screened for Hereditary Cancer Genes

By Julie Grisham, **Thursday, September 6, 2018**



Papillary renal cell carcinoma is one of several types of non-clear cell kidney cancer. Source: Steve Gschmeissner/Science Source

Summary

> Research conducted at MSK has shown that more than 20% of people with a type of kidney cancer called advanced non-clear cell renal cell carcinoma have disease that is driven by inherited cancer mutations. This number is much higher than expected.

Kidney cancer, also called renal cell carcinoma (RCC), is a relatively common cancer. It's diagnosed in nearly 65,000 people in the United States every year. Yet despite its frequency, very little is known about what causes it, beyond two broad factors linked to many common cancers: smoking and obesity.

That's now starting to change for one advanced form of the disease, called non-clear cell RCC. Recent research from a collaborative team at Memorial Sloan Kettering found that more than 20% of people with this type of RCC have disease that is driven by inherited cancer mutations. Many of the types of mutations that were found indicated that the tumors might respond to targeted therapies that would not otherwise be prescribed for kidney cancer.

"These findings suggest that everyone with advanced non-clear cell RCC should be referred for genetic counseling," says medical oncologist **Robert Motzer**, one of the authors of the **study**, published in July in *JAMA Oncology.* "Beyond a rare inherited condition called von Hippel-Lindau syndrome, as well as a few other uncommon disorders, we haven't previously known that kidney cancer had this strong hereditary component."

> Non-clear cell RCC is a catch-all term that applies to several types of kidney cancer.

Non-clear cell RCC makes up about one-quarter of RCC cases. For clear cell RCC, the more common type, the study found that only about 2% of tumors were caused by inherited cancer genes. Before this study, the rate for all kidney cancers was expected to be about 5%.

A Surprising Finding about a Diverse Group of Cancers

Over the past decade, a number of targeted drugs and immunotherapies have changed the outlook for many people with clear cell RCC. Dr. Motzer and his team have **led many of the clinical trials** that have resulted in US Food and Drug

Administration approval for these drugs, including sunitinib (Sutent®), sorafenib (Nexavar®), axitinib (Inlyta®), and **nivolumab** (Opdivo®). Thanks to these new drugs, even people with advanced kidney cancer can live for many years, often with very few side effects from their treatments.

Non-clear cell RCC has been a different story. Many of the drugs approved to treat clear cell RCC do not have the same efficacy against non-clear cell tumors. "Non-clear cell" is a catch-all term that applies to several types of cancer including papillary, chromophobe, and collecting-duct tumors.

In this current research, investigators looked at 254 people who had been treated for advanced RCC at MSK. Each person had undergone **MSK-IMPACT**™ testing to look for mutations in their cancer. As part of this test, both normal tissue and tumor cells are analyzed. This enables doctors to detect cancer-related mutations that someone may have inherited.

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Robert J. Motzer
medical oncologist

Unexpectedly, about 20% of people with non-clear cell RCC carried inherited mutations. The study found the most frequently inherited mutation in people with non-clear cell RCC was in a gene called *CHEK2.* Mutations in this gene have previously been connected to an increased risk of breast and colon cancer, but the link to RCC was not known. The researchers found mutations in other cancer-linked genes not previously known to play a role in kidney cancer as well.

The team also found several people with non-clear cell RCC who had inherited mutations in a gene called *FH*. Mutations in *FH* have already been linked to a condition called hereditary leiomyomatosis and renal cell cancer. But they were more common than what would have been expected in a group of people with RCC.

"Once we know that someone has one of these hereditary gene mutations, we can help make sure they get the right treatment," says **Maria Carlo**, a clinical geneticist

and medical oncologist on the Genitourinary Service and first author of the study. "In addition, we can offer them screening tests for other cancers that may be linked to the same mutation."

Discoveries Lead to Changes in the Clinic

At the American Society of Clinical Oncology (ASCO) meeting in June, Dr. Carlo presented **similar findings** from people being treated for advanced bladder cancer at MSK. About 16% were found to have inherited mutations. Some of these mutations suggested that they might benefit from targeted therapies that are not usually given for bladder cancer.

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Learning that someone has an inherited cancer gene has important implications for his or her close relatives as well. MSK's genetic counselors are able to offer them genetic tests. If any of them are found to have the same mutation, they can participate in screening programs for cancer as well.

In fact, due in large part to the findings reported in the *JAMA Oncology* and ASCO studies, Dr. Carlo is now leading a Genitourinary Cancer Genetics Program within MSK's **Clinical Genetics Service**. The program offers genetic testing and screening services to people with hereditary prostate, kidney, and bladder cancers and their families.

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Comments