

Targeting Lynch Syndrome to Reduce Colorectal Cancer Risk

Swati Patel, MD, points to exciting developments, including vaccines and clinical trials, to help people with Lynch syndrome avoid cancer.

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[New research](#) into Lynch syndrome — a genetic mutation that can increase the risk of several cancers, including [colorectal cancer](#) — is leading to treatments and clinical trials that can help people with the diagnosis reduce their cancer risk.

“Lynch syndrome is the most common inherited genetic predisposition to colorectal cancer,” says [University of Colorado Anschutz Cancer Center](#) member [Swati Patel](#), MD, a leading Lynch syndrome researcher. “About 10% of all colon cancer patients have some genetic or hereditary predisposition that drove them to develop that cancer, and Lynch syndrome is the most common of these genetic syndromes. The good news is that if you have that genetic diagnosis and know about it, we have effective ways to reduce colon cancer risk.”

Some of those strategies are intuitive, Patel says — including encouraging people with Lynch syndrome to avoid cancer-causing habits like smoking and excessive drinking and scheduling them for colonoscopies at an early age and higher frequency. But some are more surprising, including prescribing aspirin, which has been found to reduce the long-term risk of colon cancer by 50% in patients with Lynch syndrome.

“The big landmark study had patients on aspirin for two years, and starting at five years, their risk of colon cancer began to decrease. Following those patients out to 20 years, their risk was reduced by 50%,” Patel says. “In the general population, it’s the same effect, but it’s much more protracted. Patients have to take aspirin for at least five years, but they don’t see a benefit until 20 years down the line. Because aspirin has short-term risks including stomach ulcers and thinning of the blood, we don’t recommend it as a cancer prevention method in the general population.”

Testing a cancer vaccine

Because Lynch syndrome tumor cells tend to exhibit abnormal proteins, they are often able to be treated with targeted therapy that is aimed at those proteins, boosting a patient’s immune system to help destroy them. Because those proteins are also found in precancerous cells in patients with

Lynch syndrome, Patel and other researchers are now testing the efficacy of a vaccine shot for people with Lynch syndrome that targets suspect cells before they have the opportunity to become cancerous.

“A vaccine is much safer and easier to distribute than something like immunotherapy,” Patel says. “The CU Anschutz Cancer Center is part of a phase II trial to test a vaccine in Lynch syndrome patients. We completed accrual in 2025, and now we’re in the follow-up phase.”

In this phase, researchers will follow patients for two years to see if they develop any colorectal polyps following the vaccine. The study is randomized so that some patients receive a placebo, and it takes place in the Clinical Translational Research Center of the [Colorado Clinical and Translational Sciences Institute \(CCTSI\)](#).

“It’s a gamechanger to think about leveraging the immune system to fight cancer in patients that are susceptible to these tumors in a precancer state, targeting things that the immune system already recognizes as foreign,” Patel says.

Solving the mysteries of Lynch syndrome

As researchers learn more about Lynch syndrome and how to detect the genetic changes that cause it, they are discovering something else: Not everyone with Lynch syndrome develops cancer.

“What we want to know is, what is it that turns on risk? What is it that protects families from risk?” Patel says. “We are leading a huge North American effort at the University of Colorado to prospectively observe individuals with Lynch syndrome to understand their long-term outcomes.”

Known as the Lynch syndrome INtegrative Epidemiology And GENetics (LINEAGE) consortium and taking place at 35 sites in the U.S. and Canada, the study looks at factors including how patients were diagnosed, their medical risk factors and other medical conditions, including immunocompromised and immunosuppressed patients, and lifestyle information such as stress levels and habits.

“We also will take tissue samples and blood samples to start to develop biological signatures of risk,” Patel says. “Why is it that this Lynch family has multiple people with cancer, but the same mutation in a different family, there’s no cancer? Are there differences we can identify? There are a lot of unanswered questions about risk and appropriate management, and unless we pool large amounts of data, it’s hard to answer those in a nuanced way.”

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