Study provides clearer picture of cancer risk

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(Medical Xpress)—A University of Vermont researcher has helped to develop a more accurate way of studying genetic changes to identify people at high risk for colon and other cancers. The findings are published in *Nature Genetics*.

Marc Greenblatt, M.D., an associate professor of medicine and oncologist at the University of Vermont (UVM) and Fletcher Allen Health Care, and faculty member at the Vermont Cancer Center's Familial Cancer Program, co-led a collaborative global effort to interpret genetic data related to hereditary colon cancer. The team's findings will both allow doctors to access publicly-available data to more effectively interpret risks and give patients a more accurate picture of familial risk for colon and other cancers.

The identification of a high-risk mutation in a cancer patient guides the clinical management of that patient and their family, including considerations for counselling, treatment options, surgery and other risk-reducing interventions. Lynch Syndrome is an inherited condition that greatly increases the risk for colon, uterine and other cancers. It is responsible for three to five percent of all colon cancers. For patients who are suspected of genetic variations that cause Lynch Syndrome, genetic test results have been difficult to interpret, therefore limiting the ability of these patients and their families to manage cancer risks.

Greenblatt and his international collaborators focused on genetic variation in four genes that are responsible for Lynch Syndrome. Genetic testing to look for harmful mutations is frequently done. However, when

genetic changes are found, about one quarter of them are difficult to interpret. Individuals presenting with these genetic variations have traditionally been told they have "variants of uncertain significance" – the results are inconclusive and cannot be used to help guide patient care or predict risk for family members.

The team of researchers, working through the International Society for Gastrointestinal Hereditary Cancers (InSiGHT), pooled the knowledge and collective data of more than 45 researchers and clinicians across the world, each with a specific type of expertise in the area of Lynch Syndrome. Together, they developed a new model of classifying genetic changes, "in many cases turning indecipherable sequencing data into real knowledge that can have a clinical benefit," says Greenblatt.

"As a result of this work," he adds, "doctors can more conclusively say whether those patients have Lynch Syndrome, and focus prevention efforts on the family members who are at a high risk of getting cancer. We may also ease the worry of some people who've had inconclusive results that turn out not to be dangerous. This team approach can also serve as a model for research efforts in the future on other genetic conditions."

More information: "Application of a 5-tiered scheme for standardized classification of 2,360 unique mismatch repair gene variants in the InSiGHT locus-specific database." Bryony A Thompson, Amanda B Spurdle, John-Paul Plazzer, Marc S Greenblatt, Kiwamu Akagi, et al. *Nature Genetics* (2013) DOI: 10.1038/ng.2854. Received 19 September 2013 Accepted 26 November 2013 Published online 22 December 2013

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