

# Multi-institutional study identifies new form of inherited risk of cancer

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Like the subtext of a novel, the human genome sequence harbors more information than appears just in its "letters" of A, C, T and G. Since DNA is a data-packed molecule passed from generation to generation, comparing genome sequences among individuals also holds clues to ancestry.

So-called association studies that match unusual DNA sequence variations to diseases are very common nowadays. But a multi-institution group led by Dr. Francis Barany, professor of microbiology and immunology at Weill Cornell Medical College, has instead zeroed in on parts of the genome that are strikingly similar among people from a particular population group who have the same type of cancer.

This "autozygosity" (identical copies of DNA inherited from both parents) might serve not only as a way to predict susceptibility to cancer in some people, but may lead researchers to novel cancer-causing genes. More broadly, the work suggests a new type of genetic signpost that clinicians might follow for a range of cancers, in many population groups.

In a paper "The Signatures of Autozygosity Among Patients with Colorectal Cancer," to be published online on March 28, and in print on April 15, in the journal *Cancer Research*, Dr. Barany and his colleagues report Identity by Descent (IBD) segments that are the same in sequence (autozygous) among individuals who have colorectal cancer. About half the cases are of Jewish heritage. The simplest explanation for their IBD

segments is that they were inherited from a long-ago, shared ancestor. The investigators compared IBD regions among 74 colorectal cancer patients to two control groups, and found the segments to be twice as numerous and longer among the cancer patients.

Tellingly, the identical DNA stretches were more common among Jewish cancer patients. Scientifically, the power of this new approach derives from the common practice wherein individuals marry within the same ethnic or social background, known as "endogamy." (This custom carries no social stigma; on the contrary, it is a source of pride in most cultures.) Since the other half of patients with IBD are of Catholic or Protestant heritage, the results of such an analysis pertain to all populations. The IBD regions reveal where researchers should look for novel genes, which contribute to the overall risk for this cancer.

Colorectal cancer results in more than 52,000 deaths each year in the United States, with more than 153,000 new cases diagnosed. About a third of cases run in families, and some of them are caused by a handful of well-studied genes. The genetic underpinnings of most of the more than a million cases of colorectal cancer worldwide are not known. This new approach of following IBD regions may clear up some of that mystery -- and ultimately, many others.

Source: New York- Presbyterian Hospital

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