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Inherited cancer mutation is widespread in America

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A gene mutation responsible for the most common form of inherited colon cancer is older and more common than formerly believed, according to a recent study.

The findings provide a better understanding of the spread and prevalence of the American Founder Mutation, a common cause in North America of Lynch syndrome, a hereditary cancer syndrome that greatly increases a person's risk for developing cancers of the colon, uterus and ovaries.

The same investigators discovered the mutation in 2003. That research identified nine families with the mutation and concluded that a German immigrant couple brought the mutation to North America in 1727.

The latest study includes an additional 32 families and indicates that the mutation is actually about 500 years old, suggesting that it arose several generations earlier in Europeans or perhaps in Native Americans.

Of the 41 families overall, most are clustered in Kentucky, Ohio and Texas.

Scientists at the Ohio State University Comprehensive Cancer Center and Creighton University conducted the study, published recently in the journal *Cancer Research*.

"The increased age of the American Founder Mutation means that it is significantly more prevalent in the United States than previously

thought," says principal investigator Albert de la Chapelle, a researcher with Ohio State's Human Cancer Genetics program.

"Of interest is that this mutation has not been found in Europe, which is tentative evidence, along with hints from family histories, that it may have arisen in a Native American."

The new study estimates that the mutation is present in 32,150 Americans as compared with the earlier figure of 18,981. "But these numbers are theoretical and need to be substantiated by further work," de la Chapelle notes.

"This is an important public health concern," de la Chapelle says, "because individuals with a Lynch syndrome mutation can benefit from earlier and more frequent cancer surveillance."

In addition, he says, a simple, cheap genetic test can detect the mutation.

Lynch syndrome, also known as hereditary nonpolyposis colon cancer, is responsible for about one third of hereditary colon cancers, and almost 3 percent of colon cancer generally, or about 4,500 cases annually in the United States.

The initial study of nine families showed that the American Founder Mutation results in the loss of a very specific piece of a gene called MSH2 (although many other mutations also cause Lynch syndrome).

The new study linked 27 of the 41 families into seven groups through genealogic studies.

The age of the mutation was estimated using certain markers along the DNA located at either end of the mutation. Such patterns of markers are called haplotypes.

When a new person was identified for the study, the DNA on each side of the individual's mutation was tested for the markers, producing a shared haplotype. The shorter the shared haplotype, the older the mutation. This information led to the estimated age of 500 years.

"This data pushed the original founder mutation back to around 1500, plus or minus a number of years," says coauthor Heather Hampel, a genetics counselor and researcher with Ohio State's Human Cancer Genetics Program.

"The Pilgrims began arriving in the 1600s, so the mutation could have arisen first in very early settlers from Europe, or in Native Americans."

"It's unclear whether we'll ever learn who the first person was to have this mutation," Hampel says, "but it is clear that the mutation is much older than we thought and probably more widespread. For that reason, we feel it is potentially a serious public health issue, particularly in states such as Kentucky, Ohio and Texas where it is very prevalent."

Source: Ohio State University