Genetic copy-number variants and cancer risk

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Genetics clearly plays a role in cancer development and progression, but the reason that a certain mutation leads to one cancer and not another is less clear. Furthermore, no links have been found between any cancer and a type of genetic change called "copy-number variants," or CNVs. Now, a new study published by Cell Press in *The American Journal of Human Genetics* on August 2 identifies CNVs associated with testicular cancer risk, but not with the risk of breast or colon cancer.

Some cancers, including breast and colon cancer, are caused by mutations that are passed from one generation to the next. However, most cancers, including testicular cancer, are sporadic-they arise without a family history of cancer. Many of these sporadic cancers result from genetic mutations in germ cells-the cells involved in reproduction-even though neither parent has the mutation. Scientists call these "de novo" mutations.

In order to identify rare de novo mutations associated with cancer risk, Dr. Kenneth Offit and colleagues searched for CNVs, which are duplications or deletions of one or more sections of DNA, in cancer patients and their cancer-free relatives. They found a significant increase in the number of rare de novo CNVs in individuals with testicular cancer as opposed to breast or colon cancer. Although such CNVs have been associated with autism and other neurocognitive and cardiovascular disorders, they were not previously known to be associated with cancer.

The authors propose that de novo changes (as opposed to those inherited

from parents) might be indicative of conditions that have traditionally resulted in reduced fertility. Although modern treatment regimens allow more than 90% of men with testicular cancer to live long and reproductive lives, the condition traditionally left affected men childless. "We speculate that the paradigm of a de novo germline disease etiology may be less applicable to late-onset cancers," says Offit, "in part explaining the lower frequency of de novo events we found in adult-onset breast and colon cancer cases." Pinpointing the specific genetic changes that lead to cancer development will improve the understanding of the origins of cancer, leading to new treatment strategies and ultimately easing the burden on those afflicted with these diseases.

More information: Stadler et al.: "Rare De Novo Germline Copy-Number Variation in Testicular Cancer." *American Journal of Human Genetics* - August 10, 2012 print issue print issue

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