Scientists discover novel mechanism that increases colorectal cancer risk

June 29 2009

Finnish Academy Professors Lauri Aaltonen and Jussi Taipale have identified and described a mechanism whereby a single-base change in the human genome increases the risk of colorectal cancer.

The focus in this study was on a common single-base variant occurring in chromosome 8, which in itself causes only a slightly increased risk of cancer. However, the risk allele is carried by 75% of people of European origin and by almost 100% of African populations.

The high frequency of the gene variant makes it a very common cause of cancer at the population level. At the individual level, however, the variant does not cause significant disease predisposition because that can often be considerably reduced by lifestyle changes. Colorectal cancer is the third most common cancer worldwide and a major cause of cancer mortality.

Mutation mechanisms activate pathways regulating cancer

The variant that increases the risk of colorectal cancer was found to be located in a regulatory region, where it changes the function of a key regulatory element important for the development of colorectal cancer. The scientists showed that the risk allele strengthens the binding of a regulatory factor in cancer cells, which activates pathways that are central to the development of cancer. The impacts of this altered genetic

regulation on cell division are probably mediated via the MYC cancer gene, which is one of the best known accelerator genes in cancer.

Single-base changes are the most common type of variation found in the human genome. Genome-wide studies of interindividual differences in common variants can be studied using DNA chip technology, which has greatly facilitated efforts to understand the genetic basis of multifactorial diseases. To date, scientists have identified more than 400 variants in the human genome that are associated with an increased risk of common diseases, such as cancer, diabetes and cardiovascular diseases.

Multidisciplinary research

The findings of this research lend support to the theory that human disease susceptibility is explained in part by differences in regulatory regions of the genome, and in gene expression. A closer understanding of the biological mechanisms involved will help to clarify the aetiology of colorectal cancer and pave the way to more effective cancer prevention.
Apart from hereditary tumor predisposition, another area of major strength for Finnish research is gene regulation. It was hardly surprising therefore that Aaltonen's and Taipale's research teams found each other so easily. The research project supervised by Aaltonen and Taipale involved molecular biologists, medical doctors and data processing researchers from Finland and the UK. For instance, the project made use of the EEL software developed by Professor Esko Ukkonen and his team at the CoE for Algorithmic Data Analysis.

More information: The results of the study will be published in the prestigious journal *Nature Genetics*. DOI 10.1038/ng.406

Source: Academy of Finland