Scientists find genes associated with throat cancer through study of over 10,000 subjects

EurekAlert

Scientists from Singapore, China and USA have identified three new susceptibility genes in a genome-wide association study of nasopharyngeal carcinoma (NPC). The study, led by the Genome Institute of Singapore (GIS), a biomedical research institute of the Agency for Science, Technology and Research (A*STAR), and the Sun Yat-Sen University Cancer Centre, identified genetic risk factors of NPC that advance the understanding of the important role played by host genetic variation in influencing the susceptibility to this cancer.

NPC is a type of cancer that forms in the epithelial lining of the nasopharynx, the area of the upper throat that lies behind the nose. It is particularly prevalent in southern China, such as Guangdong, with an occurrence rate of about 25 times higher than that in most regions of the world. NPC is therefore referred to as the Cantonese Cancer (Cantonese is a Chinese dialect spoken in and around the city of Guangzhou in Southern China). Led by Dr Liu Jianjun, Associate Director and Senior Group Leader of Human Genetics at the GIS, and Professor Yi-Xin Zeng, President of the Sun Yat-sen University Cancer Center, the findings were published in *Nature Genetics* on May 30, 2010.

To search for the genetic risk factors for NPC, the scientists carried out a comprehensive genetic analysis of the human genome in a large clinical sample of southern Chinese descent - approximately 5,000 patients and 5,000 controls. The researchers found that the genetic variation within the human leukocyte antigen (HLA) [1] and the three genes known as TNFRSF19, MDSIEVI1 and CDKN2A/2B can significantly influence a person's risk of developing NPC. The researchers also noticed that these three susceptibility genes for NPC have been reported to be involved in the development of leukemia, suggesting there might be some shared biological mechanism between the developments of these two diseases. This finding provides an important opportunity for biologists to understand the molecular mechanism underlying the development of this cancer, and its unusual pattern of high prevalence in southern China.

Co-lead author Dr Liu Jianjun said, "Although many groups have attempted to identify the genetic risk factors of NPC, the findings of previous studies were limited by the small number of genes and clinical samples used. Because of this large-scale study of approximately 10,000 subjects in total, we are able to break through with more robust evidence compared to previous studies."

Co-lead author Prof Zeng added, "This finding confirmed the strong genetic effect of HLA locus in the risk of NPC. By using the high density of genetic markers, our finding helps to narrow down the chromosome region to search for the causative gene variant(s) associated with HLA loci. The identification of susceptibility genes

involved in the risk of NPC will help to develop a model for risk prediction and then screen for high risk populations, which in turn will be helpful for early diagnosis of NPC."

Dr Malcolm Simons, Chief Scientific Officer of Simons Haplomics Limited who first discovered the association of HLA genes with NPC in Singapore in 1974, said, "This confirmatory study finalises the evidence produced over the past three decades from case-control and linkage studies of single NPC cases and of multiple case families that the HLA gene system is principally involved in risk for NPC development in Chinese. There is no longer a need to perform any more studies for evidence of the HLA association. The challenge is now to identify the location within or outside the HLA complex that underlies this genetic association or associations, and to determine whether the genetic change is required to be present on both of the pair of chromosomes (known as recessive homozygosity). The indication of three new genes contributing risk, albeit at a much lower level of significance than that of HLA, provides a focus for molecular biological analysis of these candidate risk genes".

SOURCE [1]

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