International Agency for Research on Cancer



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IARC study identifies new genetic factors linked to HPV-related cancers

Lyon, France, 17 October 2016 – A new large-scale genetic study of head and neck cancers shows why some individuals infected with human papillomavirus (HPV) may go on to develop oropharyngeal cancer while others do not. Head and neck cancers are a related group of cancers that involve the oral cavity, pharynx (oropharynx, nasopharynx, and hypopharynx), and larynx. The study, published today in *Nature Genetics*, identifies seven new genetic loci (locations of a gene on a chromosome): one that is linked to oropharyngeal cancer and six that are associated with oral cavity cancer, thus providing new insights into the development of these diseases.

The study, led by researchers from the International Agency for Research on Cancer (IARC) in partnership with 40 other research groups, compared about 6000 people with cancer of the oral cavity or pharynx (cases) with about 6000 people without the disease (controls). The researchers conducted extensive DNA analysis of more than 7 million variants for each individual.

The most prominent finding was an association between oropharyngeal cancer and genetic variation in the human leukocyte antigen (HLA) region, a genetic region important for regulation of the immune system.

One particular set of variants in the HLA region was associated with a more than 4-fold protective effect against developing oropharyngeal cancer associated with HPV infection. The same genetic variants have previously been shown to protect against cervical cancer, which is known to be associated with HPV infection.

"These results indicate that genes that control the immune system play a fundamental role in influencing whether an HPV infection goes on to develop into an HPV-related cancer," says study co-author Dr Paul Brennan, Head of IARC's Section of Genetics. "Understanding why this happens may help us to identify additional methods to protect against HPV-related cancers."

HPV-related cancers

The most significant causes of all head and neck cancers are tobacco use and alcohol consumption. These exposures account for the development of approximately 80% of such cancers globally, with some variation for different subsites (65% for the oral cavity vs 86% for the larynx).¹

However, oral infection with HPV, which is linked to sexual practices, and particularly with HPV type 16, is an increasingly important cause of oropharyngeal cancer,² especially in the USA and northern Europe.

¹ Stewart BW, Wild CP, editors (2014). World Cancer Report 2014. Lyon, France: International Agency for Research on Cancer. Available from: <u>http://publications.iarc.fr/Non-Series-Publications/World-Cancer-Reports/World-Cancer-Reports/World-Cancer-Report-2014</u>.

² Gillison ML, et al. (2015). Epidemiology of human papillomavirus–positive head and neck squamous cell carcinoma. *J Clin Oncol.* 33:3235–42.

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The proportion of HPV-related cases of oropharyngeal cancer varies widely and is estimated to be approximately 60% in the USA, 30% in Europe, and lower in South America.³

HPV is also well known for causing cervical cancer, which is the fourth most common cancer in women worldwide, with an estimated <u>528 000 new cases and 266 000 deaths in 2012</u>.⁴ HPV type 16 is also associated with cancers at a variety of other sites, including the <u>vulva</u>, <u>vagina</u>, <u>penis</u>, <u>anus</u>, <u>and</u> <u>oropharynx</u>.⁵

"There are many aspects of the development of head and neck cancers that we still don't understand," says IARC Director Dr Christopher Wild, "but these exciting results shed new light on genetic factors specifically linked to HPV-related cancers, which could play an important role in developing preventive strategies."

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The International Agency for Research on Cancer (IARC) is part of the World Health Organization. Its mission is to coordinate and conduct research on the causes of human cancer, the mechanisms of carcinogenesis, and to develop scientific strategies for cancer control. The Agency is involved in both epidemiological and laboratory research and disseminates scientific information through publications, meetings, courses, and fellowships. If you wish your name to be removed from our press release emailing list, please write to <u>com@iarc.fr</u>.

³ Chaturvedi AK, et al. (2011). Human papillomavirus and rising oropharyngeal cancer incidence in the United States. *J Clin Oncol.* 29:4294–301; Kreimer AR, et al. (2005). Human papillomavirus types in head and neck squamous cell carcinomas worldwide: a systematic review. *Cancer Epidemiol Biomarkers Prev.* 14:467–75; Ribeiro KB, et al. (2011). Low human papillomavirus prevalence in head and neck cancer: results from two large case–control studies in high-incidence regions. *Int J Epidemiol.* 40:489–502; Lopez RV, et al. (2014). Human papillomavirus (HPV) 16 and the prognosis of head and neck cancer in a geographical region with a low prevalence of HPV infection. *Cancer Causes Control.* 25:461–71.

⁴ Stewart BW, Wild CP, editors (2014).World Cancer Report 2014. Lyon, France: International Agency for Research on Cancer. Available from: <u>http://publications.iarc.fr/Non-Series-Publications/World-Cancer-Reports/World-Cancer-Report-2014</u>.

⁵ IARC (2012). Human papillomaviruses. In: Biological agents. *IARC Monogr Eval Carcinog Risks Hum*. 100B: 1–441. Available from: <u>http://monographs.iarc.fr/ENG/Monographs/vol100B/mono100B-11.pdf</u>.