

Review Summary
NTP Executive Committee Working Group for the Report on Carcinogens
(RG2)

Nomination: Human Papilloma Viruses (HPV)

Date: July 22, 2003

Major issues discussed

Application of criteria

Exposure: HPV is one of the most common sexually transmitted infections. In the US more than two million people per year develop HPV infections that result in cytologic abnormalities of the genital tract.

Human studies: In 1995, IARC classified HPVs 16 and 18 as *known human carcinogens*, HPV 31 and 33 as *probably carcinogenic to humans* and some other HPVs types other than 16, 18, 31 and 33 as *possibility carcinogenic to human*. At the time of the IARC review, there were few studies available on HPV types other than 16 and 18. Since the 1995 IARC review, there have been numerous case-control and cohort studies confirming a causal relationship for cervical cancer for HPV 16 and 18 and establishing a causal relationship for other HPVS of the genital-mucosal type such as 31, and 33, 35 45, 51, 52, 58 and 59.

Experimental animal studies: HPVs do not infect experimental animal; thus studies in experimental animals are limited to other animal papillomaviruses and transgenic mice studies expressing HPV genes. Studies in monkeys, cattle, rabbit and sheep have shown that animal papillomasviruses cause cancer in their natural hosts. Studies in transgenic mice have shown that mice expressing specific regions in HPV 16 or HPV 18 develop cervical and other types of cancer; some studies involved co-treatment with estrogen.

Genotoxicity and mechanistic concerns: HPV infection caused by some HPVs (such as HPV 16 and 18) is associated with genetic instability and chromosomal aberrations. Some HPVs can integrate into the host DNA, and immortalize and transform cells. HPV proteins, E6 and E7 appear to be important for HPV-associated neoplasia. HPV E6 interacts with p53, resulting in degradation of p53 and interference with apoptosis. HPV E7 disrupts pRB and related cell cycle proteins. Most mechanistic studies are on HPV 16 and HPV 18.

Recommendations

Motion 1:

Recommend that title of nomination should be “Some Human Papilloma Viruses, Genital Mucosa Type”.

Vote on the motion: 8 yes votes to 0 no votes.

Motion 2:

Recommend that some Human Papilloma Viruses, genital mucosa type be listed as *known to be human carcinogens* based on strong evidence from human studies that demonstrate a causal relationship between infection with Human Papilloma Viruses, genital mucosa type and cervical cancer.

Vote on the motion: 8 yes votes to 0 no votes.