



**Karolinska
Institutet**

Institutionen för Onkologi-Patologi

STUDIES ON HUMAN PAPILLOMAVIRUSES IN HEAD AND NECK CANCER

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentlig försvaras i
Föreläsningssalen, CancerCentrum Karolinska R8:00, Karolinska Universitetssjukhuset, Solna

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av

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Abstract

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide. The traditional risk factors for HNSCC are smoking and alcohol. However, recently IARC has also recognized human papillomaviruses (HPV) as an etiological factor for oropharyngeal cancer, a subset of head and neck cancers. Among oropharyngeal cancer, tonsillar and tongue base cancer dominate, both often associated with HPV. The aim of the present study was to examine the involvement of human papillomavirus (HPV) in two subtypes of HNSCC, tonsillar and hypopharyngeal cancer. For tonsillar cancer the purpose was to evaluate the prevalence of HPV over time and in relation to clinical outcome. In addition we wanted to evaluate if EGFR or phosphorylated EGFR were useful as markers, together with HPV, to predict response to treatment. For hypopharyngeal cancer, the aim was to analyze the prevalence of HPV and if HPV was a risk factor for this tumor type.

In the first paper, we found a 7-fold increase in the incidence of HPV positive tonsillar cancer, between 1970 and 2006, in the County of Stockholm, highlighting HPV as the causative factor for the increased incidence of this tumor type. In addition we found a decline in the incidence of HPV negative tonsillar cancer.

In the second paper, we found a high 5-year disease specific survival for HPV positive tonsillar cancer (81%), as compared to 36% for patients with HPV negative tonsillar cancer. HPV E6 and/or HPV E7 RNA were present in 94% of the samples analyzed, demonstrating the involvement of HPV in carcinogenesis.

In the third paper, we analyzed the presence of HPV in HNSCC from Greece and found that HPV is common in tonsillar carcinoma also from this country.

In the fourth paper, the presence of HPV and overexpression of p16 in hypopharyngeal cancer from patients in Stockholm, was evaluated. Only 6% were HPV positive, indicating that HPV is not an important risk factor for this disease.

In the fifth paper, overexpression of EGFR and presence of phosphorylated EGFR in tonsillar cancer, were evaluated in relation to tumor HPV status and clinical outcome. We found a correlation between the presence of phosphorylated EGFR and HPV, but not between phosphorylated EGFR and clinical outcome, when HPV positive and negative tumors were evaluated separately.

Our studies revealed HPV as a major factor behind the increased incidence of tonsillar cancer in the Stockholm area and an important prognostic factor for this disease, while HPV was not an important risk factor for hypopharyngeal cancer in this area.