Rise of HPV Associated Oropharyngeal Cancer, and Its Oncogenic Risks.

Human Papilloma Virus, also known as HPV, is one of the most common sexually transmitted diseases around the world and is consisted of around 120 different types. Among these 120 different HPVs, only 40 types spread through sexual contact but around 80 percent of oropharyngeal cancer is caused due to type 16 (HPV-16). Oropharyngeal cancer, which is the 6th highest incidence rate of cancer, occurs in the back of the tonsil or the pharynx because the tumors appear in the oral cavity, oropharynx, and larynx, hypopharynx, and sinonasal tract. In addition, HPV-associated oropharyngeal cancer would overtake HPV cervical cancers because of the rapid increase in the rate of people diagnosed with oropharyngeal cancer in the last ten years. The reason why I chose this topic is that I am also interested in oral health, which led me to study both oral cavity and cancer biology.

HPV is a non-enveloped DNA virus, which means that the virus only contains the genome (DNA) and virus-coded protein capsid that surrounds the genome. The genome includes 8 similarly structured oncoproteins: six early proteins, E1, E2, E4, E5, E6, E7, and two late proteins, L1 and L2. Among these 8 proteins, E5, E6, and E7 oncoproteins are known to be the main contributors to malignant transformation. And the oncogenic high risk in HPV-associated oropharyngeal cancer is due to the oncoproteins E6 and E7, which immortalize, alter the cell cycle, and control apoptosis of cells. Also, these oncoproteins become the reason for cancer by targeting the p53 and RB tumor suppressor genes, which are key to inhibiting cell proliferation and tumor development. To prevent any HPV-related cancer, the desired treatment for HPV is to get vaccinated at the age of 11 to 12 years old, before having sexual contact, and receive a total of two doses of 6 to 12 months apart.

As HPV enters the mouth, it will linger around the oropharyngeal area and then turn normal cells into tumor cells, which will lead to cancer. To complete this process, it first binds to the cell surface receptor, HSPG, a widely expressed and evolutionary conserved cell surface receptor, and the interaction results in the exposure of the secondary cell surface receptor, which sends signals received by HSPG to effector proteins. These effector proteins alter host cells to facilitate infection by a pathogen, which is HPV in this case. During this process, oncoproteins, E6 and E7, that are directly responsible for the development of HPV-induced carcinogenesis, are encoded and infect the basal cells of the epithelium. The viral life cycle is now dependent upon the keratinocytes, one of the most common skin cells, and because HPV does not have its replicative function, it depends on the cellular division of the epithelium, which allows to replicate and produce new viruses. In this process, oncoproteins E6 and E7 target p53 and RB tumor suppressor genes that are involved in the regulation of cell cycle control and apoptosis enabling the virus to maintain cell proliferation and allow viral genome amplification to occur. These activities can apply to several hallmarks of cancer especially evading growth suppressors, genome instability & mutation, and sustaining proliferative signaling.

Around 80% of adults (ages 18~59) are exposed to HPV but only a few of them will have an infection with HPV-related oropharyngeal cancer. Despite this fact, the number of people diagnosed with HPV oral cancer is increasing but there aren't any approved tests or screenings for HPV-associated oropharyngeal cancer. So, what medical or dental professionals will do is to screen through a visual and tactile exam and look for the lump in the throat or ask for oral history taking for signs and symptoms that the patient had to find out whether the patient is infected to HPV or not. Even if you are infected with HPV and tumor cells are expanding, there are surgeries and therapies, such as transoral laser microsurgery, transoral robotic surgery, radiation therapy, and chemotherapy, available to treat the tumor, which will allow long-term survival.

A change that will lead to better health care in developing an approved test for HPV-related oropharyngeal cancer. Approved HPV-related oropharyngeal cancer screening will allow the doctor to have a more appropriate and detailed stage of how much the tumor cells have spread and plan a tailored matching therapy for the patient. This will lead to better treatments that can actually treat the patients diagnosed with cancer.