

The human papillomaviruses (HPV) are commonly occurring sexually transmitted viruses which infect the anogenitals, mouth and throat. There are more than 100 types of HPV. The different HPV types are classified into low and high risk based on their association with cancer. Infection with "low risk" types may be asymptomatic or cause benign skin warts. However, approximately 15 types of HPV have oncogenic potential (notably HPV16). The experts assess that about 80% of individuals during their life time faces the cancer-causing HPV, but in most cases this infection is transient. In some people, due to the weakening of the immune system or other undiscovered reasons, infection with oncogenic types of HPV can lead to cervical, vaginal or anal cancers. Oncogenic types of HPV can also cause cancer of head and neck, especially in oral cavity and pharynx regions.

In recent times, the increase in incidence of head and neck cancer depended on HPV infection is observed. Patients with HPV-associated tumours appear to be younger (under 45 years old), with higher social status and not tobacco or alcohol users. The HPV infection is related to sexual history - early sexual initiation, frequent changing of partners and oral sex. Interestingly, HPV positive patients carries better prognosis than HPV negative. The difference in prognosis between patients with and without HPV infection is so high that it has resulted in development of clinical trials concerning safe deescalation schedules of cancer treatment. Such deescalation should lead to maintain the enhanced prognosis and reduction of treatment related morbidity.

One of the conditions of effective and safe deescalation is the development of predictive and prognostic factors for this type of therapy. Prognostic factor indicates prognosis of the patient and predictive one provides information on the likely benefit from treatment. Therefore, they help to choose the best kind of oncological treatment for individual patient. Thus, the development of such factors is very important because of the possibility of improving the results of anticancer therapy.

A few experimental and preclinical studies suggest that HPV infection may deregulate EGFR/PI3K/AKT/mTOR pathway in cancer cells, what can influence the treatment effect in HPV positive head and neck cancer patients. EGFR/PI3K/AKT/mTOR signaling pathway plays a key role in the most fundamental biological processes such as: cell proliferation, differentiation, death and DNA repair. In cancer cells its functioning is often deregulated because of protein expression changes or mutations of genes encoding proteins involved in this pathway.

Therefore, the main aim of proposed project is to assess the differences in functioning of EGFR/PI3K/AKT/mTOR signaling pathway between head and neck tumours with and without HPV infection. We will also assess the influence of selected molecular features on patients survival after treatment, what will suggest their prognostic and predictive potential.

The results of the project will help in better understanding of HPV-dependend cancerogenesis. They also should be helpful in identifying new potential prognostic and predictive factors in subgroups of patients with HPV-dependent cancers and those without viral infection what may, in turn, help in the future to improve treatment outcomes in patients with these cancers.