

Abstract

Head and neck squamous cell carcinoma (HNSCC) represents the sixth most common malignancy worldwide. Despite improvements in therapeutic outcomes due to advances in surgery, radiotherapy, chemotherapy, and imaging techniques, HNSCC still has high mortality rate. For patients who are not cured with surgery and radiotherapy, there are few effective treatment options. Although HNSCC is heterogeneous in nature, current molecular classification distinguishes only human papilloma virus positive and negative tumors. HNSCC in general are characterized by considerable resistance and high rate of locoregional recurrence. Loss of p53 control pathway and numerous alterations in components of intracellular signaling pathways are consistently observed throughout the majority of HNSCC cases, supporting uncontrolled proliferation. It was proven that common mutations in the HNSCC genome play major role in tumorigenesis as well as in resistance to chemotherapy. The aim of the thesis is to describe the important mechanisms in HNSCC, which are associated with mutations in epidermal growth factor receptor and p53, and those including PI3K/Akt/mTOR and Notch signaling pathways. Association of these pathways with chemoresistance to commonly used drugs and even to advanced targeted therapeutic agents was evidenced by many experimental and clinical observations. Some mechanisms leading to resistance to conventional chemotherapeutic agents such as cisplatin or docetaxel are discussed, as well as the possibilities how to re-establish the drug sensitivity of the tumor cells.