SUMMARY

Cancer arises in consequence of genetic and epigenetic changes in various protein coding genes involved in growth, proliferation, differentiation and cell death. The alterations cumulating in a single cell may give rise to malignant transformation. One of the mechanisms leading to excessive expression of oncogenes in cancer cells is DNA amplification. Thus, the detection of amplified genes in tumors may constitute an important diagnostic, prognostic and therapeutic factor for patients affected by this disease.

The purpose of this dissertation is the analysis of genes in three chromosomal regions: 3q25–q29, 11q13 and 22q11. These regions were selected basing on the microarray CGH profiles (array-CGH technique) of laryngeal squamous cell carcinoma cell lines (LSCC) and contain putative oncogenes.

The research material encompassed 17 LSCC cell lines and 64 tumor samples derived from neoplastic tissues removed during laryngectomy. Methods used in the study included: array-CGH, real-time PCR to DNA as well as cDNA templates, fluorescent *in situ* hybridization (FISH) and immunohistochemistry.

This study allowed to identify target genes (known also as driver genes) of the copy number gains in the analyzed regions, including: *PIK3CA* (3q25–q29), *FADD* (11q13) and *CRKL* (22q11). The role of other genes analyzed in selected regions, i.e. *MAP3K13*, *CCNL1* (3q25–q29) and *PPFIA1*, *CTTN* (11q13) has not been clearly defined in relation to larynx cancer pathogenesis. In contrast, *THPO, MUC4, MUC20* (3q25–q29) and *MAPK1* (22q11) genes were defined as associated with given aberrations (called passanger genes). The mechanism of *PIK3CA* overexpression may be the result of amplification or activating mutation, whereas the mechanism causing overexpression *CRKL* and *FADD* genes is amplification. Using fluorescence *in situ* hybridization it was determined that the 3q25-q29 region is highly heterogeneous, with predominance of derivative chromosomes containing various genes of the studied region. Furthermore, the observed nuclear localization of CRKL protein 22q11 region in cell lines and tumor specimens may suggest a pathogenic activation of this protein in cancer patients.

In summary, *PIK3CA*, *FADD* and *CRKL* genes were identified as involved in the pathogenesis of low-grade LSCC.