THESIS

The thesis deals with the glycophenotype analysis of normal squamous cell epithelia, and head and neck squamous cell carcinomas. Many research projects focus on improving patients prognosis studying biological properties of the tumor. The alterations of carbohydrate motives occur during cell differentiation and carcinogenesis.

Lectins are proteins that bind to specific carbohydrate structures. Animal lectins, including human lectins, consist of five subfamilies according to their binding specifity. Much attention is paid to the investigation of galectins - β-galactoside binding proteins. Their carbohydrate recognitive function is not dependent on the presence of Ca^{2+} ions, contrary to the other lectin types. Galectins play important roles in many biological processes, e.g. in adhesion, intercellular interactions, immunomodulation, inflammation, cell growth, apoptosis, pre-mRNA splicing. Alterations in any of these might contribute to the malignant transformation and cancer progression.

Endogenous lectins (galectins, Langerin, Manose receptor) were detected using immunohistochemistry, galectin-binding sites were localized by lectin histochemistry. Reverse lectin histochemistry was employed for the study of glycosaminoglycan binding sites. Human (squamous cell epithelia of the oral cavity, oropharynx and larynx, oral cavity, oropharyngeal, laryngeal and hypopharyngeal squamous cell carcinomas including their regional lymph node metastases, corneal epithelium, epidermis, basocelular carcinomas, trichoepithelioma were studied. Coresponding cytochemical methods were used to study phenotypic features in keratinocyte culture (human and porcine folicular and interfolicular cells, FaDu – hypopharyngeal carcinoma cell line) and glioma cell lines. Gylocophenotypic faetures in the cells of studied biopsies and cells lines were corelated with the imunohistochemical profile of markers assesing proliferation potential (pKi67, ΔNp63α), differentiation level (pancytokeratin, cytokeratin peptide pCK37, cytokeratins 8, 10, 14, 19), and other molecules (E-cadherin, β-katenin, desmoplakin-1 and -2, transferin receptor, laminin, SC 35). Expression of the selected glycophenotypic characetristics (α2,3/2,6 N-acetyl neuraminic acid residues and

galectin-3-reactive epitopes) were correlated with pathological (grading, keratinization, extent of the primary tumor and lymph node metatases) and clinical (disease free and overal surviaval rates) characteristics of the examined head and neck squamous cell carcinomas.

The expression pattern of α2,3/2,6 N-acetyl neuraminic acid residues of the sacharidic chains and galectin-3-reactive glycoepitopes is dependent on the level of cell differentiation in both squamous cell epithelias and carcinomas. Aberations N-acetyl neuraminic acid expresion are often seen in carcinomas and might contribute to their behavior. α2,6 Nacetyl neuraminic residues influence the accessibility of glycoepitopes recognized by galectin-3.

The expression of galectin-3-binding represents prospective prognostic marker in head and neck squamous cell carcinomas with potential clinical application.

Galectin-7 is specifically expressed in squamous cell epithelia. Its expression pattern seems to be correlated with the process of stratification. Decreased expression in tumors originating from these epithelia might be explained by the loss of its organization.

Ammount of Langerhans cells is reduced in basal cell cell carcinomas compared to the untransformed epidermis. Alterations of their functions could participiate in the development and progession of these tumors.

Glycobiological parameters seem to be promising tools for assessment of biological characteristics of keratinocytes (e.g. stemm cell phenotype, differentiation postmitotic phenotype, snescent phenotype) in culture and *in situ*.

Cell nuclei harbor binding sites for anionic glycosaminoglycans. Nuclear transport and localisation of glycosaminoglycans is cell/tissue specific. Heparin interacts with histone proteins and could thus contribute to the level of chromatin organization.

Employement of lectin histochemical methods seem to be very atractive tools in the field of cell biology and cell oncology and their study is further warranted. Some of the glycobiological features bear the capacity for clinical application.