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GLUCOSE STIMULATE METABOLIC REPROGRAMMING AND TUMOR PROGRESSIVE PROCESSES IN HUMAN MENINGIOMA CELLS

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Background: The warburg effect has an important role in carcinogenesis and tumor progression. The extent to which this also applies to meningiomas has not yet been investigated. The aim of this study is to investigate the influence of different glucose levels during glycolysis on tumor-promoting processes in the human meningioma in vitro.
Methods: The meningioma cell line Ben Men-1 cultured 24h in a glucose-free medium. Metabolic activity was measured by MTT assay and the proliferation rate by BrdU ELISA under 14 different glucose concentrations (in the range of 0 to 100 mM) after 24 hours. A peak fitting analysis was used to determine the concentrations for maximum proliferation and glycolysis activity. Subsequently, five concentrations were determined that promote maximum, minimum and optimal activities. The cells were seeded and further cultured under the previously defined conditions over 5 passages. Morphological changes and marker expression (EMA, vimentin, GLUT1, GLUT3, p-mTOR, HIF1a) were determined by immunocytochemistry.
Results: Based on the results of the peak fitting analysis, the cells were then cultured and analyzed with glucose concentrations of 0, 15, 40, 65 and 100 mM. It was found that long-term cultivation (>p4) with 0 and 100 mM glucose was not possible. Cultivation under 15-65 mM glucose concentrations for a longer period of time was possible. The cells fed with 65 mM glucose showed the fastest doubling times. The immunocytochemical characterization showed surprisingly decreasing vimentin and EMA signals in the 65 mM group in contrast to the other investigation groups. In addition, we found increased values for pmTOR and GLUT3.
Conclusions: Our results show that meningioma cells also respond to an increase in environmental glucose levels with an increased tumor progression. In particular, the increased expression of GLUT3 and p-mTOR suggests a possible metabolic reprogramming in this context.

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MACHINE LEARNING TECHINIQUES APPLICATION IN GLIOMA INTERACTOME STUDY: A MULTICENTRIC ANALYSIS OF 100 PATIENTS

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Background: We analyzed the correlation between radiological data, IDH mutation, gene expression profiling and metabolic signature in glioma biopsies by using supervised and unsupervised machine learning techniques as a pilot study.
Methods: Tumor biopsies from 100 patients bearing gliomas were collected during surgery in the period 2015-2020. Metabolic profile of those samples were obtained by high resolution ^{1}H magnetic resonance spectroscopy and were compared with the metabolic-related gene expression data obtained by real-time quantitative PCR. IDH ½ mutation was verified by immunohistochemistry and PCR. For that purpose, we used cluster analysis and graph networks as a machine learning framework. That study was implemented with classification regression tree regression analysis.
Results: Normalization of the data was paramount in order to being able to compare genetic and metabolic results. No differences between the metabolic or genetic profiles of glioma grade III and IV samples were found. Cluster analysis revealed no differences between first-diagnosed and recidive glioma metabolic and genetic profiles and overall survival. However, there was a statistical significant correlation between some metabolic patterns and genetic profile, where IDH-mutation, Alanine, Glycine, Glycerophosphorylcholine and Myo-inositol were the most important biomarkers. Overexpression of some metabolic and genetic pathways, particularly glycolysis and glutaminolysis, were correlated to glioma grade and overall survival.
Conclusion: Present results indicate that metabolic patterns by high resolution ^{1}H magnetic resonance spectroscopy could be a useful tool to improve our knowledge about glioma gene and metabolic expression profile. Our study shows that machine learning exploratory study is helpful to assess a more precise further regression analysis.

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WHO 2016 CLASSIFICATION AND SURGERY FOR GLIOMAS

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The work of modern glioma neurosurgery practice is focused on securing accurate diagnoses, alongside an aggressive and safe surgical pursuit of tumor removal. The evidence base that drives surgical decision-making has undergone a critical re-evaluation with the incorporation of molecular classifiers (IDH1, IDH2, TERT and others) into the revised 2016 World Health Organization (WHO) Classification of Tumors of the Central Nervous System and cIMPACT-NOW updated diagnoses of diffuse infiltrative gliomas: glioblastoma IDH wild-type, astrocytoma IDH mutant, and oligodendroglioma IDH mutant 1p/19q co-deleted. The evidence base for surgery differs for these three most-common gliomas in adults. For patients with Glioblastoma IDH wild-type, the evidence supports a surgical strategy aimed at complete resection of enhancing disease. For the rare non-enhancing glioblastoma IDH wild-type, debulking can and perhaps should be pursued if safe, but there are scant data to indicate that this practice confers a survival benefit. For patients with Astrocytoma IDH mutant, multiple independent studies support a maximal strategy aiming for complete resection of both enhancing and non-enhancing disease. An impressive prolongation of survival has been associated with minimization of residual disease in this cohort of patients. For the cohort of patients with Oligodendroglioma IDH mutant 1p19q-codeleted, the overall outcome is highly favorable due to an indolent natural history and effective radio-chemotherapeutic regimens; as such, more-extensive resection, while favored given the data for Glioblastoma IDH wild-type and Astrocytoma IDH mutant, has been difficult to definitively link with a further improvement in outcome, due to the need for prolonged follow-up allowing any potential difference in outcome, should one exist, to become apparent.

4 SKULL BASE
4.1 Meningiomas

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THE IMMUNOHISTOCHEMICAL EXPRESSION OF SSTR2A AND 5 ARE INDEPENDENT PROGNOSTIC FACTORS IN MENINGIOMAS

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Background: The expression of somatostatin receptors in meningioma is well established. First suggestions of a prognostic impact of SSTRs in meningioma have also been made. However, the knowledge is based on few investigations in small cohorts. We recently analyzed the expression of all five known SSTRs in a large cohort of over 700 meningiomas and showed correlations with WHO tumor grade and other clinical characteristics.
Methods: We therefore expanded our dataset and collected information about radiographic tumor recurrence and progression as well as other established prognostic factors for a comprehensive prognostic multivariate analysis (gender, age, primary/recurrent tumor, extent of resection (Simpson grade), WHO grade, adjuvant radiotherapy and confirmed neurofibromatosis type 2) .
Results: Male gender, recurrent tumor, incomplete resection (Simpson grade 4) and higher WHO grade (II or III) were independent negative prognostic factors for tumor recurrence while adjuvant radiotherapy was an independen positive prognostic factor (p=0.0012). An increased expression of SSTR2A was revealed as an independent negative prognostic factor for tumor recurrence (p=0.0239). A higher expression of SSTR5 was associated with a better prognosis (p=0.0024).
Conclusion: While an increased expression of SSTR2A is a negative prognostic factor for tumor recurrence, a higher expression of SSTR5 has a protective effect.