based on: 1) Absent NPAS3 expression is predominant in high grade astrocytomas, in comparison to low grade astrocytomas suggestive of an expression pattern typical of tumour suppressive-late stage progression factors. 2) Loss of function mutations of NPAS3, which are associated with a loss of heterozygosity of the NPAS3 locus are identified in glioblastomas. 3) Absent NPAS3 expression is predominant in >60% of malignant human glioma cell lines. 4) An over-expressed NPAS3 in malignant glioma cell lines suppresses the transformation potential, while the converse reduced expression promotes an increase in transformation potential. 5) A reduced NPAS3 expression (efficiency >90%) in concert with gliomagenesis pre-disposition genes transforms a well characterized TERT immortalized human astrocyte cell line and promotes the growth of malignant astrocytomas, while an over-expressed NPAS3 suppresses the transformation. 6) NPAS3 drives tumour progression by the control of cell cycle, proliferation, apoptosis, migration/invasion and angiogenesis.
Conclusions: Our data provide findings of NPAS3 as a novel gene which drives the progression of malignant astrocytomas, with tumour suppressive roles. We believe that this body of work is highly significant in our quest to better understand the biology of astrocytomas, and with prospects for improved targeted therapies in the treatment of this currently and relatively incurable disease.

8714 POSTER

Tamoxifen Interaction With Protein Kinase C Delta

E.A. Dudko[1], A.B. Ravcheeva[1], A.V. Konukhova[1], R.J. Ramanauskaite[1], E.A. Bogush[2], V.J. Kirsanov[2], T.A. Bogush[1]. *[1]N.N. Blokhin Russian Cancer Research Center of the Russian Academy of Medical Sciences, Laboratory of Medical Chemistry, Moscow, Russian Federation; [2]N.N. Blokhin Russian Cancer Research Center of the Russian Academy of Medical Sciences, Surgical Department, Moscow, Russian Federation*

Background: Tamoxifen, selective estrogen receptor modulator, is efficient in the treatment of some brain cancer tumours. This effect is thought to be related with tamoxifen influence on protein kinase C (PKC) and mechanism of antiestrogen influence on the enzyme is still unclear. We have supposed that direct tamoxifen interaction with PKC could be one of the reasons of the antiestrogen therapeutic activity in brain tumours.
Materials and Methods: A549 human non-small-cell lung cancer cells were studied by flow cytometry and fluorescent microscopy. A549 cells were incubated with Abcam antibodies: primary (PKC delta, EP1484Y or rabbit IgG) for 1.5h and with secondary FITC-conjugated antibody (ab6108) for 1.5 h. The important feature of the primary anti-PKC antibody is that the epitope resides near the C-terminus of the protein, where catalytic domain of enzyme is located.
Results:
1. It was revealed PKC delta expression in about 70% of the A549 cells in culture.
2. Tamoxifen pretreatment decreased significantly both the mean cell specific fluorescence (in about 1.6 times) and the specific stained cells number (up to 40%) after incubation with anti-PKC delta antibody.
3. In the microscopic visualization of the tamoxifen effect on specific antibody interaction with the A549 cells the result was the same: the cell specific fluorescence intensity as well as specific stained cells number after tamoxifen pretreatment were decreased significantly.
4. Tamoxifen didn't influence the isotypic antibodies interaction with the cells and didn't change the cell autofluorescence.

Conclusion: Decrease in the mean cell fluorescence intensity under tamoxifen pretreatment shows disturbed availability of the PKC delta catalytic domain to antibody binding, most likely because of the antiestrogen interaction with the PKC delta molecule. Because specific triphenylethylene-binding site is located near the catalytic domain of the PKC, there is high probability that the tamoxifen interaction with the PKC delta results in the modification of the enzyme catalytic activity and changes regulation in downstream signaling pathways of the PKC delta. We believe that tamoxifen interaction with the PKC delta could be one of the reasons of the antiestrogen therapeutic activity in some brain cancer tumours.
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8715 POSTER

Comparison of Instruments for Quality of Life Measurement in Bulgarian Patients With Malignant Glial Tumours

G. Stancheva[1], T. Goranova[2], M. Laleva[3], N. Velinov[3], R. Kaneva[1], G. Poptodorov[3], V. Mitev[1], S. Gabrovsky[3], P. Vanev[4], N. Gabrovsky[3]. *[1]Medical University − Sofia, Department of Medical Chemistry and Biochemistry/Molecular Medicine Center, Sofia, Bulgaria; [2]Medical University − Sofia, Molecular Medicine Center, Sofia, Bulgaria; [3]University Multiprofile Hospital for Active Treatment and Emergency Medicine "N.I.Pirogov", Department of Neurosurgery, Sofia, Bulgaria; [4]University Multiprofile Hospital for Active Treatment and Emergency Medicine "N.I.Pirogov", Psychiatric sector, Sofia, Bulgaria*

Background: Measuring the quality of life (QoL) has become an integral part of initial examination, choosing a therapeutic approach and for the follow-up of the neurosurgical treatment. Most commonly used questionnaires for QoL are SF-36 (Short-Form Health Survey), QLQ-C30 of the European Organization for Research and Treatment of Cancer (EORTC) and World Health Organization Quality of Life-100 (WHOQOL-100). Sofia Self-Assessment Scale (SoS-SAT) is a newly developed in Bulgaria questionnaire for QoL assessment. SoS-SAT is self-directed, mainly to patients with supratentorial processes and consists of 12 questions (5 related to physical functioning and the presence of neurological symptoms, 7 related to QoL and symptoms of depression). The objective of our study was to evaluated applicability of aforementioned instruments for measuring QoL in Bulgarian patients with malignant gliomas.
Material and Methods: In the present study 100 patients with malignant gliomas treated in the period 2003–2005 were included. QoL was measured through the SF-36 (n = 95), SoS-SAT (n = 45), QLQ-C30 (n = 40) and WHOQOL-100 (n = 35) before and after treatment. All patients were asked to answer 5 questions related to ease of completion, clartiry and comprehensiveness of each used in this study QoL questionnaires.
Results: The studied questionnaires demonstrate that all of them are clearly formulated and relevant to the health of patients with malignant gliomas. 60% of patients found WHOQOL-100 instrument more difficult to complete than others. Averaged results of this study revealed that SF-36, QLQ-C30 and SoS-SAT seems to be more appropriate for measuring QoL in patients with malignant gliomas − 80% of the patients did not have any difficulties with questions clarity or questionnaires completion. Also SoS-SAT is the instrument to which most patients show positive attitude in comparison of other.
Conclusions: The SF-36, QLQ-30 and SoS-SAT questionnaires are the most suitable existing instruments for QoL assessment in Bulgarian patients with malignant gliomas.

8716 POSTER

Novel Features That Impact the Outcome of Patients With Glioblastoma Multiforme − Multivariate Analysis From a Comprehensive Dataset

K.M. Field[1], M.A. Rosenthal[1], M. Yilmaz[2], P. Gibbs[1], K. Drummond[3]. *[1]Royal Melbourne Hospital, Department of Medical Oncology, Melbourne Victoria, Australia; [2]University of Melbourne, Department of Medicine, Melbourne Victoria, Australia; [3]Royal Melbourne Hospital, Department of Neurosurgery, Melbourne Victoria, Australia*

Background: Glioblastoma multiforme (GBM) is the most common malignant adult brain tumour. While the impact of variables such as age and performance status on outcome is well known, the potential impact of other variables such as socio-econonomic status and clinical trial participation to date have not been well explored.
Materials and Methods: Data on patients (pts) with GBM were accessed from a prospective neuro-oncology dataset collected over 12 years (1998–2010) at two institutions (one public, one private). Death data were obtained from the state Cancer Registry. Data linkage and analyses were performed by BioGrid Australia. Both univariable and multivariate logistic regression analyses were performed to look for relationships between clinical and socio-demographic variables and overall survival.
Results: In total 541 pts were evaluated; the median age was 60 years. Sixty-five patients (12%) were enrolled in a clinical trial. In univariable analysis, positive predictors for longer survival were: clinical trial participation (HR for death 0.43, 95% CI 0.33–0.60, $p < 0.0001$), higher IRSAD (index of relative socio-economic advantage and disadvantage) score (socioeconomically advantaged) (HR 0.85, 95% CI 0.8–0.95, $p = 0.0093$), macroscopic resection versus biopsy alone (HR 0.5, 95% CI 0.4−0.6, $p < 0.001$), and more than one operation (HR 0.5, 95% CI 0.4−0.6). Older age (HR for death 3.0, 95% CI 2.4−3.7, $p < 0.0001$), worse ECOG performance status (HR 1.5, 95% CI 1.3−1.7, $p < 0.0001$) and multifocal disease (HR 1.5, 95% CI 1.2–1.97, $p = 0.001$) were significantly associated