Background: Meningiomas are usually benign tumors and cytogenetically well-characterized. Most tumors show either monosomy 22 or a diploid karyotype. Progression of meningiomas is correlated with increasing hypodiploidy and the loss of the short arm of chromosome 1. The aim of this study was to assess intratumoral patterns of clonal chromosomal evolution in order to identify tumor progression pathways and to analyze their correlation with time to recurrence.
Methods: From 1973 to 2004, 661 patients with complete tumor resections and cytogenetic characterization were followed up. We have developed oncogenetic trees mixture models for estimating the most likely order of cytogenetic aberrations.
Results: Overall, in 8.0% (53/661) of the tumors at least one recurrence was documented during the study. Our results showed a significant correlation between cytogenetic data and recurrence ($p < 0.001$), location ($p < 10^{-5}$) and WHO grade ($p < 10^{-15}$). The estimated model was used to assign a genetic progression score (GPS). The GPS of a tumor is a quantitative measure and allows precise assessment of genetic progression. We classified tumors in three groups with low genetic progression (GPS < 2), intermediate genetic progression ($2 \leqslant$ GPS < 6) and advanced genetic progression (GPS $\geqslant$ 6). The recurrence rate is 7.9% (27/343) in the low progression group, 4.0% (11/273) in the medium progression group, and 33.3% (15/45) in the high progression group.
Conclusion: Therefore, cytogenetic classification of meningiomas is a powerful tool to predict tumor recurrence and a valuable parameter for the postoperative management protocol.

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P36. THE CALCIUM BINDING PROTEINS S100A8 AND S100A9 AS NOVEL MARKERS FOR HUMAN PROSTATE CANCER

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Background: S100 proteins comprise a family of calcium-modulated proteins that have recently been associated with epithelial tumours.
Methods: We examined the expression of two members of this family, S100A8 and S100A9 in human prostate adenocarcinomas by means of histochemical staining procedures. S100A9 was additionally analysed in patient serum using ELISA. Furthermore, the function of the two proteins was investigated in prostate derived cell lines using expression constructs and recombinant proteins.
Results: S100A8 and S100A9 were upregulated in prostatic intraepithelial neoplasia and preferentially in high-grade adenocarcinomas, whereas benign tissue was negative or showed weak expression of the proteins. Moreover, the analysis of S100A9 in patient serum revealed significantly elevated S100A9 serum levels in cancer patients compared to BPH (benign prostatic hyperplasia) patients or healthy individuals.[1]

In cell culture experiments S100A8 and S100A9 were identified as extracellular factors which induce MAP kinase and NF-κB signalling pathways and stimulate the migration of prostate epithelial cells.[2]
Conclusion: The data show that S100A8 and S100A9 are linked to the activation of important features of prostate cancer cells. Furthermore, S100A8 and S100A9 represent novel markers for prostate cancer, which may prove useful for future diagnostic and/or therapeutic approaches.

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P37. Gd-DOTA AND FLUOROPHORE SUBSTITUTED POLYAMINES AS INTRACELLULAR CONTRAST AGENTS FOR MAGNETIC RESONANCE AND FLUORESCENCE IMAGING OF TUMORS

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Background: Upregulation of polyamine transporters on the surface of tumor cells and the internalisation of biogenic polyamines by active transport processes may be exploited for the accumulation of millimolar quantities of reporter molecules.
Methods: Novel intracellular contrast agents for magnetic resonance imaging with high tumor uptake have been developed, based on Gd(III)-DOTA. Uptake of these agents into cultured tumor cell lines B16 (mouse melanoma), MH3924A (Morris hepatoma), A493 (kidney carinoma) and 3T3 NIH (mouse fibroblasts) was quantitated by ICP-MS. Furthermore fluorescence tagged polyamines were evaluated as optical imaging agents using confocal laser scanning microscopy to investigate uptake into B16 and MH3924A tumor cells.
Results: At 10 μM incubation with Gd(III)-DOTA-polyamine conjugates for 1 h, an uptake of 0.02–0.23 fmol/cell was achieved, corresponding to intracellular concentrations of 11–110 μM Gd. The cell uptake increased in the order A493 (0.02 fmol/cell) < 3T3NIH (0.03 fmol/cell) < B16 (0.05 fmol/cell) < MH3924A (0.23 fmol/cell). 0.017–0.17 fmol/cell internalized Gd is needed to achieve a detectable contrast enhancement via T_1-weighted MRI. Evidence for intracellular uptake of the fluorophore labeled polyamines in MH3924A and B16 tumor cells, investigated by confocal lase scanning microscopy, resulted in comparable uptake values as compared to the Gd(III)-DOTA derivatives. Initial in vivo studies showed that fluorophore labeled polyamines can be imaged in the tumor.
Conclusions: This study illustrates the potential of polyamine transporters which are upregulated in proliferating cells can be used for contrast agent enhanced MRI and optical imaging of tumors.

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