radiosensitive individuals with low spontaneous level of γH2AX foci (n=3) and 2) radioresistant individuals with high spontaneous level of γH2AX foci (n=3).

Results: An inverse correlation was found between the spontaneous level of γH2AX foci and the frequency of micronuclei after irradiation (R=-0,37, p=0.025). After gene expression analysis with microarrays, several genes were identified whose differential expression could be associated with an efficiency of DNA repair and radiation sensitivity. XRRA1 gene with unknown functions, recently associated with radioresistance in tumor lines, was down-regulated both before and after irradiation in radioresistant group. Furthermore, in unirradiated samples of radioresistant individuals thrombospondin gene (THBS1), well-known radiosensitizer, was down-regulated. However, several genes were significantly up-regulated, including HERC2, important player in the assembly of DNA repair foci, and histone genes (H1, H2A, H4). After irradiation, several DNA repair genes (WHSC1, POLN, ERCC5, DCLRE1C) were significantly up-regulated, but EIF2A and PNPLA5 genes, involved in apoptosis and autophagy, were down-regulated in radioresistant group. This is consistent with low levels of apoptosis and increased proliferation in lymphocytes of these individuals.

Conclusion: The obtained results indicate that spontaneous γH2AX foci activate DNA damage response in human somatic cells and provide opportunities to clarify the role of the expression of identified genes in the formation of chromosomal aberrations in human cells after exposure to radiation.

EP-2066

Phospholipase Cε as a biomarker of prostate cancer radioresistance

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Purpose or Objective: Radiotherapy is a curative treatment option in prostate cancer. Nevertheless, many men with prostate cancer develop recurrence of their disease. Identification of the predictive biomarkers and signaling mechanisms indicative of tumor cell radioresistance bears promise to improve cancer treatment. In our study we show that Phospholipase C epsilon (PLCε) might contribute to prostate cancer radioresistance.

Material and Methods: Gene expression profiling of prostate cancer cells and theirradioresistant derivatives, western blotanalysis to assess PLCε expression in the parental and radioresistantcells and in cell cultures after irradiation, radiobiological cell survivalanalysis of the cells with genetic modulation of PLCεexpression by siRNA or cDNA transfection as well as chemical inhibition of PLCε activity,fluorescent microscopy to analyze co-expression of PLCε withother markers of radioresistance. Normal 0 21 false false false EN-US X-NONE X-NONE

Results: The results of gene expression analysis, which were validated by western blotting revealed significant upregulation of PLCe in prostate cancer radioresistant cells that can also be seenafter irradiation of the parental cells with a single dose of 4Gy. Radiobiologicalsurvival assays demonstrated that siRNA induced PLCε knockdown or chemicalinhibition of PLCε activity by Edelfosine leads to prostate cancer cellradiosensitization. In contrast, overexpression of PLCε in cells transfected withplasmid DNA results to an increase in cell radioresistance. Microscopicanalysis revealed a high expression level of ß-catenin in prostate cancer cellsoverexpressing PLCε.

Conclusion: These results indicate that PLCε plays a role in prostate cancer radioresistance that can be mediated through activation of the WNT/ ß-catenin signaling pathway.

EP-2067

The adhesion of tumor cells to endothelial cells is increased by photon irradiation

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Purpose or Objective: In general the prognosis for cancer patients is poor even though only 10% die from the primary tumor. The majority of the deceases are due to metastasis. Given the fact, that more than 70% of cancer patients receive radiotherapy it seems important to clarify if radiation is involved in initial steps of the metastatic cascade – despite of innumerable clinical studies that confirm no enhanced risk of metastasis after radiotherapy. In this project we investigated whether the irradiation with photons increases the adhesion of cultured tumor cells (TC) to a layer of endothelial cells (EC) macroscopically and whether this might be caused by the induction of adhesion proteins.

Material and Methods: The experiments were performed with glioblastoma (U87, U373) and breast cancer cell lines (MDA-MB-231, MCF7), and with primary HUVEC cells. The cells were irradiated with 0, 0.5, 2, 4, or 8 Gy. Adhesion of TC to EC, both irradiated or not, was determined with 2 different methods: the VybrantTM cell adhesion assay and the Ibidi pumpsystem that allows to mimic the physiological blood stream in the vasculature. In addition, the expression of the adhesion-related proteins E-selectin, VCAM1, ICAM1, N-cadherin, integrin ß1, and PECAM1, 4h after irradiation with 4 Gy, was analyzed by qRT-PCR and by Western blotting.

Results: Irradiation increased significantly the adhesion of TC to EC. With glioblastoma cells the highest increase of about 40% was observed when both cell types were irradiated. In contrast, with breast cancer cells the highest effect of about 25% was obtained for irradiated TC in combination with non-irradiated EC. Analysis of the expression patterns in all cell types revealed an significant increase of adhesion proteins after irradiation in more than 80% of the experimental data sets.

Conclusion: We assume that the irradiation of tumor cells as well as of endothelial cells with photons might enhance adhesive interactions of these cells and thereby might promote the first steps of metastasis. Since clinical studies reveal no enhanced risk of metastasis due to irradiation we speculate that the therapeutic effect of radiotherapy might be additionally enhanced when the induced stickiness could be blocked effectively.

EP-2068

Effect of a 0.2 T magnetic field during radiation on DNA damage and repair in prostate cancer cells

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