subsequently deacetylated NF-kB p65 and p53 in WT, however not in NQO1−/− mice thereby attenuating AIC.

Conclusion Dunnione has a cardioprotective effect against ADR-induced cardiomyopathy through NQO1 enzymatic action. Thus, modulation of NAD+/NADH by NQO1 could be therapeutic targets in the future.

PO-252 IMPAIRED GLUCOSE METABOLISM IN HUMAN GLIOMA STEM CELLS UPON TREATMENT WITH A CELL-PENETRATING PEPTIDE BASED ON CONNEXIN43

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Introduction Connexin43 (Cx43), the main gap junction channel-forming protein in astrocytes, is downregulated in glioma stem cells (GSCs). Restoring Cx43 in GSCs reverses their phenotype through the inhibition of c-Src and consequently reduces GSCs tumorigenicity. We have developed a cell-penetrating peptide (TAT-Cx43266–283) containing the region of Cx43 that interacts with c-Src that mimics the effect of Cx43 on GSC phenotype. GSCs reprogram their metabolism to compete for glucose resources through HIP-1-alpha, which can in turn be regulated by c-Src. Therefore, the aim of this work was to study the effect of TAT-Cx43266–283 on GSC metabolism.

Material and methods G166 (human GSCs), Wistar rat organotypic brain slices, neurons and astrocytes from primary culture.

2-NBDG uptake: Cells were incubated with 146 μM 2-NBDG for 1 hour, lysed, and supernatant fluorescence intensity was measured by spectrofluorimetry and normalised to mg of protein.

The glycolytic activity and oxygen consumption, glycolytic activity, energy substrates oxidation were measured by Seahorse technique. Furthermore, the amount and the activity of several proteins related mTOR (mammalian target of rapamycin) and other metabolic pathways were studied.

Results and discussions The glycolytic activity and oxygen consumption rates of the four cell lines show differences. The wild type U251 MG cell line has higher glycolytic activity and lower basal respiration than its IDH1 mutant variant glioma cell line pair. Addition of D-2-HG (72 hour) to wild type U251 MG cells increased the basal respiration and decreased the glycolytic activity of U251 MG cells. Using various bioenergetic substrates, it has been shown that U251 MG cells can oxidise glutamine, glutamate and malate at significantly higher level than IDH1 mutant U251 MG cells. This may be due to the alternative use of glutamine, we found that glutamine is the main source of D-2-HG production in these IDH1 mutant glioma cells. Furthermore, differences were found in the expression pattern of proteins which regulate energy metabolism in the studied glioma cells.

Conclusion Based on the results of the examined glioma cells, IDH1 mutant cells showed a lower glycolytic capacity, a higher respiration and altered glutamine metabolism, which could be therapeutic targets in the future.

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PO-253 CHARACTERISTICS OF CELLULAR RESPIRATION, GLYCOLYTIC ACTIVITY AND RELATED METABOLIC FEATURES IN WILD TYPE AND IDH1 MUTANT GLIOMA CELLS

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Introduction IDH mutations are expressed in 80% of low grade gliomas and secondary glioblastomas with a favourable prognosis comparing to non IDH mutant gliomas [According to WHO (2016)] classification, IDH1 mutation is an important marker to classify gliomas. Our main interest is to study the role of certain metabolic alterations in glioma models, especially mitochondrial functions, glycolytic activity, IDH1 mutations and its regulation.

Material and methods U87 MG, U373 MG and U251 MG and U251 MG IDH1 R132H (kind gift of Dr. W. Leenders) overexpressing cells were used in vitro. Cellular oxygen consumption, glycolytic activity, energy substrates oxidation were measured by Seahorse technique. Furthermore, the amount and the activity of several proteins related mTOR (mammalian target of rapamycin) and other metabolic pathways were studied. The proliferation and apoptosis rates of in vitro cell cultures were also studied. We analysed extra- and intracellular metabolite levels (citrate, succinate, fumarate, alfa-ketoglutarate, malate, 2-hydroxyglutarate – D-2-HG, glutamate) using LC-MS measurements. Addressing the question what are the sources of D-2-HG in IDH1 mutant U251 MG cells, we fed the cells with 13C-labelled energy substrates.

Results and discussions The glycolytic activity and oxygen consumption rates of the four cell lines show differences. The wild type U251 MG cell line has higher glycolytic activity and lower basal respiration than its IDH1 mutant variant glioma cell line pair. Addition of D-2-HG (72 hour) to wild type U251 MG cells increased the basal respiration and decreased the glycolytic activity of U251 MG cells. Using various bioenergetic substrates, it has been shown that U251 MG cells can oxidise glutamine, glutamate and malate at significantly higher level than IDH1 mutant U251 MG cells. This may be due to the alternative use of glutamine, we found that glutamine is the main source of D-2-HG production in these IDH1 mutant glioma cells. Furthermore, differences were found in the expression pattern of proteins which regulate energy metabolism in the studied glioma cells.

Conclusion Based on the results of the examined glioma cells, IDH1 mutant cells showed a lower glycolytic capacity, a higher respiration and altered glutamine metabolism, which could be therapeutic targets in the future.

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PO-254 G PROTEIN-COUPLED OESTROGEN RECEPTOR ACTIVATION DECREASES PROSTATE CANCER CELLS VIABILITY CONCOMITANTLY WITH ALTERED PROLIFERATION, APOPTOSIS, AND METABOLIC PROFILE

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