principle for PDT and SDT. Therefore, in vitro comparison of PDT and SDT effects can provide insight into SDT mechanism of action. We have investigated PDT and SDT effects on human melanoma and fibrosarcoma cell lines, previously exposed to 5 aminolevulinic acid (Ala), through cell proliferation, cell death, and gene expression analysis.

Patients (or Materials) and Methods: The human melanoma, A2058, and fibrosarcoma, HT-1080, cell lines were previously exposed to Ala (0.45 mM) for 12 and 4 hours, respectively. SW generated by a piezoelectric device (Piezoson 100, Wolf) were used for SDT. In particular, A2058 were treated with an energy flux density (EFD) of 0.32 mJ/mm², for 1000 shots (4 shots/sec) while HT-1080 were treated with an EFD of 0.43 mJ/mm², for 500 shots (4 shots/sec). A LED lamp at 15 mW. Cell growth was evaluated by WST-1 assay, cell death by flow cytometric analysis with SYTOX Green and APC-Annexin V and mRNA expression by real-time RT-PCR.

Results: In A2058 both treatments determined a significant cell growth reduction even if SDT produced a progressive cell growth decrease compared with PDT reaching the greatest decrease at 72 hours (P < 0.01). Moreover, cell death evaluation highlighted a 25% increase of apoptotic cells at 48 hours from SDT. Both PDT and SDT determined a significant overexpression of the pro-apoptotic gene BAX and of the genes involved in the oxidative stress, NQO1 and SOD2. In HT-1080, SDT was more effective than PDT with a more significant increase of apoptotic cells compared with PDT (P < 0.01). After both treatments a significant overexpression of the pro-apoptotic gene APAF1 was observed.

Conclusion: After PDT and SDT a similar gene expression profile was observed in both cell lines, even though SDT seems more effective on fibrosarcoma cells and PDT on melanoma cells.

Disclosure of Interest: None declared.

**PP119—EFFECT OF LIPOSOMAL CURCUMIN ON RED BLOOD CELLS IN VITRO**

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Introduction: Curcumin possesses anticancer, anti-inflammatory, antioxidant, and antimicrobial properties. Curcumin has a poor oral bioavailability and solubility in plasma. Accordingly, various drug delivery systems, such as liposomal preparation, have been developed for intravenous administration. However, animal studies have shown dose-dependent hemolysis after infusion of liposomal curcumin. Because blood cells are the first point of contact for liposomal curcumin when administered intravenously, we investigated the influence of curcumin on human red blood cell (RBC) morphology in vitro.

Patients (or Materials) and Methods: Whole blood buffered with EDTA was incubated with different concentrations (1, 10, 100 µg/mL) of free or liposomal formulations of curcumin. RBC morphology and mean cellular volume were examined after 30 minutes, 1 hour, 2 hours, and 4 hours of incubation.

Results: Dose-dependent echinocyte formation was observed after incubation with free and liposomal Curcumin, with a threshold concentration of 10 µg/mL and peak effect after 30 minutes of incubation. Treatment with empty liposomes also resulted in RBC shape change. A concomitant increase in mean red blood cell volume was detectable.

Conclusion: Curcumin, liposomes and liposomal curcumin dose-dependently change RBC morphology. This effect is additive and may represent a first sign of toxicity following intravenous administration.


**PP120—CHEMOTHERAPEUTIC ANTITUMOR ACTIVITIES OF CURCUMIN**

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Introduction: In search for drugs that can target cancer cell microenvironment in as much as being able to halt malignant cellular transformation, the natural dietary phytochemical curcumin was currently assessed in DMH-induced colorectal cancer rat model.

Patients (or Materials) and Methods: The study enrolled 50 animals divided into a control group (n = 10) and DMH-induced colorectal cancer control group (n = 20) (20 mg/kg.-body weight for 28 weeks) versus curcumin-treated group (n = 20) (160 mg/kg suspension daily oral for further 8 weeks).

Experimental Procedures: ACF Assay: The colonic lesion biopsies were stained by 30% methylene blue for light microscopic examination [using a 40 magnification to transilluminate the specimens] in search for lesions fulfilling Mc Lellan and Bird criteria.

Histopathological Examination: By using light microscopic assessment.

Biochemical Estimations in Colonic Tissues: Malondialdehyde (MDA) Assay, reduced glutathione (GSH) Assay, Cyclooxygenase-2 (COX-2) activity measurement, tumor necrosis factor-α (TNF-α) Determination, platelet activating factor (PAF) activity measurement, transforming growth factor-β (TGF-β) determination.

Results: Treatment by curcumin succeeded to significantly decrease the percent of ACF and tended to normalize back the histologic changes retrieved in adenomatous and stromal cells induced by DMH. The drug also significantly elevated GSH and significantly reduced most of the accompanying biochemical elevations (namely MDA, TNF-α, TGF-β, and COX2) observed in colonic carcinomatus tissue, induced by DMH, thus succeeding to revert that of MDA, COX2 & TGF-β back to near normal as justified by being nonsignificantly altered compared with normal controls. The only exception was PAF, which was insignificantly altered by the drug.

Conclusion: When taken together, it could be concluded that curcumin possess the potentiality to halt some of the orchestrated cross-talk between cancerous transformation and its microenvironmental niche that contributes to cancer initiation, progression, and metastasis in this experimental cancer colon model. Envisioning these merits to a drug with an already known safety preferentiality, awaits final results of current ongoing clinical trials, before curcumin can be added to the new therapeutic armamentarium of anticancer therapy.

Disclosure of Interest: None declared.

**PP121—CYP2C9 GENOTYPES ASSOCIATED WITH HIGHER SULFOLANE LEVELS IN CHILDREN RECEIVING INTRAPODUS BUSULFAN PRIOR TO HEMATOPOIETIC STEM CELL TRANSPLANTATION**

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Introduction: Cytochrome P 450 enzymes (CYPs) were presumed to play a role in the oxidation of intermediate metabolites of busulfan (Bu). In vitro elucidation of involvement of CYPs in the oxidation of Bu metabolites is cumbersome due to the volatile nature of tetrahydrothiophene and nonavailability of sensitive quantitation methods. This study is aimed at exploring the association of CYP2C9, CYP2C19, CYP2B6, FMO genotypes, and sulfolane (Su) levels in children undergoing hematopoietic stem cell transplantation (HSCT). The relation of genotypes with the outcomes of HSCT was also explored.

Patients (or Materials) and Methods: Sixty-six children receiving IV Bu-based myeloablative conditioning regimens were genotyped for common functional variant alleles in CYP2C9 (*2 and *3), CYP2C19 (*2 and *17), FMO3 (rs2266780, rs2266782 and rs1736557) and CYP2B6 (*5 and *9). Plasma levels of Bu and its metabolite Su were measured after dose 9 from a subset of 44 patients for whom plasma samples after dose 9 were available. The ratio of Bu to Su was taken as a metabolic ratio (MR) to compare among genotype groups. The MRs (Bu/Su), Bu and Su levels between different genotype groups were compared using nonparametric tests. The distribution of age, and gender between the groups was compared using t test and chi-square test, respectively. Cumulative incidence of overall survival and event-free survival were estimated using Kaplan-Meier curves and log-rank test was used to compare the difference between genotype groups or groups divided on the basis of MR, in a univariate analysis. Multivariate analysis was performed using cox-regression analysis.

Results: Higher metabolic ratios (MRs, Bu/Su) were observed in CYP2C9-*2 and *3 allele carriers (mean [SD], 7.8 [3.6] Vs 4.4 [2.2]; P = 0.003). Lower event-free survival was seen in patients with MR above the median 5 (40% vs 79%; P = 0.009) and carrying reduced function alleles of CYP2B6 (40% vs 84%; P = 0.005).

Conclusion: This study suggests the role of the CYP2C9 in the oxidation reactions of THT and CYP genotypes along with Bu MRs to be important at predicting outcomes of Bu based myeloablative conditioning before HSCT.

Disclosure of Interest: None declared.

PP1123—TARGET GENE EVALUATION OF TWO MIRNAS DIFFERENTIALLY EXPRESSED IN FOCAL AND NON-FOCAL BRAIN TISSUE OF THERAPY-RESISTANT EPILEPSY PATIENTS
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Introduction: Resistance to anticonvulsants affects one third of all epilepsy patients. Limited bioavailability of the drug at the target site caused by increased expression of efflux transporters on the blood brain barrier or alterations of target genes as well as seizure-induced neural reorganization are potential mechanisms for therapy resistance. There is increasing evidence that expression of microRNAs (miRNAs) is deregulated in neuronal disorders. We hypothesize that an altered miRNA regulation of target genes is involved in drug resistance in epilepsy.

Patients (or Materials) and Methods: Hippocampal focal and cortical nonfocal brain tissue samples from 13 patients diagnosed with MTS (mesial temporal sclerosis) who underwent neuurosurgery have been screened for miRNA expression using TaqMan® low-density arrays. To compare miRNA expression between brain regions, a microarray approach for both hypothesis-based (efflux-transporter and target gene) as well as a hypothesis-free approach were used.