involved in colon cancer, suggested by our previous expression profiling data. To investigate its functional role, we generated SC1D deficient colon cancer cells.

**Material and methods** SC1D, SREBP1, FASN and ELOVL6 were quantified by qPCR in 78 patients with stage III colon cancer, and clinical and prognostic significance was assessed by Kaplan-Meier analysis. SC1D and SREBP1 were further analysed on protein level. SC1D-deficiency was implemented in colon cancer cells HCT116 by the CRISPR-Cas9 system. Mass spectrometry (MS) analysis was used to analyse the activity of SC1D; cell proliferation and survival of the SC1D deficient clones were compared to parental cells.

**Results and discussions** Expression of SC1D and FASN was highly significantly increased in tumours, whereas SREBP1 and ELOVL6 were significantly reduced. However, SC1D and SREBP1 were upregulated in tumour tissue on protein level and their mRNA was significantly co-expressed. SC1D was significantly associated with tumour grading and worse post-operative survival, and elevated expression of FASN and ELOVL6 with increased metastatic relapse.

SC1D deficiency was verified by DNA sequencing and immunoblotting, and MS analysis confirmed the deprivation of MUFAs. KO of SC1D led to significantly decreased cell proliferation and survival under normal growth conditions, which was even more pronounced under reduced serum. This was fully rescued by addition of the SC1D product oleate, suggesting that SC1D is necessary for growth and survival especially in the absence of exogenous lipids.

**Conclusion** SC1D, FASN and ELOVL6 are negative prognostic markers in stage III colon cancer. Functionally, SC1D is essential for cell survival under serum depletion. Together, these data suggest that the cell-autonomous synthesis of fatty acid species in cancer cells is due to reduced access to exogenous lipids. Enhanced lipogenesis rises the requirement for the production of MUFAs by SC1D, e.g., to maintain survival and circumvent lipotoxicity.

**PO-230** EFFECT OF C. COCHINCHINENSE EXTRACT ON V-ATPASE INHIBITION TRIGGERING APOPTOSIS IN HUMAN CANCER CELL LINES

R. Watanapokasin*, S. Innajak, S. Nilsaranggoen. Srinakharinwirot University, Biochemistry, Bangkok, Thailand

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**Introduction** V-ATPase is a family of proton pumps that balances the proton between intracellular and extracellular compartments. High metabolism could be found in cancer cells resulting in overproduction of protons. Thus, highly activated V-ATPase is necessary to balance cytosolic pH in cancer cells to protect cell death from acidosis. As V-ATPase is important for cancer cell survival, invasion, migration, and metastasis in cancer cells, therefore the development of anti-cancer therapeutics selectively targeting V-ATPases function in cancer cells is necessary.

**Material and methods** To investigate the effect of *C. cochinchinense* extract on V-ATPase inhibition, the cancer cells were treated with *C. cochinchinense* for 24 hour then were stained with acridine orange for 30 min compared with a positive control (bafilomycin A1). Then, the effect of V-ATPase inhibition on apoptosis cell death induction was conducted by staining with Hoechst 33 342 to determine nuclear morphological changes.

**Results and discussions** The results showed that *C. cochinchinense* extract inhibited V-ATPase activity in malignant melanoma cell line A375, triple-negative breast cancer cell line MDA-MB-231, colorectal cancer cell line HCT116 and epidermoid carcinoma cell line A431 compared with bafilomycin A (as a V-ATPase inhibitor). In addition, *C. cochinchinense* extract showed apoptosis induction by inducing apoptotic bodies in *C. cochinchinense* extract treated cells.

**Conclusion** Our results indicated that *C. cochinchinense* extract is an inhibitor of V-ATPase triggering apoptosis induction in various cancer cell lines including A431, A375, and MDA-MB-231 cells. Thus *C. cochinchinense* extract may be further developed as an anti-cancer drug possessing V-ATPase inhibition. However, the underlying mechanisms of V-ATPase inhibitor and apoptosis induction in cancer cells should be further studied.

**PO-231** MTOR ACTIVITY DIFFERENCES AND RELATED METABOLIC ACTIVITY IN HUMAN BREAST CANCER CELL LINES

1. G. Petőváni*, 2. Z. Hujer, 3. T. Dankó, 4. N. Szabolcsai, 1. I. Krencz, 5. M. Hajdu, 6. Ú. Kulka, 1. M. Tókés, 1. A. Jeney, 1. A. Sebestyén. Semmelweis University, First Department of Pathology and Experimental Cancer Research, Budapest, Hungary; 2. Eötvös Loránd University, Laboratory of Environmental Chemistry and Bioanalytics - Department of Analytical Chemistry- Institute of Chemistry, Budapest, Hungary; 3. Semmelweis University, Second Department of Pathology, Budapest, Hungary

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**Introduction** The mTOR (mammalian target of rapamycin) is a receptor tyrosine kinase which plays an important role in cell growth regulation, proliferation and tumour cell survival in cancer cells. Differences of mTOR activity were described in tumours. mTOR dependent and independent metabolic activity of tumour cells could be essential in survival and therapy resistance of breast cancer. Changes of mTOR and metabolic activity of breast cancer could correlate to the patients’ treatment outcome.

**Material and methods** In our work, the correlations between the metabolic phenotype and mTOR activity of breast cancer cell lines were studied. Furthermore, the expressions of mTOR activity related proteins and several metabolic transporter, enzymes were studied by Western blot, ICC and IHC using breast cancer cell lines and human tissue samples. The metabolic phenotypes were also analysed using LC-MS. Moreover, the effect of mTOR, metabolic inhibitors and chemotherapeutics were also studied in vitro.

**Results and discussions** Subtypes independent differences in mTORC1/C2 complex and metabolic activities were detected in breast cancer cell lines. Certain cell lines were characterised with high glucose uptake, high mTORC1 complex activity and high lactate production, while other cell lines showed balanced mTORC1 and mTORC2 activity, well-functioning oxidative phosphorylation capacity and higher levels of TCA metabolites which were related to intact mitochondrial functions. The metabolic phenotype and mTORC1/C2 activity correlated to the detected mTOR inhibitors, metabolic inhibitors and chemotherapeutic sensitivity of breast cancer cell lines in vitro. The metabolic and mTOR activity differences can be observed in human tissue samples independently of breast carcinoma cell subtypes, as well.
Conclusion Differences of metabolic and mTOR related protein levels may explain the different therapeutic sensitivity. We suggest evaluating the metabolic phenotype and mTOR activity in breast cancer subtypes, which may help to introduce therapeutic drug combinations and predict therapy resistance.

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**PO-232 LEWIS GLYCAN AND THEIR EPIGENETIC REGULATION ARE ASSOCIATED WITH NEUROBLASTOMA AGGRESSIVENESS**

H Cuello*, V Segatori, M Alberto, C Gulino, R Aschero, Galluzzo Muttii, Madauss, D Alonso, F Lubieniecki, M Gabr, Molecular Oncology Laboratory—Quilmes National University, Science and Technology, Bernal, Argentina; Pediatric Hospital Prof. Dr. Juan P. Garrahan, Department of Pathology, Buenos Aires, Argentina; GlaxoSmithKline, Alt Discovery and Development, Philadelphia, USA

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**PO-233 CHEMORESISTANT NSCLC CELLS ARE HYPERSENSITIVE TO METABOLIC DRUGS DUE TO mTOR-MEDIATED INHIBITION OF AUTOPHAGY**

M Warzab*, N Gremke, L Schmoll, A Pagenstecher, J Schneikert, T Stiewe, Philipp University of Marburg, Institute of Molecular Oncology, Marburg, Germany; UKGM, Neuropathology, Marburg, Germany

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**PO-234 TRANSWELL CO-CULTURE WITH HUMAN BREAST ADIPOCYTES ALTERS THE PROTEOME EXPRESSION PROFILES OF MCF-7 AND MDA-MB-231 HUMAN BREAST CANCER CELLS**

R Crake*, E Phillips, T Keffmann, H Morin, M Strother, B Robinson, M Currie, University of Otago, Christchurch, Department of Pathology, Christchurch, New Zealand; University of Otago, Department of Biochemistry, Dunedin, New Zealand

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Introduction In non-small cell lung cancer (NSCLC) cisplatin is the first line chemotherapy and triggers a strong apoptotic response mainly by inducing DNA interstrand crosslinks. However, the effectiveness of cytotoxic cancer therapy is often limited by the emergence of drug resistant tumour cells. Here, we identify strategies for overcoming resistance to DNA interstrand crosslinkers such as cisplatin.

Material and methods We treated the NSCLC cell line H460 continuously with DNA crosslinking agents resulting in resistant subclones that displayed cross-resistance to multiple DNA-damaging cancer drugs, which are commonly used in the clinic.

Results and discussions Drug resistance was found to be mediated by mTOR-dependent upregulation of DNA repair via the Fanconi anaemia pathway. Strikingly, despite being multidrug-resistant, resistant cells were highly sensitive to treatment with the metabolic drugs 2-deoxyglucose (2-DG) and dichloroacetate (DCA), whereas parental H460 cells failed to respond. Moreover, xenograft studies in mice revealed, that DCA preferentially reduces growth of resistant tumour cells. Interestingly, mTOR inhibition by RNAi or pharmacological inhibitors not only reversed resistance to crosslinking drugs but in parallel mitigated the apoptotic response to metabolic drugs, thereby linking sensitivity to metabolic drugs with mTOR signalling in chemoresistant cells. Mechanistically, inhibition of autophagy by mTOR was found to be decisive. We observed elevated levels of the mTOR-induced inhibitory S757 phosphorylation of the central autophagy-initiating kinase Ulk1 in chemoresistant tumour cells. Matching these observations, autophagosomal formation was detected only in parental, but was abrogated in resistant tumour cells upon DCA treatment.

Conclusion Together these results demonstrate that mTOR-triggered resistance to DNA-damaging cancer drugs generates a therapeutic vulnerability to metabolic drugs due to mTOR-mediated inhibition of autophagy.

Introduction Breast tumours grow within adipose tissue, and stromal adipocytes are likely the first cell type encountered by