Introduction The dysregulation of glycolysis has been suggested to lead to the alteration of cell drug resistance signals, proliferation and metastasis. Emerging evidence indicates that lncRNAs play a key role in the cellular processes of tumour cells, including glycolysis, growth, and movement. However, the role of lncRNAs in glycolysis-mediated metastasis and the potential mechanism has not been explored.

Material and methods First, microarrays were performed to explore the lncRNA, mRNA and miRNA profiles in 4 pair OSCC and adjacent non-tumour tissue samples. qRT-PCR and bioinformatic analysis were used to confirm the expression and coding capability of lnc-p23154 in OSCC cell lines. Then, functional experiment, the nude mouse model and RNA sequence were performed to demonstrate that lnc-p23154 could promote OSCC metastasis and glycolysis both in vitro and in vivo. Furthermore, we verified lnc-p23154 promoted OSCC metastasis via Glut1-mediated glycolysis through a rescue assay. At last, luciferase assay, FISH assay, RNA immunoprecipitation and RNA pull down was utilised to prove that lnc-p23154 inhibited miR-378a-3p transcription by interacting with its promoter region, then regulated miR-378a-3p targeted gene Glut1 expression and promoted Glut1-mediated OSCC metastasis.

Results and discussions In this study, we identified a novel lncRNA, Lnc-p23154, which is up-regulated in oralsquamous cell carcinoma (OSCC) tissues and cell lines, is associated with OSCC patient metastasis and promotion of OSCC cell migration and invasion in vitro and in vivo. Furthermore, we found that lnc-p23154 also participates in OSCC glycolysis by facilitating Glut1 expression. Rescue of lnc-p23154 reversed the suppression of OSCC cell migration and invasion induced by Glut1 knockdown. More importantly, lnc-p23154 is mainly located in the nucleus and binds to the promoter region of miR-378a-3p, which represses Glut1 expression by targeting to its 3’UTR directly.

Conclusion In summary, we described a novel mechanism of lnc-p23154-miR-378a-3p/Glut1 axis in Glut1-mediated glycolysis and OSCC metastasis regulation. Meanwhile, we provided evidence that overexpression of lnc-p23154 is significantly associated with higher metastasis tendency in both OSCC cells and patients with OSCC. These results indicated that lnc-p23154 may act as a metastasis driver in OSCC and a potential biomarker for OSCC diagnosis and treatment.

PO-365 ISOTHIOCYANATES AS POTENT EPIGENETIC REGULATORS IN HUMAN MALIGNANT MELANOMA CHEMOPREVENTION

1M Mitsiogianni*, 2A Pappa, 3M Panagiotidis. 1Northumbria University, Department of Applied Sciences, Newcastle Upon Tyne, UK; 2Democritus University of Thrace, Department of Molecular Biology and Genetics, Alexandroupolis, Greece; 3Northumbria University, Department of Applied Sciences, Newcastle Upon Tyne, UK.

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Introduction Glucosinolates (GLs) are phytochemicals abundant in cruciferous vegetables, which are hydrolysed, by myrosinase, to a range of isothiocyanates (ITCs). These molecules are biologically active metabolites capable of mediating a plurality of anticancer effects including cell cycle arrest, inhibition of proliferation and apoptotic induction. Their wide range of biological properties may be reflected by their ability to interfere with the epigenetic machinery at both DNA and histone levels. The aim of the current study is to investigate how ITCs interact with the epigenetic pathway(s) response in order to induce apoptosis by modifying the expression of key apoptotic genes in an in vitro model of human malignant melanoma.

Material and methods Our in vitro human malignant melanoma model consists of (i) immortalised normal keratinocyte (HaCaT) cells; (ii) malignant melanoma (A375) cells and epitheloid carcinoma (A431) cells subjected to the following ITCs: R, S-Sulforaphane (SFN), Phenethyl Isothiocyanate (PEITC), Benzyl Isothiocyanate (BITC), Allyl Isothiocyanate (AITC) and Iberin (IBN) over different concentrations and time points of exposure. Apoptotic induction was confirmed by TaqMan qPCR gene expression profiling arrays while involvement of the epigenetic machinery was assessed by western immunoblotting for determining protein expression levels of histone deacetylases (HDACs), histone acetyltransferases (HATs) and various other histone modification tags.

Results and discussions Our results showed that all ITCs were capable of inducing apoptosis as evident by the differential expression of key target genes in a manner where PEITC and IBN were involved primarily in up-regulation compared to SFN and AITC both of which were involved in down-regulation of the majority of these apoptotic genes. Finally, differences in HDAC and HAT protein expression levels, among ITC treatments, were evident in addition to their differential compartmentalization between nucleus and cytosol.

Conclusion Overall our results suggest an ITC-dependent cytotoxicity effect which is mediated via apoptotic induction and is underlined, at least partially, by epigenetic pathway(s) response mechanism(s). Our data support the notion that ITCs may be promising candidates in the context of epigenetic therapy for the treatment of human malignant melanoma.
expression was performed using SPSS. The Broad Institute Morpheus tool was used for hierarchical cluster analysis of the TCGA RNA-Seq data to identify associations of lncRNA expression with UC molecular subtypes.

Results and discussions Consistent with the TCGA RNA-Seq data, qRT-PCR analysis of our large tissue set revealed both TINCR and DANCER to be upregulated in UC and in B-SCC compared to benign tissues. According to the qRT-PCR data, DANCER expression was significantly elevated in non-invasive over invasive tumours. Kaplan-Meier analysis did not reveal associations of patient outcome with upregulated lncRNA expression, except that high TINCR expression was associated with worse metastasis-free survival. Hierarchical cluster analysis indicated that the BASQ subtype, which is defined by low expression of luminal marker genes (FOXA1, GATA3) and high expression of basal and squamous marker genes (KRT5, KRT6, KRT14), is also characterised by intermediate TINCR expression.

Conclusion Both TINCR and DANCER expression are frequently upregulated in UC, but are not strongly associated with clinical parameters. Instead, our data support the emerging consensus that specific lncRNA expression patterns are associated with and may contribute to the characteristics of UC molecular subtypes.

**PO-367 DFNA5 METHYLATION: A POTENTIAL BIOMARKER FOR BREAST CANCER, ON THE BASIS OF A LARGE SCALE ANALYSIS IN TCGA**

1. L. Croes*, 1 M. Beyens, 2 F. Fransen, 1 I. Ibrahim, 1 W. Vanden Bergh, 1 A. Suls, 1 M. Peeters, 1 P. Pauwels, 3 G. Van Camp, 1 K. Op de Beeck. 1 University of Antwerp and Antwerp University Hospital, Center of Medical Genetics and Center for Oncological Research, Antwerp, Belgium; 1 University of Antwerp, Center of Medical Genetics and Statixa Center for Statistics, Antwerp, Belgium; 1 University of Antwerp, Laboratory of Protein Chemistry-Proteomics and Epigenetic Signaling PRS, Antwerp, Belgium; 2 University of Antwerp and Antwerp University Hospital, Center of Medical Genetics, Antwerp, Belgium; 3 University of Antwerp and Antwerp University Hospital, Center for Oncological Research, Antwerp, Belgium

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Introduction Breast cancer is the most frequent cancer among women worldwide. Biomarkers for early detection and prognosis of these patients are needed. We hypothesised that DFNA5 (also known as Gasdermin E (GSDME)) may be a valuable biomarker, based upon strong indications for its role as tumour suppressor gene and its function in regulated cell death. In this study, we aimed to analyse DFNA5 methylation and expression in the largest breast cancer cohort to date using publicly available data from TCGA, in order to further unravel the role of DFNA5 as detection and/or prognostic marker in breast cancer.

Material and methods We analysed Infinium HumanMethylation450k data, covering 22 different CpGs in the DFNA5 gene (668 breast adenocarcinomas and 85 normal breast samples) and DFNA5 expression (Agilent 244K Custom Gene Expression: 476 breast adenocarcinomas and 56 normal breast samples; RNA-seq: 666 breast adenocarcinomas and 71 normal breast samples).

Results and discussions DFNA5 methylation and expression were significantly different between breast cancer and normal breast samples. Overall, breast cancer samples showed higher DFNA5 methylation in the putative gene promoter compared to normal breast samples, whereas in the gene body and upstream of the putative gene promoter the opposite is true. Furthermore, DFNA5 methylation, in 10 out of 22 CpGs, and expression was significantly higher in lobular compared to ductal breast cancers. An important result of this study was the identification of a combination of one CpG in the gene promoter (CpG07504598) and one CpG in the gene body (CpG12922093) of DFNA5, that was able to discriminate between breast cancer and normal breast samples (AUC=0.93). This model was externally validated in three independent datasets. Moreover, we showed that oestrogen receptor state is associated with DFNA5 methylation and expression. Finally, we were able to find a significant effect of DFNA5 gene body methylation on 5-year overall survival time.

Conclusion We conclude that DFNA5 methylation shows strong potential as detection and prognostic biomarker for breast cancer.

**PO-368 EPIGENETIC REGULATION OF GLYCOSYLATION AND THE IMPACT ON CHEMORESISTANCE IN OVARIAN AND BREAST CANCER**

1. G. Greville, 2 L. Ucko, 3 R. Peracaula Miró, 4 A. McConnell, 2 P. Rudd, 5 A. Saidova*. 1 The National Institute for Bioprocessing Research and Training, NIBRT GlycoScience Group, Dublin, Ireland; 2 University College Dublin, UCD School of Medicine - College of Health and Agricultural Science and UCD Conway Institute of Biomolecular and Biomedical Research, Dublin, Ireland; 3 University of Girona, Biochemistry and Molecular Biology Unit - Department of Biology, Girona, Spain

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Introduction Glycosylation is epigenetically regulated and is a fundamental post-translational modification altered in cancer. These alterations impact on tumour progression, and promote tumour survival. In the literature, there is a clear link between chemoresistance and hypoxia, hypoxia and epigenetics and more recently glycosylation and epigenetics. Our remit is to bring these paradigms together, to open up new avenues of approach for the detection, diagnosis and treatment of ovarian and breast cancer.

Material and methods Ovarian and breast cancer cells were treated with the DNA methyltransferase inhibitor, 5-AZA-2-deoxycytidine (5-AZA-dC). Cells were exposed to normoxia and differential hypoxic conditions. Methylation status of hypoxia-exposed cells and the normoxia-controls as well as demethylation following 5-AZA-dC treatment was confirmed by flow cytometry. N-glycans from cell secreted glycoproteins were analysed using hydrophilic interaction liquid chromatography (HILIC) and mass spectrometry. Western blot analyses assessed apoptosis, senescence, autophagy and epithelial to mesenchymal transition (EMT). The Oris Migration Assay monitored the cell migration, while qRT-PCR measured candidate glycosyltransferases and transcription factor (TFs) gene expression in these samples.

Results and discussions Branching and sialylation known to aid in tumour survival, were increased on secreted N-glycans from chemoresistant cells compared to chemoresistant cells following treatment with 5-AZA-dC and in all cells under hypoxic conditions. These changes correlated with increases in MGAT5 and ST3GAL4 expression in demethylated ovarian cancer cells. GATA2/3 were identified in-silico, as possible TFs for these genes. Results show that there is a correlation between, ST3GAL4 and GATA2 and MGAT5 and GATA3, respectively. 5-AZA-dC-treated and hypoxia-exposed cells displayed increased migration, with a greater effect in chemosensitive...