node metastasis in young TNBC patients. Our results showed that NOS3 expression level was reciprocally up-regulated.On the molecular level, sONE siRNAs resulted in an increase in NOS3 levels and NO production in MDA-MB-231. On the functional level, knocking down of sONE levels resulted in a significant increase of cellular viability and cellular proliferation rates of MDA-MB-231

Conclusion This study highlights a novel prognostic value of sONE in young TNBC patients where sONE expression level was negatively correlated with the aggressiveness of the disease. Moreover, this study validated sONE/NOS3/NO as a novel tumour suppressor signalling axis in BC patients.

PO-348 TWO NOVEL SYNTHETIC ANALOGUES OF MIR-1207–3 P, NB5 AND NB1207, TARGET AR-V7 AND C-MYC AND DEMONSTRATE *IN VIVO* THERAPEUTIC EFFICACY IN METASTATIC CASTRATE-RESISTANT PROSTATE CANCER (MCRPC)

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Introduction Chromosome 8q24 prostate cancer (PCa) susceptibility region encodes miR-1207–3 p which directly targets fibronectin type III domain containing 1 (FNDC1) to regulate fibronectin (FN1) and subsequently the androgen receptor (AR), and FNDC1/FN1/AR is overexpressed in metastatic PCa (Das *et al*, Exp Cell Res, 2016).

Material and methods Expression of miR-1207–3 p and c-MYC in histologically confirmed normal prostate, benign prostatic hyperplasia (BPH) and PCa from prostatectomy or transrectal ultrasound-guided biopsies was analysed. Molecular mechanisms were elucidated using mCRPC cell lines. Effects of NB1207 and NB5, two novel synthetic analogues of miR-1207–3 p, on AR-V7 (implicated in PCa therapeutic resistance), mCRPC tumour growth in mice were studied.

Results and discussions miR-1207–3 p is underexpressed in PCa (0.10±0.02, 95% CI [0.1, 0.2], p=0.000) in comparison to normal prostate (1.02±0.17, 95% CI [0.7, 1.4], p=0.000) and BPH (0.74±0.15, 95% CI [0.4, 1.1] p=0.004). c-MYC was overexpressed in PCa (34.76±8.11, 95% CI [18.1, 51.4], p=0.000; normal: 1.99±0.34, 95% CI [1.3, 2.7]; BPH: 1.01 ±0.21, 95% CI [0.6, 1.4], p=0.000). miR-1207–3 p was underexpressed by nearly 3-fold in PCa with Gleason score ≥8 versus those with Gleason score <8, while c-MYC was overexpressed by nearly 5-fold in PCa with Gleason score ≥8 versus those with Gleason score <8. NB1207 significantly inhibited c-MYC expression in mCRPC cell lines: PC-3, E006AA-hT and C4-2B. miR-1207–3 p regulates c-MYC expression via the miR-1207–3 p/FNDC1/FN1/AR pathway: c-MYC protein expression is inhibited in mCRPC cell lines by overexpression of miR-1207–3 p, and by inhibition of expression of FNDC1, FN1, and AR. In AR-V7-expressing mCRPC cell lines, NB1207 and NB5 significantly reduced AR-V7 expression, and NB1207 and NB5 more effectively inhibited AR-V7 compared to abiraterone, enzalutamide and apalutamide. In mCRPC cell lines, abiraterone, enzalutamide, and apalutamide failed to significantly inhibit cell proliferation or induce apoptosis. However, NB1207 and NB5 significantly inhibited proliferation and induced apoptosis. In mCRPC 22RV1 tumor-bearing mice, NB5 and NB1207 significantly inhibited tumour growth and metastatic spread. While enzalutamide minimally inhibited growth of 22RV1 tumours in mice, apalutamide and abiraterone had no inhibitory effects on tumour growth.

Conclusion This study shows potential diagnostic and prognostic value of miR-1207–3 p in mCRPC, and that NB5 and NB1207, novel analogues of miR-1207–3 p, may be candidate therapeutics for mCRPC.

PO-349 IDENTIFICATION OF DIFFERENTIALLY EXPRESSED LNCRNAS IN METFORMIN RESISTANT SH-SY5Y NEUROBLASTOMA CELLS

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Introduction Of the total human DNA only 1.2% o codes for proteins, with the rest only being transcribed into regulatory RNA, known as non-coding RNA. Long non-coding RNAs (lncRNAs) are non-coding RNAs that have no or limited protein-coding potential, are >200 nt in length and include-among other categories- long/large intergenic/intervening RNAs (lincRNAs), intronic lncRNAs, natural antisense transcripts (NATs) and pseudogenes. lncRNAs are key regulators of several cellular processes and have been associated with a variety of diseases, including cancer. Metformin (N, N-dimethyl biguanide) is an oral biguanide already in clinical use against diabetes and has also been suggested to decrease the incidence of various cancers, including neuroblastoma, the most common extracranial paediatric cancer arising at the sympathetic nervous system.

Material and methods The present study aimed at assessing the differential expression of protein-coding and, primarily, non-protein-coding RNAs between control untreated SH-SY5Y neuroblastoma cells and cells resistant to 3 mM Metformin via a paired-end RNA sequencing approach.

Results and discussions In the first data set (untreated cells compared to cells resistant to 3 mM Metformin), out of 13 741 genes measured, 7855 genes were found to be differentially expressed with 108 of them falling within the lncRNA category. Among these 33 comprise lincRNAs, 24 are NATs and 18 pseudogenes. In the second data set (untreated cells compared to cells treated with 20 mM Metformin) 13 481 genes were tested, of which 5652 showed perturbed expression. Among them, 86 belong to the lncRNA category, and in particular, 33 are lincRNAs, 19 are NATs and 13 are pseudogenes. Interestingly, 34 of the assessed lncRNAs display differential expression in both data sets. The results were obtained using a threshold of 0.05 for statistical significance (p-value) and a log fold change of expression with an absolute value of at least 0.6.Neuroblastoma cells' response to Metformin, as well as the acquisition of resistance to the drug, trigger the differential expression of a great diversity of lncRNAs.

Conclusion Given that Metformin is an appealing and promising therapeutic approach against neuroblastoma, these lncRNAs could, in turn, be used as molecular biomarkers

towards better prediction, prognosis and diagnosis of the disease. Moreover, such an approach would be of interest as part of a combination therapy.

PO-350 MIRNAS AND THEIR RELATION TO BIOLOGICAL PATHWAYS IN LEFT- AND RIGHT-SIDED COLORECTAL CANCER

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Introduction MicroRNAs (miRNAs) are involved in the regulation of gene expression in colorectal cancer (CRC), which has specific biological pathways that are predominant in either left- or right-sided CRC. However, it is unclear how miRNAs are associated with biological pathways in these two forms of CRC. Our hypothesis is that a comprehensive understanding of the fundamental biological signalling pathways in the two sides of CRC may aid in developing a decisive step towards precision medicine. We aim to clarify specific biological pathway differences of differentially expressed miRNAs between left- and right-sided CRC.

Material and methods We extracted total RNA from 24 of left- and right-sided CRC tumour samples from Finnish patients using the mirVana™ miRNA Isolation Kit (Thermo Fisher Scientific) in the discovery cohort. Libraries for small RNA sequencing were prepared using TruSeq® Small RNA Library Prep Kit (Illumina) and run on Illumina MiSeq. Differentially up-regulated miRNAs were identified using DeSeq2. For validation purposes, we used the mature miRSeq dataset of 201 CRC samples from The Cancer Genome Atlas. We analysed biological pathways of site-specific miRNAs from the discovery and validation cohorts using the DIANA/mirPath tool.

Results and discussions We found 17 and 15 differentially up-regulated miRNAs in left- and right-sided CRC, respectively, in the discovery cohort. The left miRNAs were involved in the mTor, Wnt, PI3K-Akt signalling pathways. These pathways are the predominant pathways in left-sided CRC. The Wnt signalling pathway was also significant (false discovery rate <0.05) in the left miRNAs from the validation cohort. In the discovery cohort, the right miRNAs were involved in the TGF-β signalling pathway. This pathway is dominant in right-sided CRC also in earlier reports. Alongside with the pathway findings, we found that the discovery and validation cohorts share six miRNAs. One of these (hsa-miR-196b-5p) was differentially up-regulated in left-sided CRC and the rest of them (hsa-miR-625–3 p, hsa-miR-155–5 p, hsa-miR-625–5 p, hsa-miR-31–5 p and hsa-miR-330–5 p) in right-sided CRC.

Conclusion Our findings highlight that there are site-specific miRNAs in left and right-sided CRC. The results also indicate the involvement of these left and right miRNAs in different predominant biological pathways of the two forms of CRC. This exploration may be useful for further studies on the development of diagnosis in left- and right-sided CRC.

PO-351 MELATONIN SUPPRESSES TPA-INDUCED ORAL CANCER CELL MIGRATION VIA LNCRNA-LNC310-MEDIATED PRUNE2 ACTIVATION

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Introduction Long non-coding RNAs (lncRNAs) are kind of non-coding RNAs (ncRNAs). The length of lncRNAs is more than 200 nucleotides. A few decades ago, lncRNAs were regarded as useless parts of the genome, but more and more studies demonstrate that lncRNAs play an important role in growth, development, metabolism and cancer. Very few lncRNAs have been characterised in detail at the present time. However, it is clear that lncRNAs are important regulators of gene expression and have a wide range of functions in cellular and developmental processes. Previous studies have shown that development of cancers is accompanied by abnormal expression of lncRNAs that participate in the regulation of cancer metastasis, apoptosis and proliferation. Melatonin is a hormone secreted from pineal gland and play an important role in the regulation of the immune system. Melatonin is also a potent antioxidant agent. Previous studies have shown that melatonin inhibits the growth and metastasis of breast cancer cells, cervical cancer cells and ovarian cancer cells. However, the detailed effects and mechanisms of melatonin and lncRNAs on oral cancer cell metastasis were still unclear.

Material and methods RNA-seq and quantitative real-time PCR analyses were used to detect the lncRNAs and mRNAs expression in HSC-3, HSC-4 and OECM-1 oral cancer cells. Transwell migration assay was performed to evaluate the migration of tumour cells. Fluorescent *in situ* hybridization (FISH) assay was used for determining the lncRNAs levels in oral cancer cell. Protein levels were accessed by western blotting assay.

Results and discussions The results show that melatonin could induce the PRUNE2 through decreasing lncRNA-LNC310 to improve the migration inhibition of oral cancer cells. On the other hand, melatonin could partially inactivate Src/STAT3 signalling cascade targeting LNC310 to induce the expression of PRUNE2 in oral cancer cells. Additionally, LNC310 knockdown upregulated PRUNE2 expression and suppressed cell migration in oral cancer cells.

Conclusion This results suggested that melatonin inhibited oral cancer migration by inducing lncRNA-LNC310-mediated PRUNE2 expression and indicated that melatonin could be a promising treatment for oral cancer.

PO-352 THE EFFECTS OF LAPATINIB RESPONSIVE MIRNA ON CELL PROLIFERATION AND CELL INVASION IN HER2 +BREAST CANCER CELL LINE

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Introduction Lapatinib is a dual receptor tyrosine kinase inhibitor that blocks EGFR (HER1) and HER2 activation in breast cancer. microRNAs (miRNA) are non-coding RNAs involved in the regulation of protein-coding genes and these regulatory