into medulloblastoma cells via endocytosis and siRNA was trafficked to the cytoplasm. Star-siRNA inhibited PLK1 protein expression by 70% ($p<0.001$, $n=3$) when compared to control cells (star-non-functional siRNA). Knockdown of PLK1 resulted in G2 cell cycle arrest ($p<0.001$) and DNA damage. This led to the induction of apoptosis and cell death ($p<0.001$). Star-PLK1 siRNA also sensitised cells to cisplatin.

Conclusion This is the **first** study to demonstrate that star nanoparticles can deliver siRNA to medulloblastoma cells. This nanomedicine may be a new therapeutic tool which has potential to revolutionise medulloblastoma treatment and could enhance *precision-medicine* where it can be used to inhibit the expression of any tumour-promoting gene or cocktail of genes personalised to the genetic profile of a patient's tumour.

PO-355 ANTITUMOR ACTIVITY OF HSA-MIR-X IN HER2 POSITIVE CELLS IS MEDIATED BY THE REGULATION OF AKT AND ERK

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Introduction HER2 overexpression has been reported in approximately 30% of human breast tumours, and is associated with poor clinical outcome and recurrent disease. Herceptin is a humanised monoclonal antibody targeting HER2. PI3K-AKT is a downstream effector of the HER2 signalling pathway. microRNAs (miRNA) are small non-coding RNAs of 19–22 nucleotides that can negatively regulate gene expression at post-transcriptional levels. Herceptin plays an important role in treating metastatic breast cancer by targeting Erbb2 (HER2), therefore, combining Herceptin with miRNAs might enhance its antitumor activity. In this study the antitumor activity of hsa-miR-X, which was found to be Herceptin–responsive by our group, with Herceptin in HER2 positive breast cancer cell lines was identified in SK-Br-3 and BT-474 cells.

Material and methods We investigated the synergistic effect of Herceptin and miRNA mimic combination on tumorigenic activities of the cells. To check its role in migration and invasion, wound healing and invasion assays were performed respectively. Cell invasion was monitored over a period of 24 hours by xCELLigence real-time cell analyzer measuring impedance-based signals. Furthermore, viability of breast cancer cells was measured by the WST1 assay after transfection with hsa-miR-X miRNA mimic. We measured the expression of AKT and ERK in HER2 positive cells treated with miR-X mimic plus Herceptin by Western blot analysis.

Results and discussions We showed that increased expression of hsa-miR-X significantly inhibits migration and invasion of HER2 (+) breast cancer cells. Additionally, western blot experiments demonstrated that transfection of hsa-miR-X with Herceptin treatment decreased the protein level of AKT and ERK in these cells.

Conclusion It may be concluded that hsa-miR-X may increase the activity of the drug by pulling down its effective concentration and regulating PI3K-AKT pathway in HER2 positive cells. hsa-miR-X could decrease proliferation, motility and invasion via inhibiting Akt phosphorylation and may represent a new strategy for treating HER2 positive breast cancer.

PO-356 MICRORNA MEDIATED REGULATION OF MORGANA, A NEW ONCOSUPPRESSOR IN CHRONIC MYELOID LEUKAEMIA

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Introduction Morgana is a chaperone protein encoded by the *CHORDC1* gene. Its deletion is embryonic lethal due to apoptosis of the cells of the inner cell mass. We recently characterised the role of Morgana in myeloid malignancies, as the haploinsufficiency of the protein in mice is able to induce a fatal and transplantable myeloproliferative disease resembling human Atypical Chronic Myeloid Leukaemia (aCML). 5 out of 5 aCML patients and 16% of Philadelphia-positive CML patients express low/undetectable levels of Morgana in their bone marrow. As we never found mutations or deletions of *CHORDC1* gene, we decided to investigate if Morgana can be targeted by miRNAs. Five miRNAs are predicted to target Morgana: miR-15a/b and miR-16 sharing the same seed sequence and miR-26a/b.

Material and methods HEK-293T cells were used to overexpress miRNAs predicted to target Morgana mRNA. The level of miRNAs overexpression and Morgana mRNA was assessed with qRT-PCR and Morgana protein level with Western Blot at different time points. The seed sequences for the selected miRNAs in the 3'UTR of *CHORDC1* gene were than mutagenized to validate the specificity of the binding. Bioinformatic analysis were used to correlate miRNAs and Morgana expression levels in leukaemia and lymphoma.

Results and discussions We demonstrated that miRNA-15a/b and miRNA-26a/b are able to bind to Morgana 3'-UTR and, in this way, mediate its mRNA deregulation leading to a reduction of Morgana, both at mRNA and protein level. We were able to highlight an anti-correlation between Morgana and miRNAs expression in haematological tumours: in particular miR-15b in Chronic Lymphocytic Leukaemia and Lymphomas, miR-15a in aCML and CML and miR-26a and miR-16 in Lymphomas.

Conclusion Morgana is able to act both as proto-oncogene and as oncosuppressor depending on tissue type and levels of expression as it is frequently found both overexpressed and downregulated. Different approaches to elucidate its mechanisms of regulation failed and we believe that miRNAs are just one of them. Further investigations are needed to clirify how Morgana expression is regulated in different type of tumours.

PO-357 MIR-145–5 P, MIR-196A-5P, MIR-222–3 P AND LNCRNA MALAT1 AS NON-INVASIVE MARKERS IN ADVANCED LARYNGEAL SQUAMOUS CELL CARCINOMA

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Introduction Non-coding RNAs are become one of the most investigated biomarkers in non-invasive diagnostics of cancer