molecular prognostic markers in several tumour types. However, the underlying mechanism of miR-146b in relation to its oncogenic behaviour in PTC and its putative targets remain to be fully elucidated.

Material and methods We used genome-wide microarray, computational analysis and 3 UTR reporter gene assays to identify IRAK1 as a miR-146b target gene. *In vitro* gain/loss-of-function experiments were fur- ther performed to determine the effects of IRAK1 on proliferation, colony formation, and wound- healing in PTC cancer cell lines. Expression levels of miR-146b and IRAK1 of 50 cases of PTC and its adjacent normal thyroid specimens were assessed via quantitative real-time polymerase chain reaction.

Results and discussions Microarray expression profile revealed that the mRNA level of IRAK1 gene was down- regulated by miR-146b. The 3 UTR of IRAK1 mRNA was found to be a molecular target of miR-146b posttranscriptional repression in BCPAP cells by reporter gene assays. MiR-146b promoted the migration and proliferation of PTC cells by downregulating IRAK1 expression, whereas restoration of IRAK1 expression reversed this effect. In addition, the expression of IRAK1 mRNA was significantly lower in PTC clinical tissue samples than normal adjacent thyroid specimens and showed a strong inverse correlation with the expression of miR-146b in PTC specimens. Our results demonstrated that IRAK1 is a direct target of miR-146b and has functional roles to inhibit various aggressive PTC cell activities.

Conclusion In conjunction with current therapeutic regimens, targeting the miR-146b-IRAK1 axis not only may provide a potential approach for PTC management but also serve as a unique supplemental tool for diagnosis and predicting prognosis for PTC in the near future.

PO-344 MIR-302B AS ADJUVANT THERAPEUTIC TOOL TO IMPROVE CHEMOTHERAPY EFFICACY IN HUMAN TRIPLE NEGATIVE BREAST CANCER

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Introduction MiRNAs are a class of non-coding regulatory RNAs playing key roles in different biological processes including cancer. Triple-negative breast cancer (TNBC) accounts for 15%–20% of all breast cancer cases, with the worst outcome of all subtypes. For TNBC, still lacking targeted therapies, the only therapeutic option is chemotherapy. MiRNAs can modulate chemotherapy response by affecting DNA repair, cell cycle progression, apoptosis and also tumour microenvironment. Macrophages constitute a major component of the immune microenvironment of cancer and pro-tumour M2 macrophages have been associated with response to chemotherapeutic treatments. Here, we investigated the potential of miR-302b as a therapeutic tool to enhance cisplatin sensitivity in a TNBC mouse model and which pathways are involved in this mechanism both in tumour cells and microenvironment.

Material and methods TNBC cells were injected into the mammary fat pad of female SCID mice and then treated with lipid nanoparticles containing miR-302b or cel-67 control, alone or in combination with cisplatin. Gene expression profile on collected tumours was performed by microarray. ITGA6 expression was assessed on tumour samples and siRNA tranfection was performed to evaluate the cisplatin response. Tumour sections were stained with anti-arginase 1 (M2 marker) to assess the number of M2 macrophages, and luciferase assay was used to evaluate Irf4 (M2 marker) as a direct target of miR-302b.

Results and discussions Our results show that combination of miR-302b with cisplatin significantly impaired tumour growth in comparison with control cel-67. Gene expression profile identified ITGA6 as a regulatory target of miR-302b and cisplatin activity. Indeed, ITGA6 expression is down-modulated in mice treated with miR-302b plus cisplatin compared with control mice. Furthermore, TNBC cell lines increase their cisplatin sensitivity upon ITGA6 silencing. These data confirm the role of ITGA6 in cisplatin response mediated by miR-302b. Moreover, in xenograft tumours collected from the *in vivo* miR-302b delivery experiment, we observed a reduced number of M2 macrophages in the tumour microenvironment and gene expression confirm immune system modulation. Finally, luciferase assay validate Irf4, a key gene involved in M2 recruitment, as a direct target of miR-302b.

Conclusion Our data demonstrate that miR-302b can be exploited as a new therapeutic tool to improve the response to chemotherapy, modulating ITGA6 expression in tumour cells and M2 recruitment in tumour microenvironment.

PO-345 IDENTIFICATION OF AR-MODULATORY MICRORNAS FOR PROSTATE CANCER PROGRESSION AND THERAPY

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Introduction Prostate cancer (PCa) is the most common type of cancer affecting the male population. It is an androgen dependent malignancy that initially responds well to androgen ablation therapy. However, despite hormonal treatment, castrate resistant prostate cancer eventually emerges. MicroRNAs (miRs), a class of small non-coding RNAs, modulate gene silencing through inhibition of translation and mRNA degradation. MiRs and/or miR inhibitors that reduce AR activity represent a promising therapeutic strategy, therefore a high-throughput miR inhibitor screen was performed in PCa cell lines, expressing a luciferase-based AR reporter. We sought to validate and characterise AR-modulatory miRs and identify their targets in PCa cell lines.

Material and methods Prostate cancer cell lines that stably expressed an AR reporter element were transfected with specific miR inhibitors and mimics. The effect of miR modulation on potential alteration of AR activity was investigated (through a luciferase assay), as well as the potential impact on cell growth by an SRB assay and on apoptosis, using a caspase 3/7 assay. Real-time qPCR and western blot assays were performed, to check the potential effect of miR manipulation on mRNA and protein levels of AR and miR specific target genes.

Results and discussions MiR-1271–5 p inhibitor significantly reduced AR activity and increased apoptosis in a castrate resistant cell line and the opposite effect was seen with the use of the mimic. MiR-1271–5 p inhibitor significantly