MicroRNA-21 Alters Cell Survival Mediated Responses of MDA-MB-231 Breast Cancer Cells in The State of Methionine Deprivation

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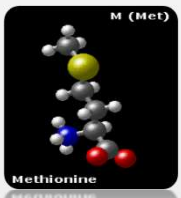
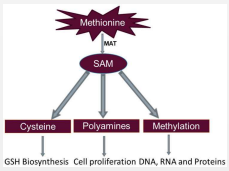
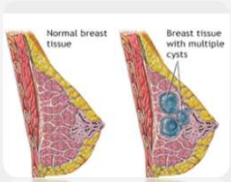
INTRODUCTION

Breast cancer (BCa) is one of the most common types of cancer worldwide and is the second most common cause of cancer-related death. microRNA-21(miR-21) is upregulated and promotes metastasis in various tumor types, also can induce cell proliferation and migration in MDA-MB-231 breast cancer cells. Methionine is a key amino acid, and its deprivation inhibits cell proliferation via mTOR and AMPK signaling cascade. Since, metabolic responses of cells in the case of miR-21 deficiency in selected breast cancer were investigated, this study highlights the role of miR-21 in the case of methionine deprivation in aggressive MDA-MB-231 BCa cells as metabolism targeted.

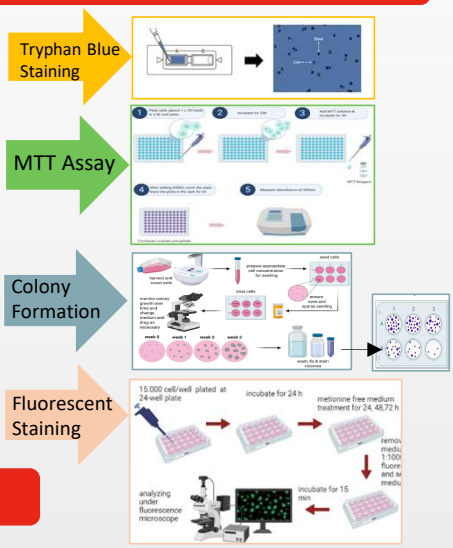


Met: $C_5H_{11}NO_2S$





METHODS



RESULTS

➢ Methionine Deficiency Reduced Cell Viability in MDA-MB-231 Bca Cells in a Time Dependent Manner

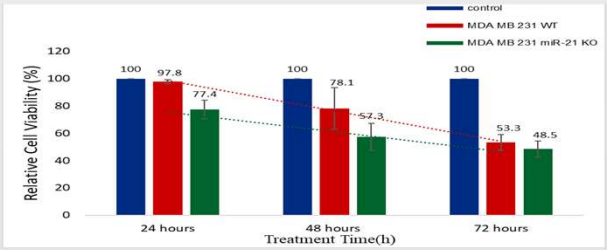


Figure 1: Colorometric MTT cell viability assay of MDA-MB-231 Bca cells were performed to observe the effect of methionine deficiency on cell viability. Results showed an obvious decrease in cell viability in both cell groups after treatments. But this decrease was more in miR-21 -/- MDA-MB-231 than MDA-MB-231 wt Bca cells.

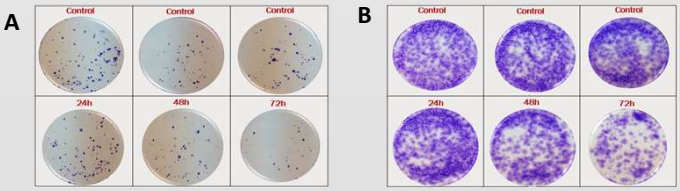


Figure 2: A. Colony Formation Assay of miR-21 -/- MDA-MB-231 and **B.**MDA-MB-231 wt Bca cell lines after treatment with methionine free cell culture medium for 24, 48 and 72 hours. Colony formation potentials of both group of cells were examined with colony formation assay under the light microscopy. Results showed reduced colonization in both cell groups after treatments. After miR-21 inhibited, colony formation of MDA-MB-231 cells were obviously decreased.

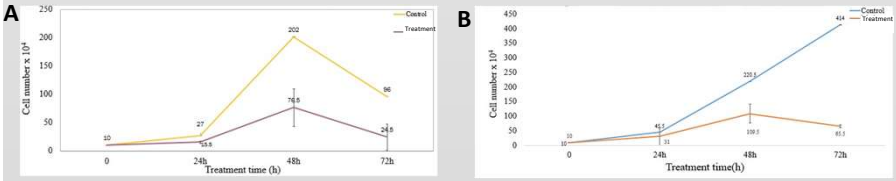


Figure 3: A. Proliferation graph of miR-21 -/- MDA-MB-231 and **B.**MDA-MB-231 wt Bca cell lines by using tryphan blue staining. Cell survival and death rates were obtained by counting both groups of cells by staining them with typhan blue everyday after treatment. Culturing cells with methionine free medium caused a decrease in cell proliferation for both groups of cells.

➢ Methionine Deficiency Reduced Cell Viability, Increased ROS and Lipid Formations in MDA-MB-231 BCa Cells

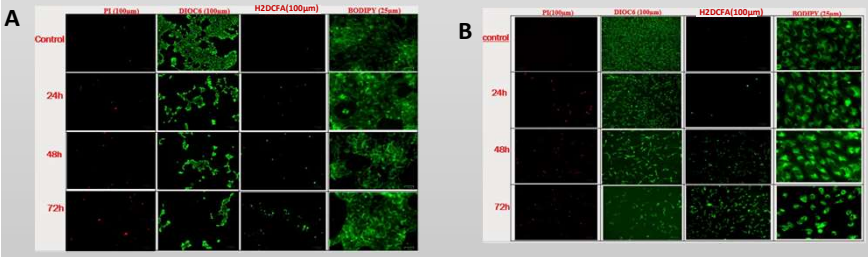


Figure 4: A. Fluorescent staining of miR-21 -/- MDA-MB-231 and **B.**MDA-MB-231 wt Bca cell lines with PI, DIOC6, DCFDA, BODIPY after treatment. Cell viability was observed by using DiOC6 and PI while ROS and lipid formations examined with H2DCFDA and BODIPY fluorescent dyes. In both groups of cells, DIOC6 dye showed decreased live cells, PI dye showed increased dead cells under fluorescent microscope. Also, H2DCFDA and BODIPY dyes showed increased ROS and lipid formation,respecticely after treatments.

CONCLUSION

MiR-21 could be a useful target for BCa. Obtaining the decreased cell viability and colony formation in methionine deprivation indicates that methionine starvation has a therapeutic importance on breast cancer. Although we highlighted the importance of miR-21 in methionine deprivation, its novel genes, molecular mechanisms, clinical potential still need further investigation.

REFERENCES

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