Natural Killer based cellular therapy as a treatment for melanoma

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Melanoma accounts for only 1% of the total skin cancers but causes the highest number of deaths due to skin cancer. Studies have stated that the incidence of melanoma is increasing by about 3% every year. Therefore, this calls for the development of effective therapeutics against melanoma. One of the therapies that is becoming highly exciting is metabolism modulating drugs such as glycolysis inhibiting drugs. These therapies utilize one of the cancer cell's hallmark features, upregulation of glycolysis, which can be inhibited by glycolytic inhibitors. Unfortunately, when glycolysis is inhibited in cancer cells, by systemic administration of the glycolytic inhibitors they prevent immune cell functions as well. This glycolytic inhibition of the immune cells can prevent them from effectively killing the tumor cells, thus reducing the efficacy of the therapy. Therefore, a strategy needs to be developed to enhance glycolysis in the immune cells during cancer cell glycolysis inhibition. One way to execute this is to introduce a metabolite involved in glycolysis pathways to the immune cells to accelerate their glycolytic pathway so that they remain unaffected by the addition inhibition of glycolysis. This study proposes a method to introduce Natural Killer (NK) cells, known for their tumour-killing properties, laden with Fructose 1,6-Bisphosphate as a cell-based therapy against melanoma.

Methods: NK-92 cell line will be used for this study. They were cultured in AMEM media supplemented with Fetal Bovine Serum and Horse Serum. Liposomes, generated using probe sonication, were used to introduce Fructose 1,6-Bisphosphate into NK cells. *In-vitro* studies with PFK15 and human melanoma cell line will be performed to understand the efficacy of tumour killing abilities of this formulation. Following this, *in-vivo* studies will be done in mice, and the following parameters will be observed and measured after tumour injection and administration of formulation: Survival, Weight, Size of Tumour, and immune responses.

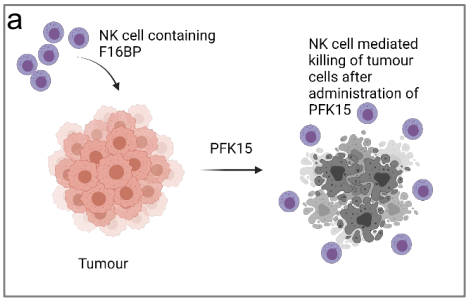

Figure: A schematic of the overall study.

Results: *In-vitro* studies of F16BP containing NK cells have shown promising results with regard to alteration in rates of glycolytic pathway in these cells on exposure to PFK15, a glycolytic inhibitor. A noticeable increase in glycolysis was observed in them compared to the controls. Additionally, the NK cell containing F16BP also exhibited a higher tumour-killing ability *in-vitro* even in the presence of PFK15.

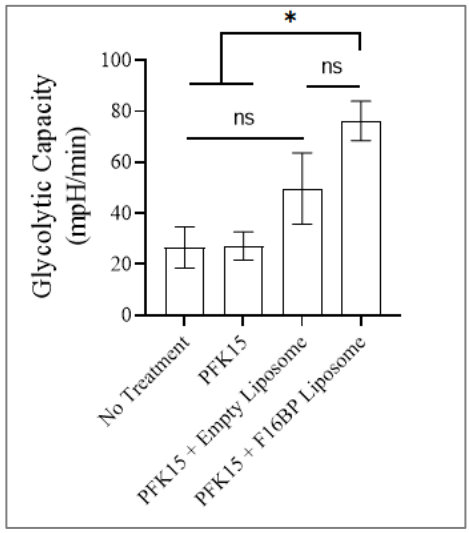

Figure: Acceleration of glycolysis rates in NK-92 cells on receiving the F16BP-liposome formulation, measured using Seahorse assay.

References:

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