Elucidating the role of peripheral blood immune cell versus Intratumoral Immune Cells (IICs) in a tumor histo-culture model in response to Immune checkpoint inhibitors

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INTRODUCTION:

Immune cells in the Tumor Immune Microenvironment (TIME) play an important role in mounting response to immunotherapy. The relative distribution and functional status of Intratumoral Immune Cells (IICs) are distinct from the peripheral blood immune cells from the same patient[1,2]. Model systems that can co-culture Peripheral Blood Nucleated Cells (PBNCs) with tumor cells, spheroids or tumors have helped assess response to immunotherapeutic agents. However, these models are ineffective in capturing the complex immunobiology of native human tumors.

Farcast™ TIME is a human tumor histo-culture platform which retains the tumor, stroma and functional IICs post culture. In this study we used the Head and Neck Squamous Cell Carcinoma (HNSCC) TIME model to evaluate the added benefit of PBNC co-culture in modulating response to Immune Checkpoint Inhibitors (ICIs).

METHODS:

Patient tissue samples: Fresh, surgically resected HNSCC tissue samples were collected from consenting patients. A matched blood sample from the patient was also collected.

Flow cytometry analysis: The tumor explants were dissected post culture with various treatments into single cells and stained with Live/Dead dye, and cocktail of immune cell lineage makers (CD45, CD3, CD8, CD14, CD11b, CD68). Data was acquired using BD LSR Fortessa Flow cytometer with appropriate control antibodies and analysed using FlowJo software.

Cytokine analysis: The cultured supernatants of T0, T48, T72 were tested for the presence of various cytokines (FN, Granzyme-B, Perforin, IL-10 and TNF-alpha) using Luminex Magpix instrument and data was analysed using MILLIPLEX® Analyst software.

RESULTS:

Cancer tissue was observed in S1 on drug treatment in absence of PBNC co-culture

REFERENCES:


SUMMARY & CONCLUSIONS

1. For IC therapy, IICs are sufficient to elicit response.
2. Co-culture with PBNCs did not enhance efficacy of immune check point inhibitor drugs like Nivolumab and Ipilimumab.
3. Infiltrating PBNCs, in fact, modified the immune environment of the tumor leading to a response that differed from IC driven response.
4. Inclusion of PBNCs is not universally beneficial to elicit response across different drug platforms.
5. The choice of platform should be driven by the class of agent to be tested and the PBNC platform used provides this unique and flexible option.