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Preclinical development of tumor-infiltrating lymphocyte therapy for ovarian cancer

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Background

Immunotherapy has become an effective cancer therapy, particularly in the case of checkpoint blockade and adoptive T cell therapy (ACT). ACT exploits the presence of tumor-infiltrating lymphocytes (TIL) by exponentially expanding their numbers *ex vivo* and re-infusing them into the patient in an autologous setting. With the effectiveness of TIL therapy already well established in multiple Phase II studies in melanoma, there is a push to translate it to other malignancies such as ovarian cancer (OvCa) [1].

Methods

The presence of TIL is correlated with greatly increased survival in OvCa [2,3] suggesting that TIL effectively control the disease and provide a rationale to test TIL therapy in this setting. To assess the feasibility, we characterized the immune component of OvCa, explored the ability to grow & expand TIL from tumor fragments, and tested their functionality.

Results

Extensive flow cytometry analysis detected a robust, activated T cell infiltrate that can be grown from OvCa samples obtained pre- and post-chemotherapy. The addition of an agonistic anti-41BB antibody to the cultures preferentially increased $CD8^+$ TIL outgrowth as well as favored the expansion of NK cells. Importantly, success rate of TIL growth was increased from 40% to 90% for cultures grown without and with anti-41BB respectively. It was established next that the $CD3^+$ TIL initially grown with anti-41BB could be rapidly expanded at least 1000 fold over two weeks. Finally, the rapidly expanded T cells exhibited anti-tumor capabilities in the context of re-directed killing assays.

Conclusions

In conclusion, further flow cytometry analysis to identify other agonistic and inhibitory targets is needed along with additional *in vitro* and *in vivo* experiments. However, the initial data suggest that TIL therapy for OvCa could be a viable therapeutic option in the future.

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