TUMOUR ASSOCIATED T CELLS FROM HIGH-GRADE SEROUS OVARIAN CARCINOMA PATIENTS RECOGNIZE THE CANCER TESTIS ANTIGEN LACTATE DEHYDROGENASE C

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Although the presence of intraepithelial $CD8^+$ T cells is a positive predictive marker of survival in high grade serous carcinoma (HGSC), the paucity of known tumour-specific T cell targets is a notable barrier to the rational design of immunotherapies for this disease. In our cohort of HGSC cases, we found that the Cancer Testes (CT) antigen lactate dehydrogenase C (LHDC) is expressed in 75% of tumours. Therefore, we hypothesize that LDHC is a potential immunological target in HGSC, and that T cells that recognize LDHC can be activated and used for adoptive immunotherapy. We first sought to examine whether endogenous LDHC specific T cells were present in ascites of HGSC patients. Patients were prioritized based on expression of LDHC within their tumours by qPCR. CD8+ T cell cultures derived from each ascites sample were expanded using a standard Rapid Expansion Protocol. These cultures were screened for reactivity to a peptide library encompassing all possible epitopes of the LDHC protein via interferon-γ ELISpot. Reactive CD8+ T cells were sorted based on antigen-dependent 4-1BB upregulation, further expanded, and used to identify the minimal epitopes recognized. We identified five T cell clones that reacted to LDHC peptides. We are currently evaluating these clones' ability to differentiate between LDHC and its ubiquitously expressed isoform, Lactate Dehydrogenase A. Additionally, we are testing whether the LDHC minimal epitopes are naturally processed by antigen processing and presentation machinery of HGSC tumour cells.

At this time, we can conclude that there are T cells harboured within the patient repertoire which can recognize LDHC. An LHDC specific T cell response within the tumour environment provides strong rationale to develop T cell therapies targeting this antigen in HGSC.