195 STIMULATION OF TUMOR INFILTRATING B-CELLS IMPROVES EX-VIVO TIL EXPANSION FOR MELANOMA IMMUNOTHERAPY

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Background The immunogenic nature of melanoma has been exploited for the development of adoptive transfer of ex-vivo expanded tumor infiltrating lymphocytes (TIL). This adoptive cell transfer therapy has overall response rates of around 50%. Multiple factors may determine the quality of the TIL product including components of the tumor microenvironment. B-cells are frequently found in melanoma metastasis, and display signs of antigen experience. Recently, B-cell tumor infiltration has been associated with improved clinical responses to immune checkpoint inhibitors,[1 2] but their role in TIL therapy remains unexplored. Considering the potential role of B cells, we aim to develop strategies to enhance the quality of TIL products through B-cell stimulation during ex-vivo TIL expansion.

Methods We stimulated melanoma infiltrating B-cells using human recombinant CD40L on the first day of ex-vivo TIL expansion. Thirteen samples were expanded from melanoma tumor single cell suspensions, in high dose IL-2 alone (standard protocol), or in high dose IL-2 plus CD40L. After up to four weeks of expansion, the TIL phenotype was analyzed by flow cytometry.

Results The expansion success rate from the frozen tumor digests was 69% (95% CI: 38.6–90.9%) in the CD40L treatment condition compared to 23% with the standard protocol. Also, TILs cultured in the presence of CD40L expanded to higher numbers than with the standard protocol ($P = 0.02$). Interestingly, most of the samples expanded with CD40L had a significant increase in the percentage of CD4+ T cells ($P = 0.03$), but not to the detriment of the absolute number of CD8+ T cells. Treatment with CD40L increased the percentage of effector memory-like T cells ($P = 0.03$) and of CD39-CD69- T cells ($P < 0.05$), which were recently associated with response to TIL therapy.[3]

Conclusions This preliminary work demonstrates that the stimulation with CD40L at the initiation of TIL culture leads to enhanced TIL expansion and an increase in CD4+ T cells with an effector memory-like and stem-like phenotype. Our group and others have previously described cases of patients who had tumor regression after receiving TIL therapy that were predominantly CD4+ T cells, suggesting that expansion of the CD4+ TIL repertoire may enhance TIL therapy.[4]

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Ethics Approval The study was approved by Advarra IRB, approval number MCC20559.

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