Abstracts

EPI-R™ P2 PROTOCOL PRODUCES A SCALABLE POLYCLONAL TIL PRODUCT WITH A GREATER EXPANSION SUCCESS RATE ACROSS HOT AND COLD TUMORS IN SHORTER CULTURE TIME

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Background Adoptive cell therapy (ACT) with tumor-infiltrating lymphocytes (TIL) can mediate durable responses in advanced solid tumors. One of the challenges with current TIL productions is long duration of culture times (4–6 weeks) that reduce TIL stemness and TCR diversity through progressive differentiation. Literature suggests that shorter culture duration is correlated with longer telomere length, increased stemness, improved persistence, and positive clinical outcomes in metastatic melanoma patients. Therefore, strategies that shorten the culture time without adversely affecting stemness, or polyclonality while maintaining high expansion success rates are warranted. Previously, we have shown that TIL expanded with the Epi-R P1 manufacturing protocols results in TIL with improved stemness, antitumor function, and maintenance of polyclonality. Epi-RTM P2 is an improved TIL expansion process that reduces the TIL culture duration to less than 3 weeks without impacting the quality of TIL.

Methods TIL products were produced from 12 tumor tissues across 3 different tumor types (melanoma, lung and colorectal cancer) treated with or without checkpoint inhibitors (CPI) using the Epi-R P2 and Epi-R P1 protocols. Characteristics of the resulting products (Epi-R P2 and Epi-R P1, respectively) were compared using a matrix of assays involving flow cytometry, co-culturing with autologous tumor cell line, and TCR beta sequencing.

Results Epi-R P2 protocol resulted in significantly higher TIL yields at the end of the first expansion step: Epi-R P2 REP1 phase (8 to 10 days) compared to Epi-R P1 pre-REP phase (10 to 14 days) in 3 different tumor types. After a second expansion step, Epi-R P2 protocol yielded an average of 60 billion T cells. TIL products derived from Epi-R P2 protocols resulted in maintenance of similar preferential skewing of CD8+ T cells compared to Epi-R P1 products and also preserved similar or better stemness qualities. Epi-R P2 significantly reduced terminally differentiated cells and increased the magnitude of most frequent clones present in the baseline tumor. Furthermore, Epi-R P2 process is scalable and can be implemented for manufacturing TIL while maintaining stemness and preservation of putative tumor-reactive clones.

Conclusions Results from research and large-scale Epi-RTM P2 demonstrated successful TIL expansion from both immunologically hot and cold tumors in less than 3 weeks. Compared to the previous Epi-R process, Epi-R P2 maintained a greater proportion of stem-like T cells and increased the magnitude of most frequent clones that were present in the baseline tumor.

REFERENCES


Ethics Approval Research was performed with tissues obtained from patients through a procurement protocol approved by WCG IRB, tracking number 20210857.