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ABSTRACT BODY: Adoptive cell therapy (ACT) of metastatic melanoma with autologous tumor infiltrating lymphocytes (TIL) is clinically effective, but TIL production can be challenging. Initial TIL culture and rapid expansion involves 4 to 6 weeks of culture in 24-well plates, tissue culture flasks and bags. Here we describe a simplified method for initial TIL culture and rapid expansion in gas-permeable flasks. TIL were initially cultured from tumor digests and fragments in 40 mL capacity flasks with a 10 cm2 gas-permeable silicone bottom, G-Rex10. A TIL rapid expansion protocol (REP) was developed using 500 mL capacity flasks with a 100 cm2 gas-permeable silicone bottom, G-Rex100. TIL growth was successfully initiated in G-Rex10 flasks from tumor digests from 13 of 14 patients and from tumor fragments in all 11 tumor samples tested. Enough TIL for REP could be obtained from one G-Rex10 flask (tumor digest) or 3 G-Rex10 flasks (tumor fragments) rather than two 24-well plates. TIL could then be expanded to 8-10 billion cells in a two-step REP which began by seeding 5 million TIL and 500 million irradiated peripheral blood mononuclear cells as feeder cells into a G-Rex100 flask. After 7 days of culture the cells were split and divided equally into 3 G-Rex100 flasks for the second step of TIL REP. This two-step G-Rex100 flask TIL REP was successful in 12 of 14 patients studied. To obtain the 30 to 60 billion cells used for patient treatment we seeded 6 G-Rex100 flasks with 5 million cells and later transferred the TIL into 18 G-Rex100 flasks. Large scale TIL REP in gas-permeable flasks requires approximately 9 to 10 liters of media, about 3 to 4 times less than other methods. In conclusion, TIL initiation and REP in gas-permeable G-Rex flasks require fewer total vessels, less media, less incubator space and less labor than initiation and REP in 24-well plates, tissue culture flasks and bags. TIL culture in G-Rex flasks will facilitate the production of TIL at the numbers required for patient treatment at most cell processing laboratories.