BIOIVT

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WHITE PAPER

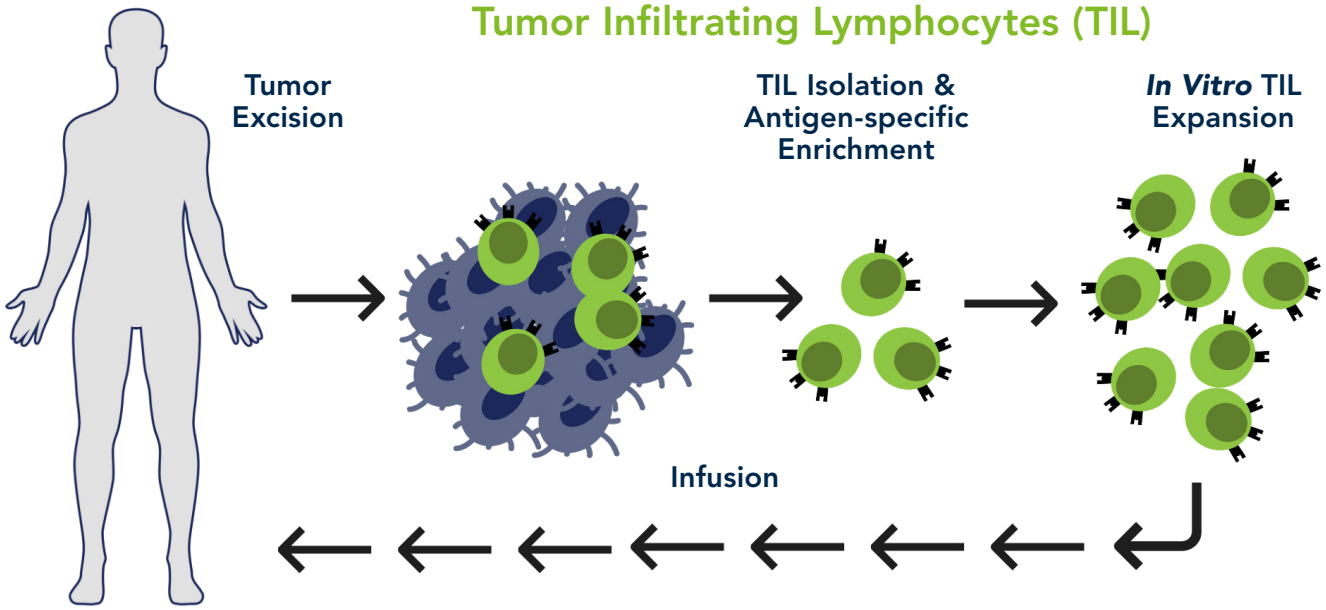
Isolation of Tumor-Infiltrating Lymphocytes From Dissociated Tumor Cells

Introduction

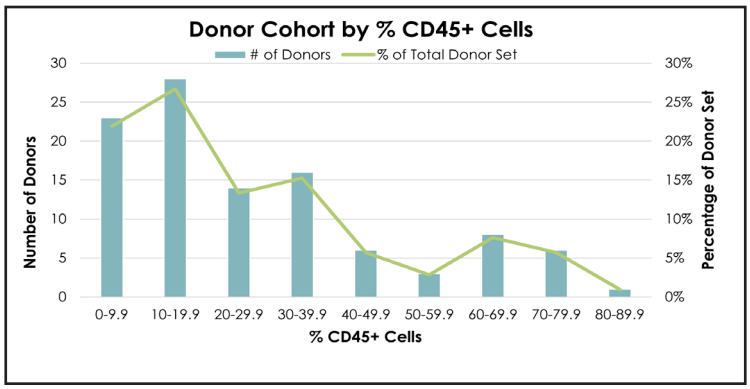
Dissociated Tumor Cells (DTCs) are a single cell suspension dissociated from a solid tumor using digestive enzymes and separated by mechanical force. This offers the flexibility of cryopreserving the cells for on-demand research, as opposed to the regulatory and scheduling restrictions associated with fresh tissue collection and shipment. DTCs are heterogeneous cell populations containing a mixture of both epithelial and fibroblast cells. In addition, they contain lymphoid cell subsets such as T cells, B cells and NK cells which can be easily isolated using standard immunomagnetic selection. As such, they are an invaluable source of tumor-infiltrating lymphocytes (TILs), which are of critical interest for cellular therapies targeting solid tumors.

TILs and the Tumor Microenvironment

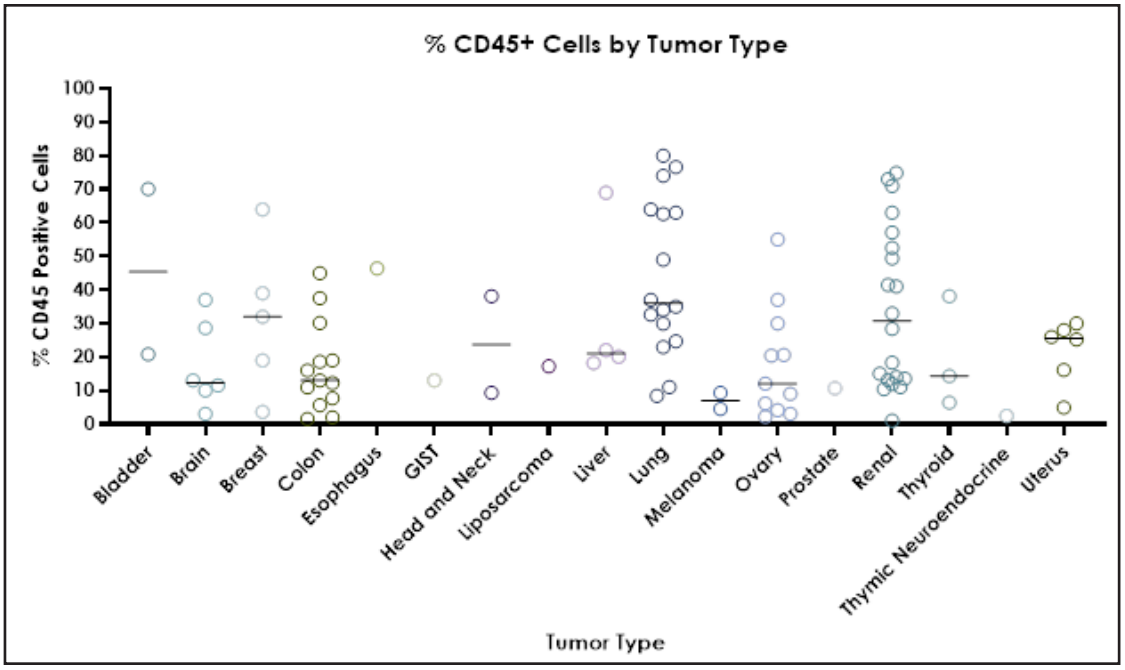
Solid tumors remain an elusive target for researchers, as each tumor microenvironment (TME) is rife with immune-evading signals that dampen the anti-tumor response. For instance, cancer-associated fibroblasts (CAFs) within the tumor may upregulate their expression of fibroblast-activation protein (FAP), resulting in increased tumor growth and reduced accumulation of intra-tumoral T cells.[1] Oncogene-driven expression of cytokines that promote an immunosuppressive environment also starves the TME of tumor-fighting signals.[2] Lymphocytes that proliferate within the tumor, therefore, show a significant advantage over peripheral lymphocytes, improving overall survival rates in cancer patients with higher levels of CD3+, CD4+ and CD8+ TILs.[3] Current TIL therapy consists of *ex vivo* expansion of TILs from resected tumor material with an adoptive transfer into the patient following a lymphodepleting preparative regiment and subsequent support of interleukin-2 (IL-2).[4] With initial successes seen in melanoma patients, the field has expanded significantly to include other solid tumor types.



Characterization of TILs From DTCs



An analysis was performed on BioIVT's DTC products, isolated from a variety of tumors, to assess the TIL populations therein. From a sample of 95 solid tumor donors, there is a high degree of donor-to-donor variability in TIL concentration. On average, solid tumors contain 27.8% CD45+ cells (21.5% standard deviation), with a range from 1.0% to 80.0%.



Broken down by tumor location, the highest CD45+ populations occur in bladder, lung and renal tumors (45.4%, 44.0% and 34.6% respectively). However, even within these tissue types, there exists a high level of donor-dependent variability.

Both DTC cell yield and viability are dependent on the quality of the tissue supplier's operating procedures throughout the production processes. Obtaining high-quality DTCs requires optimization of all facets of the upstream process, including the tissue resection time from the patient (warm ischemic time) and histopathological assessment, shipping and disaggregation times (cold ischemic time.) At BioIVT, we have spent nearly 30 years perfecting our expertise in tissue collection to ensure maximal product quality.

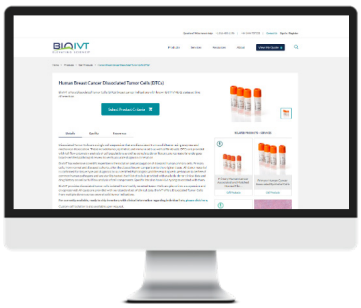
Characterization of TILs From DTCs

Different methods exist for the *ex vivo* expansion of TILs, typically induced by triggering the T cell receptor (TCR) complex through either feeder cells or T cell stimulating growth factors. Further, duration of TIL expansion has been found to give rise to new T cell clones that are barely detected in the originating tumor, likely due to differences in *in vitro* and *in vivo* environments.[5]

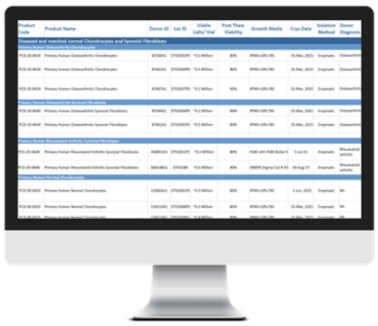
Breakthrough methodologies in single-cell analysis have helped TIL researchers identify T cell clones that maximally react to autologous tumors. Collection methods at BioIVT exist that allow researchers to obtain both DTCs and whole blood peripheral blood mononuclear cells (PBMCs) in a matched set to better compare the epigenetic differences between peripheral lymphocytes and TILs from the same donor. While TIL cell therapies may still be in the early clinical phases of development, BioIVT's technical team is on the cutting edge of this field so that we can best support your research.

BioIVT has a broad collection of DTC lots from a variety of cancer indications.

To learn more or to view available inventory, visit BioIVT.com.



Product Information



Available Inventory

Blog Post

References

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2. Binnewies, M., et al. (2018). Understanding the Tumor Immune Microenvironment (TIME) for Effective Therapy. Nature medicine, 24(5), 541–550.
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5. Poschke, I. C., et al. (2020). The Outcome of *Ex Vivo* TIL Expansion Is Highly Influenced by Spatial Heterogeneity of the Tumor T-Cell Repertoire and Differences in Intrinsic *In Vitro* Growth Capacity between T-Cell Clones. Clinical Cancer Research, 26(16), 4289–4301.

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About BioIVT

BioIVT is a leading global provider of research models and value-added research services for drug discovery and development. We specialize in control and disease-state biospecimens including human and animal tissues, cell products, blood and other biofluids. Our unmatched portfolio of clinical specimens directly supports precision medicine research and the effort to improve patient outcomes by coupling comprehensive clinical data with donor samples. And as the premier supplier of hepatic products, including hepatocytes and subcellular fractions, BioIVT enables scientists to better understand the pharmacokinetics and drug metabolism of newly discovered compounds and their effects on disease processes. By combining our technical expertise, exceptional customer service, and unparalleled access to biological specimens, BioIVT serves the research community as a trusted partner in ELEVATING SCIENCE®.

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