



Laboratory Services

Important Test Announcement

T Cell Senescence and Exhaustion Panel with TBNK by Flow Cytometry (TSEPP)

New Test Code: **TSEPP**

Live Date: **3/24/2026**

- **Methodology:** Flow Cytometry
- **Performed:** Monday - Friday
- **Turnaround Time:** 72 hours
- **Specimen Required:** EDTA
 - **Specimen Preparation:** Do not centrifuge, do not refrigerate or freeze
 - **Stability:** Whole blood (EDTA): 48 hours, room temperature
 - **Storage/Transport/Temperature/Conditions:** Transport Whole Blood EDTA samples at room temperature. Do not refrigerate.
 - **Unacceptable Conditions:** Wrong collection tubes, not received within specified time frame, refrigerated samples, clotted samples
 - **Comments:** TSEPP will include the TBNK test.

Clinical Utility:

The primary objective of this assay is to distinguish between two distinct states of T-cell dysfunction: exhaustion and senescence. While exhausted T cells (defined by PD-1 and LAG-3 markers) are characterized by a reversible loss of effector function due to chronic antigen exposure, senescent T cells (defined by the loss of CD28 and expression of CD57/KLRG-1 markers) are those, which have entered a state of irreversible cell-cycle arrest. These senescent subsets are often not inert but adopt a Senescence-Associated Secretory Phenotype (SASP). The SASP is a metabolically hyperactive program where cells transform into potent sources of systemic inflammation, secreting a complex cocktail of pro-inflammatory cytokines (such as IL-6, TNF- α , and IL-1 β), growth factors, and matrix metalloproteinases.

This assay will focus specifically on the following populations: PD-1+, HLA-DR+PD-1+, CD45RO+HLA-DR+ PD-1+, CD28-, CD57+, CD28-CD57+, CD28+CD57+, KLRG-1+, LAG-3+, CD45RO+PD-1+KLRG-1+, and CD45RO+PD-1+LAG-3+, within CD4+ and CD8+ T cell subsets.

In clinical contexts such as Inborn Errors of Immunity (IEIs), malignancies, chronic viral infections and immune dysregulation, the SASP creates a self-sustaining "amplification loop". These secretions can induce "paracrine senescence" in neighboring healthy cells, degrade tissue architecture, and recruit immunosuppressive myeloid cells (MSCs) for example, into the tumor microenvironment. This process results in a state of chronic "inflammaging", which drives multi-organ dysfunction and can promote tumor immune evasion. Furthermore, the presence of a high SASP-burden significantly diminishes the efficacy of T-cell-directed therapies like CAR-T and BiTEs, as the systemic inflammatory environment can trigger premature exhaustion in the therapeutic cells or lead to severe toxicities such as Cytokine Release Syndrome (CRS).

The frequency of exhausted and senescent T cells increases with age in immunologically healthy individuals, as well as with persistent antigen exposure and TCR stimulation during chronic infections, immune dysregulation, and malignancies. Distinguishing between senescence and exhaustion is vital for understanding the immune response. Senescent T cells are limited by their replicative capacity while exhausted T cells are identified by their progressive upregulation of inhibitory receptors. PD-1 and LAG-3 are "checkpoint" molecules, which act as "brakes" on the immune response following chronic antigenic exposure. High expression of these exhaustion molecules signals a state of functional "hyporesponsiveness", which is important to discriminate because unlike senescence, exhaustion can often be partially reversed (e.g. checkpoint inhibitors). Further, the ratio of CD28-senescent to CD28+ effector cells can serve as a biomarker for inflammaging, predicting risk for opportunistic infections or likelihood of responding poorly to vaccines.

Reference Intervals:

This test will include relevant - adult or pediatric (based on age of patient) reference intervals, for all reported subsets within the report. Additionally, an interpretive report will be provided.

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If you have any additional questions about [T Cell Senescence and Exhaustion Panel with TBNK by Flow Cytometry](#), please refer to the [Laboratory Test Directory](#) or call Client Services at 614-722-5477.