

Research: Leveraging Immunometrics to Achieve Minimally Invasive Prognostic Information for Hematopoietic Neoplasms

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Budget: **\$2000**
Flow cytometry antibodies and reagents
Costs associated with histology slide acquisition and review

Traditionally, the power of pathology to provide prognostic information has lagged considerably behind its ability to provide initial diagnoses. Particularly for hematopoietic neoplasms, this shortfall has generated a need for serial biopsies to trace the course of a patient's illness, often subjecting patients to a number of invasive, painful procedures. Current prognostic scoring systems for many hematopoietic cancers often remain in active debate and lack universal adoption. These shortfalls underscore an urgent need for novel approaches to prognostication from the laboratory that are both more predictive and rely on less invasive methods. **We hypothesize that monitoring of systemic immune responses to such neoplasms—referred to here as immunometrics—can provide an orthogonal approach to disease monitoring and prediction.** Two hematopoietic neoplasms—cutaneous T cell lymphoma (CTCL) and lymphoplasmacytic lymphoma (LPL)—are in particular need of clarification, given the absence of widely accepted prognostic indices and widely variable clinical outcomes among patients.

We focus on myeloid-derived suppressor cells (MDSCs), a recently discovered population of immunosuppressive innate immune cells related to neutrophils and monocytes, because their expansion in a number of solid tumor settings have correlated reliably with poorer patient outcomes. Whether circulating MDSCs in the bloodstream relates to or predicts disease stage or progression in CTCL or LPL remains largely unexplored. **Our objectives are to use flow cytometric techniques to quantify and track MDSC frequency in the peripheral blood of patients with CTCL and LPL, associate these frequencies with initial clinical stage, and correlate them with clinical progression.** Our preliminary data suggests that expansion of bloodstream MDSCs (compared with healthy controls) corresponds with CTCL disease stage, even while the disease remains localized to the skin (Fig. 1). We intend to verify and expand upon these results through pursuit of the following independent aims.

Aim 1: To verify and expand the circulating MDSC analyses of our cohort of CTCL patients at varying disease stages and clinical treatment states, compare these results with skin biopsy histology, and correlate initial MDSC frequency with disease progression kinetics.

Aim 2: To assess the generalizability of circulating MDSC immunometrics through application of similar methods to the peripheral blood of lymphoplasmacytic lymphoma patients, another hematopoietic neoplasm with currently poor prognostic approaches and previously demonstrated to exhibit tissue-localized MDSC expansions.

Completion of these aims may generate a novel, minimally invasive approach to providing prognostic information to patients with highly unpredictable clinical outcomes in a tractable manner achievable within one year or less.

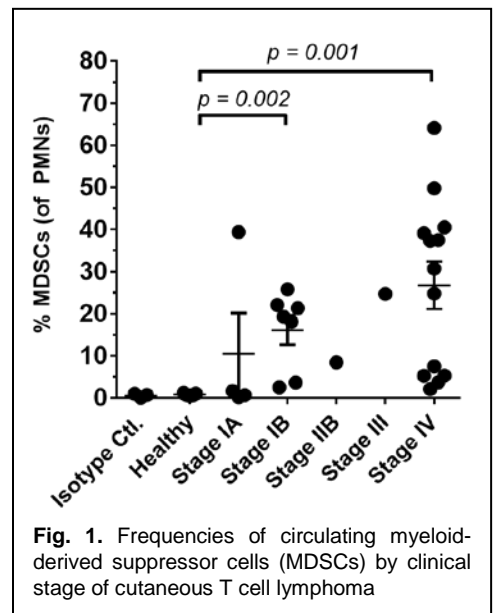


Fig. 1. Frequencies of circulating myeloid-derived suppressor cells (MDSCs) by clinical stage of cutaneous T cell lymphoma