REGULAR ARTICLE

blood advances

A germinal center–associated microenvironmental signature reflects malignant phenotype and outcome of DLBCL

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Key Points

- The DLBCL microenvironment signature scoring system was established using nCounter-based profiling of GC-related microenvironmental genes.
- DMS scores stratified DLBCL patients with different prognosis independently of existing prognostic models.

Diffuse large B-cell lymphoma (DLBCL) is the most common B-cell malignancy, with varying prognosis after the gold standard rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). Several prognostic models have been established by focusing primarily on characteristics of lymphoma cells themselves, including cell-of-origin (COO), genomic alterations, and gene/protein expressions. However, the prognostic impact of the lymphoma microenvironment and its association with characteristics of lymphoma cells are not fully understood. Using the nCounter-based gene expression profiling of untreated DLBCL tissues, we assess the clinical impact of lymphoma microenvironment on the clinical outcomes and pathophysiological, molecular signatures in DLBCL. The presence of normal germinal center (GC)-microenvironmental cells, including follicular T cells, macrophage/dendritic cells, and stromal cells in lymphoma tissue indicates a positive therapeutic response. Our prognostic model, based on quantitation of transcripts from distinct GC-microenvironmental cell markers, clearly identified patients with graded prognosis independently of existing prognostic models. We observed increased incidences of genomic alterations and aberrant gene expression associated with poor prognosis in DLBCL tissues lacking GC-microenvironmental cells relative to those containing these cells. These data suggest that the loss of GC-associated microenvironmental signature dictates clinical outcomes of DLBCL patients reflecting the accumulation of "unfavorable" molecular signatures.

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of B-cell non-Hodgkin lymphomas (NHL) with heterogeneous clinicopathologic features. By performing global gene expression profiling (GEP), Alizadeh et al have grouped DLBCL cases into 2 subtypes based on the cell-of-origin (COO) of lymphoma cells. The germinal center B-cell-like (GCB) type exhibits the signature of B cells in the germinal center (GC) of normal secondary lymphoid organs, while lymphoma cells of the activated B-cell (ABC)-like type resemble post-GC B cells that transit from the GC for plasmacytic differentiation.[1] Among DLBCL patients treated with multiagent chemotherapy consisting of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), patients with ABC-type disease generally show significantly

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The full-text version of this article contains a data supplement.