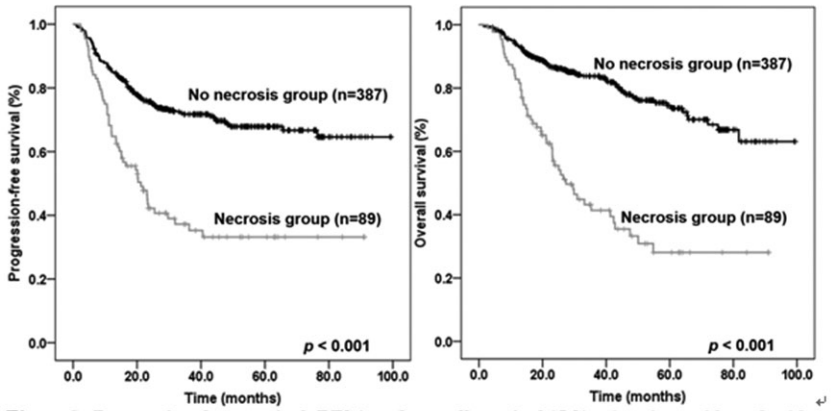

Figure 1. Progression-free survival (PFSs) and overall survival (OS) of patient with and without tumor necrosis. PFS and OS of the tumor necrosis group were significantly lower than the nonnecrosis group (PFS, $p < 0.001$; OS, $p < 0.001$).

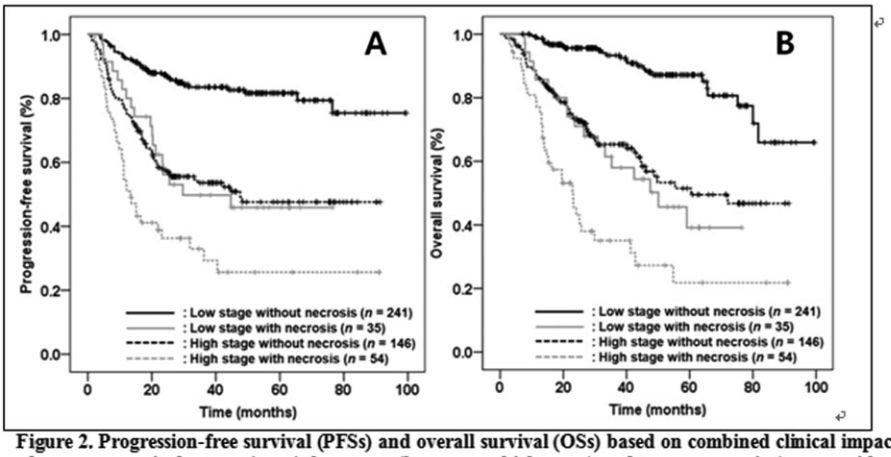

Figure 2. Progression-free survival (PFSs) and overall survival (OSs) based on combined clinical impacts of two prognostic factors: Ann-Arbor stage (low versus high stage) and tumor necrosis (versus without necrosis). PFS and OS of the group having low stage without necrosis were significantly higher than other patient groups (PFS, $p = 0.001$; OS, $p = 0.004$). Survival of high stage patients with necrosis were significantly lower than other groups (PFS, $p = 0.005$; OS, $p = 0.009$). However, low stage patients with necrosis had similar survival to as high stage patients without necrosis (PFS, $p=0.687$; OS, $p= 0.225$).

cyclophosphamide, doxorubicin, vincristine, and prednisone) therapy. Eighty-nine (18.7%) patients had TN at diagnosis. Patients with TN had a progression-free survival (PFS) and overall survival (OS) of 39.3% and 46.7%, whereas patients without TN had a PFS and OS of 73.4% and 82.6%. Adverse clinical factors of poor Eastern Cooperative Oncology Group performance status ≥grade 2 (P = .005), elevated lactate dehydrogenase ratio >1 (P < 0.001), advanced Ann Arbor stage (P = .002), and bulky disease (P = .026) were more prevalent in the TN group than the non-TN group. Cox regression model analysis revealed TN as an independent prognostic factor for PFS and OS in DLBCL (PFS, hazard ratio [HR] = 1.967, 95% confidence interval [CI], 1.399-2.765, P < .001; OS, HR = 2.445, 95% CI, 1.689-3.640, P < .001). The results indicate that TN could reflect adverse clinical features and worse prognosis in DLBCL patients receiving R-CHOP therapy.

Keywords: diffuse large B-cell lymphoma (DLBCL); prognostic indices; R-CHOP

317 MICROENVIRONMENT EXPRESSION IN DIFFUSE LARGE B-CELL LYMPHOMAS

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Diffuse large B-cell lymphoma (DLBCL), the most common type of non-Hodgkin lymphoma, is recognized as a heterogeneous disease with distinct molecular subtypes derived from different stages of B-cell differentiation. The contribution of the tumor microenvironment to the pathogenesis and tumor survival of DLBCL is poorly understood. However, several recent studies have yielded intriguing findings and shed some light on the possible roles of the microenvironment.

In this retrospective study, data from 29 patients diagnosed with DLBCL between 2009 and 2013 were reviewed. All patients had pathologically confirmed DLBCL and had been treated with the R-CHOP regimen. In these patients, we correlated the expression of CD3 staining for T cells, tryptase staining for mast cells, CD68 for tumor-associated macrophages (TAMs), and CD31 staining for blood vessels.

CD68 and tryptase expression, as well as MVD, were increased in chemo-resistant patients compared to chemosensitive patients. Tryptase expression showed a positive correlation with MVD, supporting a role for mast cells in DLBCL tumor angiogenesis, while the CD68 correlation with MVD was not significant, indicating a different role for TAMs rather than angiogenesis in DLBCL. A statistically significant difference was observed in the expression of CD3 in patients with bulky disease. Specifically, a higher expression of CD3 was observed in nonbulky disease patients (mean expression 52.91%, n = 20) compared to bulky disease patients (mean expression 34.9%, n = 9), *P* value < .05. The reduction in T cells in bulky disease patients contributes to loosen the immune control over the tumor, resulting in an increased cell proliferation, leading to large tumor cell masses, which are predictive of poor prognostic and clinical outcomes. CD3 showed a positive correlation with tryptase and MVD, while multiple regression analysis efficaciously predicted MVD depending on CD3 and tryptase as predictors, supporting a complex interplay between these cells in sustaining tumor angiogenesis in DLBCL patients.

The improved understanding of tumor biology and of the role of the tumor microenvironment has led to advances in the diagnosis, classification, prognostics, as well as novel treatments of patients with hematologic malignancies. In particular, translational research, leading to drugs that target the interaction between the tumor microenvironment and malignant cells, has provided many promising new approaches to cancer therapy. Ongoing dynamic and correlation studies of tumor biology and the contribution of the tumor microenvironment should be promoted in the context of novel drug development in order to identify optimal therapies for various lymphomas and improve the curability of these diseases.

Keywords: diffuse large B-cell lymphoma (DLBCL)

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EBV INFECTION PROMOTES TUMOR INFILTRATING LEUCOCYTE AND IMMUNE ESCAPE IN PLASMABLASTIC LYMPHOMA ACCORDING TO GENE EXPRESSION PROFILING

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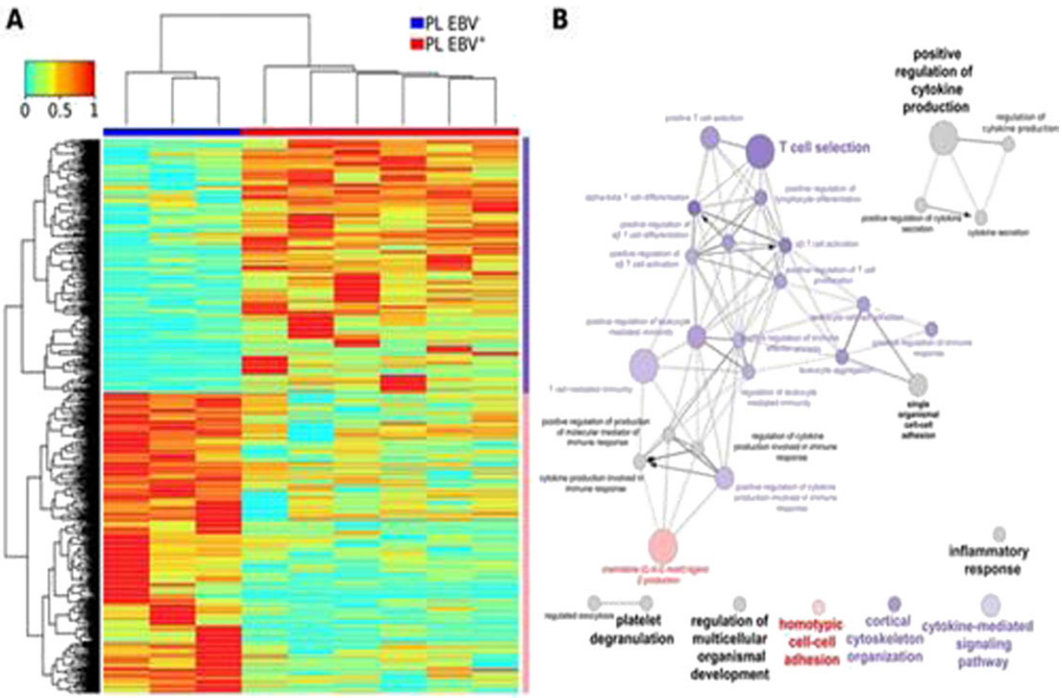

Figure 1: Molecular profiling and pathways analysis in EBV⁺ and EBV⁻ plasmablastic lymphomas. **A**: Unsupervised hierarchical clustering of 1213 genes detected as differentially expressed in EBV⁻ (n=3, blue bar) and EBV⁺ (n=6, red bar) PL. The color bar denotes z-score adjusted expression values, cyan used for lower expression and red for higher expression levels. Datas are represented in a grid format in which each column represents a single patient, and each row a single gene. The dendrogram shows the degree to which the expression pattern of each gene is correlated with that of the other genes. **B**: Functional network of the differentially expressed genes in EBV⁻ and EBV⁺ PL, using the GO biological process terms. The node circle size represents the number of genes in the pathway and the node circle colors (pink and purple) correspond to the genes clustering (genes up-regulated in EBV⁻ or EBV⁺ PL respectively).