

<https://doi.org/10.7124/bc.000B78>

**L.M. Kovalevska¹, S.A. Lytvyn¹, A.S. Matveeva¹,
I.B. Tytorenko², I.D. Holodnyuka³, I.A. Kryachok²**

¹ R.E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, NASU,
45 Vasylykivska str, Kyiv-22, 03022, Ukraine

² National Cancer Institute,
43 Vasylykivska str, Kyiv-22, 03022, Ukraine

³ Riga Stradiņš University Research Centre
5, Rātsupītes iela, Riga, Latvia, LV-1067
krey1@yahoo.com

CHEMOKINE DYSREGULATION AND TRANSCRIPTIONAL COLLAPSE OF B-CELL DIFFERENTIATION IN CHRONIC LYMPHOCYTIC LEUKEMIA

Background. Chronic lymphocytic leukemia (CLL), the most common adult leukemia, arises from clonal expansion of dysfunctional CD5⁺ B lymphocytes and remains incurable despite modern targeted therapy. A central feature is active remodeling of the tumor microenvironment, which sustains leukemic survival and shields the clone from immune clearance. **Methods.** This study profiled the coordinated expression of three chemokines (CCL3, CCL4, CCL5), β 2-microglobulin (B2M), and five B-cell differentiation transcription factors in peripheral blood B-lymphocytes from 34 CLL patients versus age-matched healthy donors, using RT-qPCR and the 2^{- $\Delta\Delta C_t$} method. **Results.** CCL3 (MIP-1 α) and CCL4 (MIP-1 β) were significantly upregulated, consistent with tonic and antigen-driven BCR-NF- κ B signaling. Via CCR1/CCR5 they recruit T-regulatory and nurse-like cells that deliver pro-survival signals (APRIL, BAFF, IL-6), confirming active immunosuppressive niche construction. In contrast, CCL5 and B2M were downregulated. Reduced CCL5 – primarily a T/NK-cell product – reflects impaired cytotoxic recruitment and T-cell exhaustion, while B2M loss compromises MHC class I surface display and antigen presentation. Together they form a dual immune-evasion mechanism: diminished effector recruitment and reduced target recognition. A hierarchically graded suppression of differentiation transcription factors was observed (2- to 15.5-fold). The earliest-acting regulators were most affected – EBF1 (15.5-fold) and PU.1 (14-fold) – indicating dismantling of core B-lineage identity. BLIMP1 (4-fold) explains the block in terminal plasma-cell maturation, while IRF8 (3.5-fold) and IRF4 (2-fold) consolidate arrest at intermediate stages. The gradient – deepest at progenitor-commitment factors and milder downstream – suggests the transcriptional block acts most forcefully on B-lineage identity itself, favoring sustained self-renewal over terminal maturation. **Conclusions.** CLL B-lymphocytes run a coordinated, mechanistically linked dual program of immune evasion and differentiation arrest. The CCL3/CCL4-CCR5 pathway (targetable by repurposed CCR5 antagonists), B2M loss (relevant to CAR-T responsiveness), and EBF1/PU.1 restoration as a differentiation-induction strategy emerge as actionable therapeutic directions. **Fundings.** Supported by NRFU grant No. 0124U003787, “Activation of signaling cascades for elimination of transformed B-cells in CLL”.

Keywords: CLL, chemokine, transcription factors, B-lymphocytes.

Received: 06.07.2026; Accepted: 08.09.2026; Published: 29.09.2026

Citation: Kovalevska L.M., Lytvyn S.A., Matveeva A.S., Tytorenko I.B., Holodnyuka I.D., Kryachok I.A. (2026) Chemokine dysregulation and transcriptional collapse of B-cell differentiation in chronic lymphocytic leukemia. *Biopolymers & Cell*, Special issue(42), 61. <https://doi.org/10.7124/bc.000B78>

© Publisher PH "Akademperiodyka" of the NAS of Ukraine, 2026. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited