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# Chronic lymphoproliferative disorder of NK cells with *TNFAIP3* and *DNMT3A* mutations

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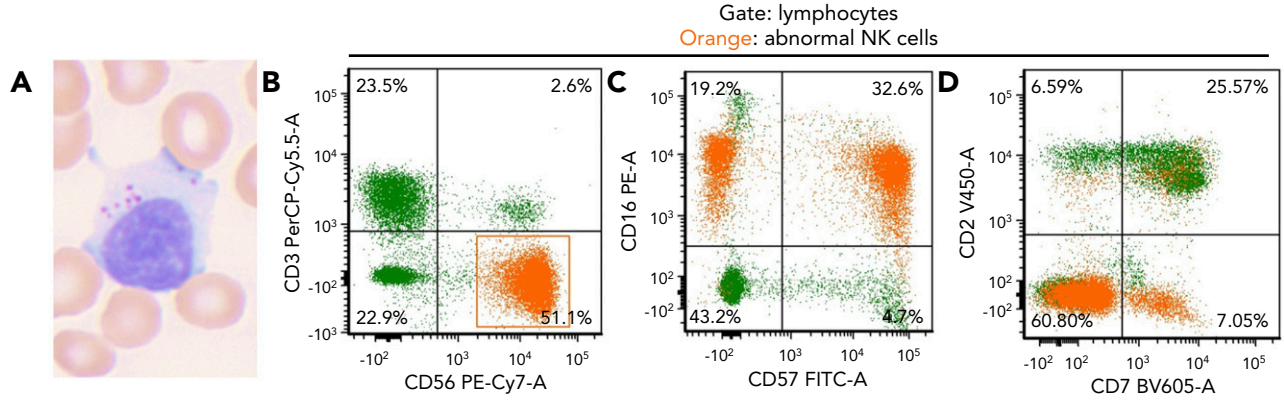


An 82-year-old woman presented with a history of lung and breast cancer, both treated surgically, and persistent asymptomatic lymphocytosis for 8 years. Peripheral blood showed increased large granular lymphocytes without other abnormalities (white blood cell count, 10.5 × $10^9$/L; neutrophils, 47.8%; lymphocytes, 39.8%; monocytes, 8.6%; eosinophil, 3.2%; basophil, 0.6%) (panel A; Wright-Giemsa stain, original magnification ×60 objective, ×600 total magnification). Flow cytometry showed an abnormal natural killer (NK) cell population, 26% of leukocytes (2.7 K/μL), expressing CD56, CD16, subset CD57, minor subset CD7, and negative for CD3, CD2, and CD5 (panels B-D; orange). This NK population was identified 4 years prior and was thought to be due to a "reactive etiology." Targeted mutational analysis (Stanford Actionable Mutation Panel for Hematopoietic and Lymphoid Malignancies) of the peripheral blood revealed *TNFAIP3 p.R278fs*, *DNMT3A p.? (c.856-2A>G)* and *TP53 p.P177L* mutations with variant allele frequencies of 8%, 22%, and 4%, respectively. Mutations in *STAT3* or *STAT5B* were not identified.

Chronic lymphoproliferative disorder of NK cells (CLPD-NKs) shares morphologic features with reactive NK proliferations; thus, molecular techniques are often required to make a definitive diagnosis. This case of CLPD-NKs with *TNFAIP3* and *DNMT3A* mutations is the second reported case of CLPD-NKs with *TNFAIP3* mutation and highlights that CLPD-NKs, like T-cell large granular lymphocytic leukemia (T-LGLL), can show coexisting myeloid-associated mutations. It is unclear if the coexisting *DNMT3A* and *TP53* mutations are within myeloid or NK cells to suggest concurrent CLPD-NKs and clonal hematopoiesis of indeterminate potential, or CLPD-NKs with myeloid-associated mutations, both phenomena reported to occur in T-LGLL.



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