Repurposing CD19-directed immunotherapies for pediatric t(8;21) acute myeloid leukemia

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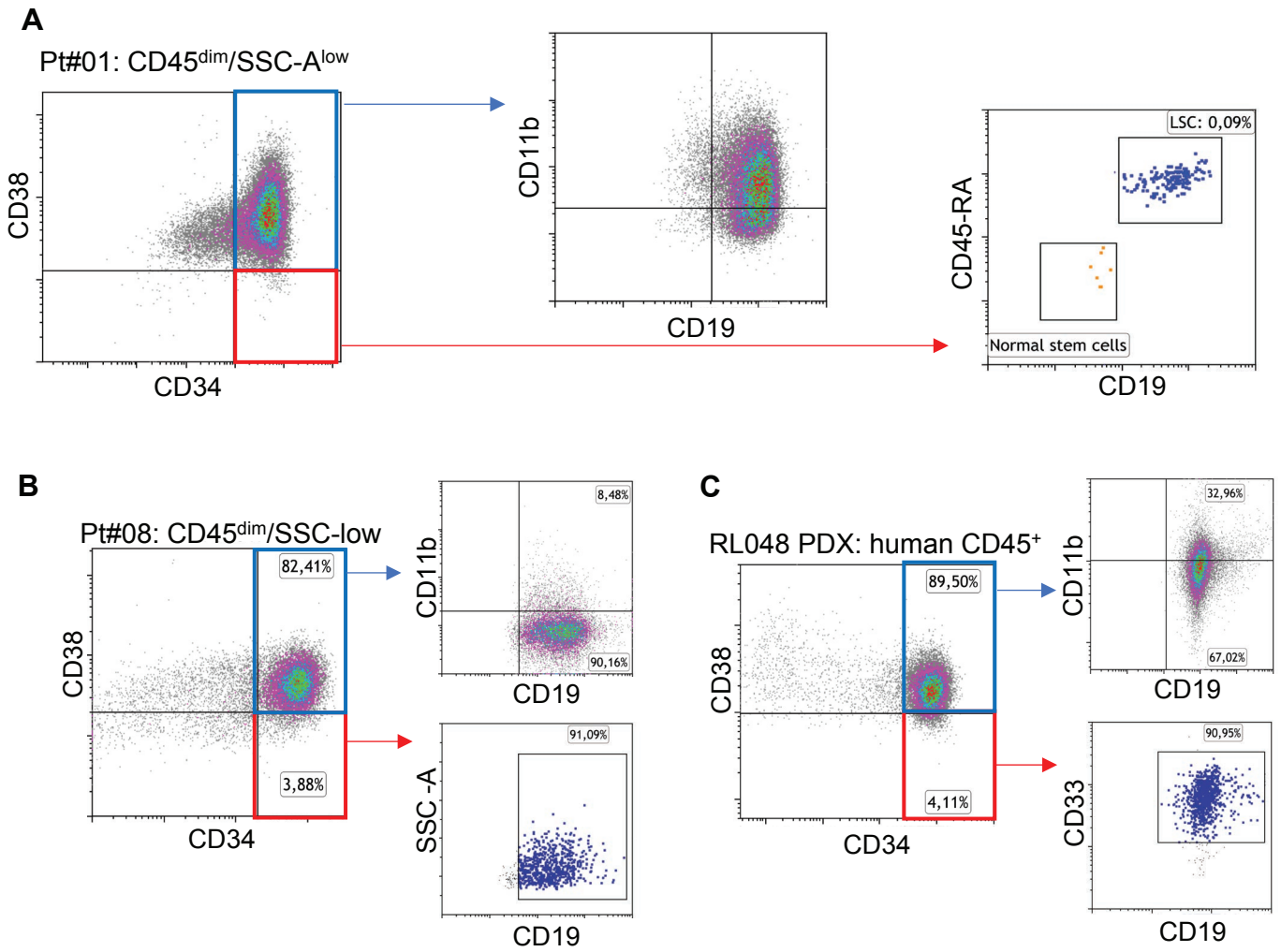
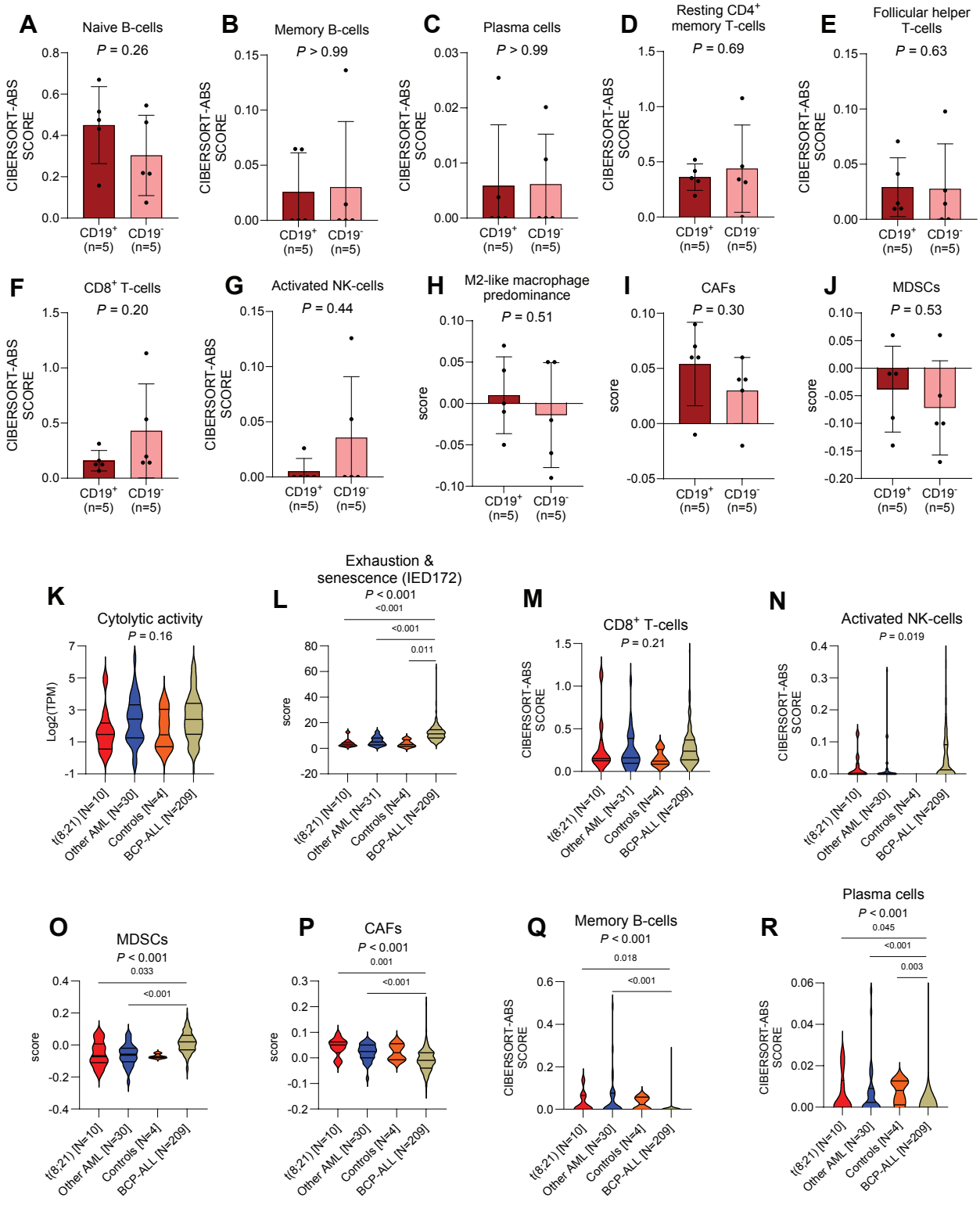
https://doi.org/10.3324/haematol.2024.285707

Received: April 18, 2024.
Accepted: July 30, 2024.
Early view: August 8, 2024.

Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure legends

Supplementary Figure 1. CD19-expression on AML subpopulations. (A) CD19-expression among putative leukemic stem cells (LSCs; $CD34^+CD38^-CD45RA^+$) and more mature subpopulations ($CD34^+CD38^+CD11b^+$, $CD34^+CD38^+CD11b^-$) from patient #01. (B) CD19-expression among $CD34^+CD38^-$ and more mature subpopulations ($CD34^+CD38^+CD11b^+$, $CD34^+CD38^+CD11b^-$) from patient #08. (C) CD19-expression among $CD34^+CD38^-$ and more mature subpopulations ($CD34^+CD38^+CD11b^+$, $CD34^+CD38^+CD11b^-$) from RL048 PDX cells.

Supplementary Figure 2. Characterization of the bone marrow immune microenvironment of t(8;21) AML using immunogenomic analyses. (A-J) Comparison of the deconvoluted absolute (ABS) abundance of various cell populations among $CD19^+$ and $CD19^-$ t(8;21) AML. Data are presented as mean with standard deviation. The Mann-Whitney test was used to test for statistical differences between groups. (K-R) Comparison of gene signature scores (cytolytic activity[1]: *GZMA, GZMB, PRF1, GNLY, GZMH* (K) and IED172: 172-gene immune effector dysfunction signature[2] (L)) and the absolute abundance of various cell populations among t(8;21) AML patients, AML patients with other cytogenetic alterations, non-leukemic controls, and BCP-ALL patients (all treatment-naïve). Data are presented as median with quartiles and range. Kruskal-Wallis test with Dunn's post-hoc test is performed for multiple comparisons. In case multiple *P* values are shown, the upper one indicates the result of the Kruskal-Wallis test and the lower one(s) the result of Dunn's test. M2-like macrophage predominance: ratio of M2- to M1-like macrophages; NK: natural killer; MDSC: myeloid-derived suppressor cell; CAF: cancer-associated fibroblast.

References

1. Dufva O, Pölönen P, Brück O, et al. Immunogenomic landscape of hematological malignancies. Cancer Cell 2020;38:380-399. e13.

2. Rutella S, Vadakekolathu J, Mazziotta F, et al. Immune dysfunction signatures predict outcomes and define checkpoint blockade–unresponsive microenvironments in acute myeloid leukemia. The Journal of Clinical Investigation 2022;132.

(Reference 14 and 15, respectively, in the main file)