# (PS1581) A MULTI-OMICS PLASMACYTOID DENDRITIC CELL SIGNATURE PREDICTS PROGNOSIS AND REFINES RISK STRATIFICATION IN ACUTE MYELOID LEUKEMIA

**Topic:** 03. Acute myeloid leukemia - Biology & translational research

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## Background

Although the European Leukemia Net (ELN) 2022 risk stratification system provides a framework for precise diagnosis and treatment of acute myeloid leukemia (AML), its genetic-based stratification still fails to fully account for the clinical heterogeneity observed among patients. The tumor immune microenvironment (TME) plays a crucial role in disease progression and treatment response, potentially harboring important complementary information. Among TME components, plasmacytoid dendritic cells (pDCs) exert dual functions in tumor immunity, yet their prognostic significance in AML remains unclear.

## Aims

Our aim is to integrate immune features to optimize the AML prognostic risk stratification system.

## Methods

We collected bone marrow samples at diagnosis from 8 patients with AML who received the ABC-14 regimen (azacitidine, venetoclax, chidamide) at Guangdong Provincial People's Hospital between March 2023 and November 2024. Based on bone marrow assessment after two cycles of induction chemotherapy, patients were classified as complete remission (CR, n=3) or non-CR (n=5). All participants provided written informed consent, and the study was approved by the ethics committee (No.:KY-N-2022-103-01). We integrated our data with those of 13 AML patients from the GSE198681 dataset, who received "3+7" induction chemotherapy (Table 1). After single-cell analysis identified an adverse pDC subset (Fig.1A), we applied five machine learning algorithms to select 7 prognostic genes and constructed the GDPH score. This score was validated for its association with overall survival (OS), chemotherapy response, and immune features.

*Table1 Baseline Characteristics of AML Patients by Treatment Response*

| Characteristics | All patients (n = 21) | Non-CR group (n = 10) | CR group (n = 11) | P value |
|---|---|---|---|---|
| **Age, years [median ]** | 58 (45-63) | 60 (50-62.8) | 53 (38-61.5) | 0.585 |
| **Gender** | | | | |
| Male | 12 (57.1%) | 8 (80%) | 4 (36.4%) | 0.0805 |
| Female | 9 (42.9%) | 2 (20%) | 7 (63.6%) | |
| **Leukocytes, $\times 10^9$/L [median]** | 8.1 (3.2-45.3) | 6.1 (3.4-20.5) | 35.1 (4.6-69.9) | 0.379 |
| **Blasts in marrow, % [median ]** | 67.5 (45-75) | 69 (57.4-79) | 48 (44.2-71.8) | 0.409 |
| **FAB classification** | | | | |
| M0 | 2 (9.5%) | 1 (10%) | 1 (9.1%) | 1 |
| M1 | 1 (4.8%) | 0 (0%) | 1 (9.1%) | |
| M2 | 15 (71.4%) | 8 (80%) | 7 (63.6%) | |
| M4 | 1 (4.8%) | 0 (0%) | 1 (9.1%) | |
| tAML | 2 (9.5%) | 1 (10%) | 1 (9.1%) | |
| **Cytogenetics risk** | | | | |
| Adverse | 11 (52.4%) | 6 (60%) | 5 (45.5%) | 0.67 |
| Intermediate | 10 (47.6%) | 4 (40%) | 6 (54.5%) | |

## Results

The GDPH score robustly stratified patients into high- and low-risk groups with significantly distinct overall survival across training and validation cohorts(Fig.1B). The score also exhibited significant predictive value for response to induction chemotherapy (AUC > 0.7, 95% CI: 0.650–0.772, P < 0.001)(Fig.1C). Notably, this model extended beyond conventional ELN2022 stratification by uncovering a high-risk subgroup concealed within the favorable-risk category (HR = 4.15, 95% CI: 1.62–10.60, P = 0.003) and survival outcomes comparable to those of ELN2022 intermediate/adverse groups(Fig.1D). Heterogeneity in the immune microenvironment between risk groups suggested LAG3 as a potential immunotherapeutic target(Fig.1E).

## Summary/Conclusion

This study represents the first construction of a pDC-based prognostic and therapeutic response prediction model for AML, offering new insights into AML risk re-stratification and the formulation of immunotherapy strategies.

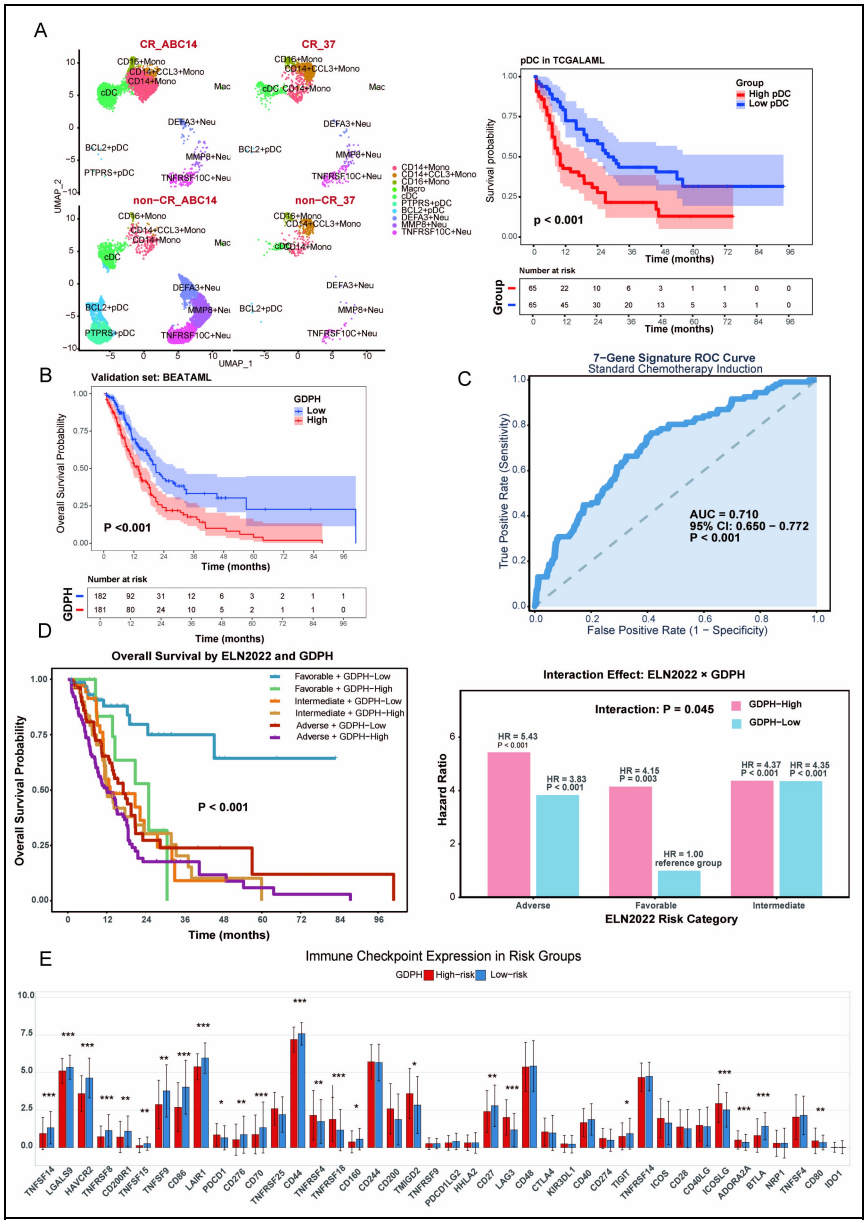


Fig. 1. Construction and validation of the pDC-based prognostic model. (A) Single-cell profiling identifies pDC subsets associated with adverse prognosis in AML. (B) Kaplan–Meier survival curves for GDPH_High vs.GDPH_Low patients in the BEAT-AML validation cohort. (C) ROC curve of the 7-gene signature for predicting response to induction chemotherapy. (D) Forest plot showing hazard ratios for mortality within each ELN2022 risk category, identifying a high-risk subgroup within the ELN2022-favorable-risk group (HR = 4.15, interaction P = 0.045). (E) Bar plot comparing expression levels of 42 immune checkpoint molecules between GDPH_high and GDPH_low subgroups.