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617.ACUTE MYELOID LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

Predicting Molecular Alterations from Blast Morphology of Acute Myeloid Leukemia Bone Marrow Aspirate Smears Using Machine Learning

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Introduction

Acute Myeloid Leukemia (AML) has enormous molecular and cytogenetic heterogeneity. Evaluation of bone marrow morphology is essential in the diagnosis of AML, however, it requires significant training and there is wide inter-observer variability. Genomic testing has been progressively relied on for AML classification, ultimately helping to dictate prognosis and guide clinical management. However, genomic testing, if performed, can be subject to prolonged turnaround times and lacks clinical penetration in low-resource settings. To overcome these challenges, we aimed to evaluate the feasibility of predicting clinically relevant genomic alterations from bone marrow cell morphology using a machine learning approach.

Methods

We scanned 799 Wright-stained bone marrow aspirate smear slides, made for routine patient care, for subjects diagnosed with AML. These subjects were linked to clinical data, including pertinent cytogenetic/molecular alterations and subclassified as cases with mutated Nucleophosmin 1 (*NPM1*), those with *TP53* mutations and those with myelodysplastic-related changes (AML-MRC). Whole slide images were screened for containing spicules and blasts, and were analyzed to detect 180 million cells (blasts and non-blasts) excluding hemodilute and particle regions. We developed a multi-instance model to predict patient molecular subtype by repeatedly sampling 512 cells from each slide and using these to train a classifier that weights cells with morphology relevant to subtype. We also trained a model to predict *NPM1* and *TP53* mutations independently, as well as other frequent variants reported to impact blast morphology.

Results

Performance in predicting NPM1/TP53/AML-MRC subtype was moderate (0.80 AUROC). Performance of the single-gene model varied, with NPM1 having the highest performance (0.85 AUROC) followed by IDH (0.80 AUROC), FLT3 (0.79 AUROC) and TP53 (0.62 AUROC).

Conclusions

This study provides promising preliminary results for prediction of genetic alterations in AML in a large-scale single-institution dataset. Interestingly, this method did not rely on the classification of individual cells, avoiding the need for manually collecting annotations to train a blast cell classifier. Future work will evaluate the morphology of cells attended by the multi-instance model, and explore the value of enriching sampled cells with blasts using cell classification methods.

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