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ORAL ABSTRACTS

803.EMERGING TOOLS, TECHNIQUES AND ARTIFICIAL INTELLIGENCE IN HEMATOLOGY

Label-Free Cell Detection of Acute Leukemia Using High-Content Morphological Profiling in Flow

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Background: Early diagnosis and prompt initiation of appropriate treatment are critical for improving the prognosis of acute leukemia. Acute leukemia is typically diagnosed through microscopic morphological examination of bone marrow smears and flow cytometric immunophenotyping of bone marrow cells stained with fluorophore-conjugated antibodies. However, these diagnostic processes require trained professionals and are time and resource-intensive. Here, we present a novel diagnostic approach using ghost cytometry (GC), a recently developed high-content flow cytometric approach that leverages machine vision-based, stain-free, high-speed morphological characterization and analysis of cells.
Methods: Label-free morphological information of cells was acquired as compressive imaging temporal waveforms. These waveforms were directly analyzed using the support vector machine (SVM) algorithm without computational image production, enabling high-speed and accurate information processing. Conventional flow cytometric data modalities, such as forward-scattering (FSC), backscattering (BSC), and fluorescence signals from biological labeling, were used as ground truth labels to identify and annotate blast and normal cells in bone marrow (BM) based on flow cytometric gating schemes. Subsequently, we trained a leukemia cell classifier using the annotated GC (compressive imaging) waveforms and evaluated its classification ability by comparing the predicted results with the ground truth labels. Finally, we applied the trained classifier to unidentified GC waveforms (a test dataset not used for classifier development) to demonstrate the detection of blast cells in BM based on their morphology, without relying on biological labels. Following this protocol, we first trained and tested a machine classifier using a human leukemia NB-4 cell line spiked into BM from a healthy donor. Next, we trained and tested two classifiers using BM aspirates from patients diagnosed with acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML), where CD45 was used as the ground truth marker of leukemic cells.
Results: The leukemia cell classifier, developed using a human NB-4 cell line spiked into BM cells from a healthy donor, demonstrated excellent classification accuracy with an ROC-AUC score of 0.9998. The high classification accuracy was reproducible across different spike-in concentrations ranging from 1% to 95%. The classifiers trained using BM cells from patients diagnosed with ALL and AML showed high ROC-AUC scores of 0.986 and 0.941, respectively. When we used the classifiers to evaluate blast cell proportions in test datasets that were not used to develop the classifiers, they were also highly accurate in identifying the percentage of blast cells: 56.8% for ALL with a decision boundary of SVM scores at 0, and 30.4% for AML with a decision boundary of SVM scores at 0.37, when compared to May-Grunwald-Giemsa staining of the same cases by medical technologists at diagnosis (60.0% for ALL and 31.2% for AML).
Conclusions: Here, we present a novel diagnostic approach that leverages machine vision-based, stain-free, high-speed morphological characterization and analysis of cells. We demonstrate that the approach can detect leukemic cells from the bone marrow cells of patients diagnosed with ALL and AML, without requiring biological staining. The method presented here holds promise as a rapid, precise, simple, and cost-effective method for the diagnosis of acute leukemia in clinical settings.

Disclosures Kawamura: *ThinkCyte K.K.:* Current Employment, Current holder of *stock options* in a privately-held company. **Murata:** *ThinkCyte K.K.:* Current Employment, Current holder of *stock options* in a privately-held company. **Teranishi:** *ThinkCyte K.K.:* Current Employment, Current holder of *stock options* in a privately-held company. **Miyazaki:** *ThinkCyte K.K.:* Current Employment, Current holder of *stock options* in a privately-held company. **Toda:** *ThinkCyte K.K.:* Current Employment, Current holder of *stock options* in a privately-held company, Patents & Royalties. **Imai:** *ThinkCyte K.K.:* Current Employment,

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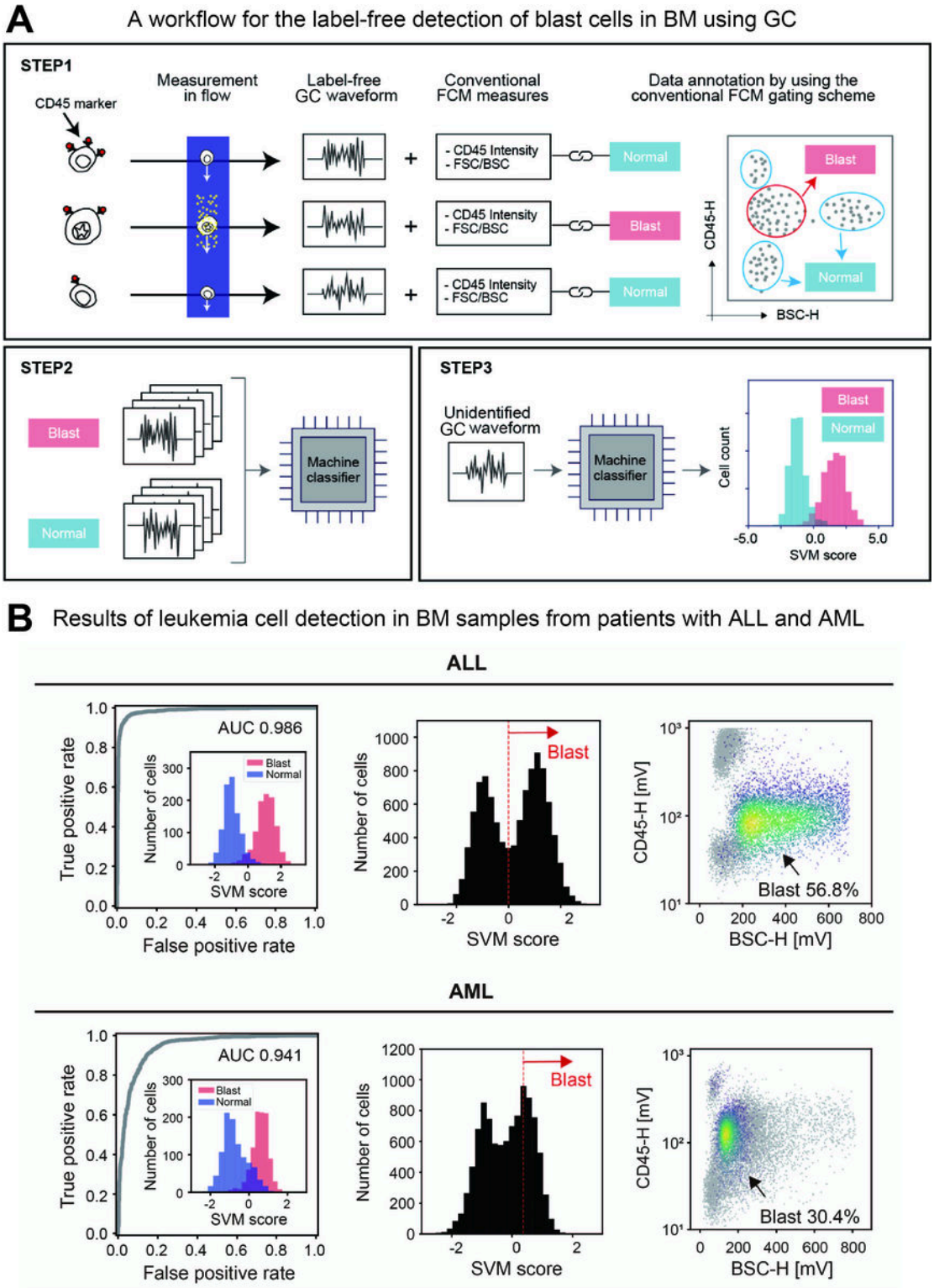

Figure 1

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