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POSTER ABSTRACTS

803.EMERGING TOOLS, TECHNIQUES AND ARTIFICIAL INTELLIGENCE IN HEMATOLOGY

Deep Learning Based Blood Abnormalities Detection As a Tool for Vexas Syndrome Screening

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Introduction

The VEXAS syndrome (vacuoles, E1 enzyme, X-linked, auto-inflammatory, somatic) described in 2020 caused by mutations of the *UBA1* gene, displayed a large pleomorphic array of clinical and biological features. Nevertheless, these criteria do not allow to discriminate VEXAS from other myeloid malignancies on complete blood count + differential, notably due to the absence of peripheral blood characterization of the disease.

This study aimed at singling out dysplastic features indicative of VEXAS among peripheral blood (PB) polymorphonuclears (PMN) from VEXAS patients compared to healthy patients and myelodysplastic (MDS) patients. As such task is tedious and subject to operator bias, a multicentric dataset has been used to design a deep learning algorithm for automatic detection of these features, finally tested on an external validation cohort.

Patient, material and methods

Patients written consents were obtained and five academic centers (number from 1 to 5) were involved in this 3 steps study. Firstly, 3 academic centers (number 1 to 3) enrolled 20 patients distributed as follow: 9 patients with UBA1 ^{mut} and 6 patients UBA1 ^{wt} with no other genetic mutation as well as 5 samples from MDS patients. A total of 25 PB smears and especially PMN images were gathered and screened for various abnormalities. Two independent morphologists blindly quantified PMN predefined characteristics. This dataset of 2,824 multilabelled PMN was evaluated and tested by a two-sample Wilcoxon Rank Sum test for statistical significance between UBA1 ^{mut} and the others.

Secondly, in order to automate the detection of these significant features on PMN images, a convolutional neural network (CNN) was trained using a multicentric image dataset gathered from 4 academic centers (number 2 to 5). Patients were selected based on clinical and biological symptoms suggesting VEXAS syndrome, namely fever, skin lesions, chondrites, vasculitis and/or anemia. After evaluation of the *UBA1* mutation status, this multicentric cohort was separated into confirmed VEXAS (n = 19) and UBA1 ^{WT} (n=20). A total of 6,615 annotated PMN images were collected from DI systems (Cellavision ®, Lund, Sweden) with 1 to 12 PB smears per patient, yielding a 48 UBA1 ^{mut} and 33 UBA1 ^{wt} smears. All patients were males, the median age was 74 year-old (IQR 67-77) and that of control patients 72 year- old (61-79).
Finally, the CNN was evaluated on an external cohort from another academic hospital (center 1), including inflammatory patients, and patients screened for VEXAS syndrome for a total cohort of 15 patients and 1,887 images.

Results

Four specific abnomalities were observed in PMNs from VEXAS patients as compared with healthy or myelodysplastic controls. The automatic recognition of anomalies was then cast in a multilabel classification task, where each PMN image could be assigned to one or more labels during interference. In order to take into account this specificity, a CNN was trained, composed of different layers of convolutions and pooling (Figure1).
The model was set-up to output an independent binary prediction for the presence or absence of each of the four anomalies of interest.
Automatic detection of these 4 anomalies by the proposed model yielded area under the curve (AUC) of 0.827; 0.837; 0.927 and 0.947 (Figure 2). Regarding the general performance on the external validation cohort, the CNN achieved a Hamming loss of 0.141, and macro and micro F1 scores of 0.588 and 0.668 respectively.

Discussion

This study suggests that computer-assisted analysis of PB smears, focusing on suspected VEXAS cases, could provide valuable insights to determine which patients should undergo molecular testing.
A deep-learning approach leveraging previously identified peripheral blood indicators and automatic analyzers is thus presented, which can help hematologists orient their suspicion before initiating further analysis.

Disclosures Heiblig: *Pfizer Inc.:* Honoraria; *Astellas:* Honoraria; *AbbVie:* Honoraria; *Jazz Pharmaceuticals:* Honoraria; *Servier:* Honoraria. **Chevallier:** *Sanofi:* Honoraria; *Mallinckrodt Pharmaceuticals:* Honoraria; *Incyte:* Honoraria, Research Funding; *Takeda:* Honoraria; *Immedica Pharma:* Honoraria; *Servier:* Honoraria.

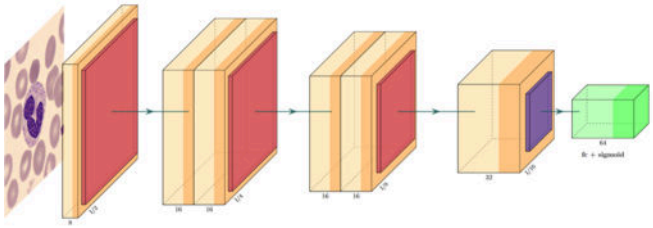

***Figure 1** : CNN used for multilabel classification. Orange marks convolution with kernel size 3x3 and stride 1 followed by ReLU activations; red marks max pooling with kernel size 2x2 and stride 2; purple marks global average pooling operation; green marks fully connected layer with sigmoid activation for each of the 4 classes considered.*

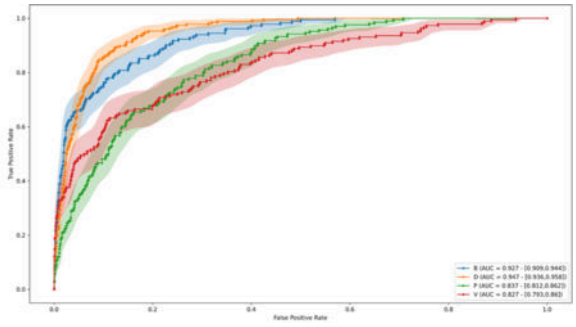

***Figure 2** : ROC-AUC for positive labels on the external testing set.*

Figure 1

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