A publicly available database for developing machine learning applications to differentiate leukocytes and recognise malignant cells in peripheral blood

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Abstract

Acute Myeloid Leukemia (AML) is a malignant disease of the myeloid lineage of the hematopoietic system. It predominantly affects the elderly population, and can be a clinically challenging disease. The routine diagnostic workup of AML and many other hematological conditions includes examination of blood smears and bone marrow samples under a microscope using high resolution. Due to its easy accessibility peripheral blood is often sampled in the initial stages of the diagnostic pipeline. While other diagnostic modalities have been increasingly automatised, cytomorphologic classification is still today mostly performed manually by human examiners using optical microscopes. Our paper aims to harness recent progress in biomedical image classification using deep learning and apply it to the field of leukemia diagnostics.

In order to achieve this aim, we digitised peripheral blood smears of 100 AML patients and 100 non-malignant controls diagnosed at Munich University Hospital at 100-fold objective magnification using oil immersion. Leukocytes were annotated manually by experienced examiners, allowing us to compile a database of over 18,000 single-cell images of malignant and non-malignant cell classes. Annotations were repeated up to three times, allowing us to estimate intra- and inter-rater variability of human annotation. The single-cell image database thus compiled has been made freely available to the community via The Cancer Imaging Archive (Matek et al., 2019a).

Using the single-cell image database, we trained and evaluated a network based on the ResNeXt architecture (Xie et al., 2016) for classification of leukocyte images into a standard scheme of 15 morphological classes, which is widely used in routine practice. The network showed very good performance for the most common malignant and non-malignant cell types. For example, segmented neutrophils, typical lymphocytes and myeloblasts were all classified with values for precision and sensitivity exceeding 0.94. We furthermore tested the network at two clinically relevant binary decisions, namely (i) if a given cell has the character of a blast, i.e. the malignant leukocyte characteristic of AML, and (ii) if a given cell belongs to the set of cell types that are expected to be absent under physiological conditions. At both binary questions, the network attains the performance level of human examiners, with ROC AUC values exceeding 0.99 in both cases.

Finally, to get a glimpse at the inner workings of the network developed, we analysed the network predictions by gradient-based saliency maps. We find that the network has learned to focus on the relevant leukocyte in the test images, and map out cytoplasmatic features and nuclear shape. The full paper and trained network were recently published (Matek et al., 2019b).

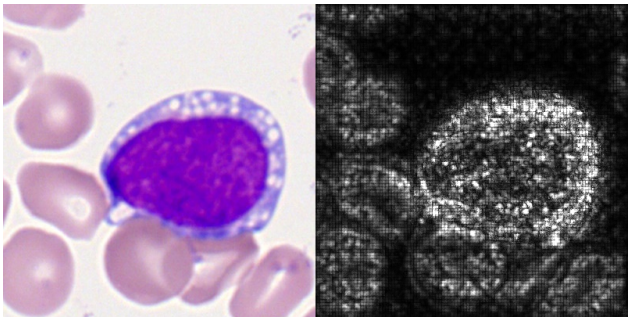

Figure 1. Left: Light microscopic single-cell image of a cell from the dataset annotated as a myeloblast, the characteristic malignant cell type of AML, at 100-fold objective magnification. Right: Gradient-based saliency map of the image on the left leading to the correct classification as a myeloblast.

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