Self-supervised learning for detection and classification of circulating tumor cells in liquid biopsy data

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Background & objectives

Circulating tumor cells (CTCs) are a critical liquid biopsy marker but rare events and extraordinarily heterogeneous in the background of millions of hematopoietic cells in patients' blood. There are several clinical CTC detection methods available, including the FDA approved gold standard CellSearch® system – however, they are expensive and time-consuming to conduct. Here, supervised deep learning has been shown to address and overcome some of these challenges but it still requires expensive labels by experts.

The use of self-supervised learning, an emerging approach in computer vision and partly in the medical domain, has the potential to result in significant decrease in labelling effort, save expert time and improve the detection and classification of CTCs.

Methods

The acquired dataset consists of 12 metastatic breast cancer patients from the CellSearch® system – each patient with a raw data of 175 3-channel (DAPI, CK, CD45) images. Segmentation of objects in CK channel images was done by StarDist (encoder-decoder CNN), resulting in a total of 69,297 images. Through consensus rating, a ground truth (CTCs: 1,101 and N-CTCs: 2,333) was labeled, leaving 65,863 unlabeled cells of which 61,865 (test patients excluded) are used as training images for the adapted DINO (knowledge distillation with no labels) self-supervised method. An "on top" classifier then performed a binary classification of CTCs vs. Non-CTCs for different training subset sizes.

Results

DINO (combined with the "on top" classifier) is compared to a state-of-the-art supervised deep learning model for different training subset sizes and is shown to outperform the latter in terms of F1 score (0.965). An investigation of the latent space of the learned cell representations in DINO reveals distinct cell clusters for CTCs and Non-CTCs, even though DINO extracted the features of the cells without any annotation information during training.

Conclusion

Using the proposed self-supervised learning pipeline (DINO + classifier), we demonstrate that it can be used for CTC detection to reduce labelling effort and that it exceeds the F1 score for CTCs and Non-CTCs differentiation compared to classical end-to-end supervised deep learning. In the future, usage of unlabeled data of more patients is planned.