

## Supplementary Materials

Table S1 displays the training dataset used for tissue segmentation, lymphocyte detection, and TIL score prediction in this study. The training dataset of the TIGER challenge largely comprises WSIBULK, WSIROIS, and WSITILS. In this experiment, the WSIROIS dataset with ROI-level annotation (patch type) was used for tissue segmentation and lymphocyte detection.

Table S1. Structure and content of training dataset of the TIGER challenge.

| Datasets | Data Configuration                |                                | Num_images | Use status |
|----------|-----------------------------------|--------------------------------|------------|------------|
| WSIBULK  | images                            |                                | 92         | not used   |
|          | tissue-masks                      |                                | 93         | not used   |
|          | annotations-tumor-bulk            | masks                          | 93         | not used   |
|          |                                   | xmls                           | 93         | not used   |
| WSIROIS  | WSI-level-annotation (WSI type)   | images                         | 196        | not used   |
|          |                                   | tissue-masks                   | 196        | not used   |
|          |                                   | annotations-tissue-bcss-masks  | 151        | not used   |
|          |                                   | annotations-tissue-bcss-xmls   | 151        | not used   |
|          |                                   | annotations-tissue-cells-masks | 168        | not used   |
|          |                                   | annotations-tissue-cells-xmls  | 168        | not used   |
|          | ROI-level-annotation (patch type) | tissue-bcss-images             | 151        | used       |
|          |                                   | tissue-bcss-masks              | 151        | used       |
|          |                                   | tissue-cells-images            | 1,879      | used       |
|          |                                   | tissue-cells-masks             | 1,879      | used       |
|          |                                   | tiger-coco.json                | -          | used       |
| WSITILS  | images                            |                                | 82         | used       |
|          | tissue-masks                      |                                | 82         | not used   |

|  |                              |   |      |
|--|------------------------------|---|------|
|  | tiger-til-scores-wsitils.csv | - | used |
|--|------------------------------|---|------|

Some tissue-bcss dataset within WSIROIS are annotated with only certain parts of the image as shown in (a) and (b) of Figure S1. Therefore, the image was rotated and cropped as shown in (c) and (d) of Figure S1 using the annotation information in the 'annotation-tissue-bcss.xmls'.

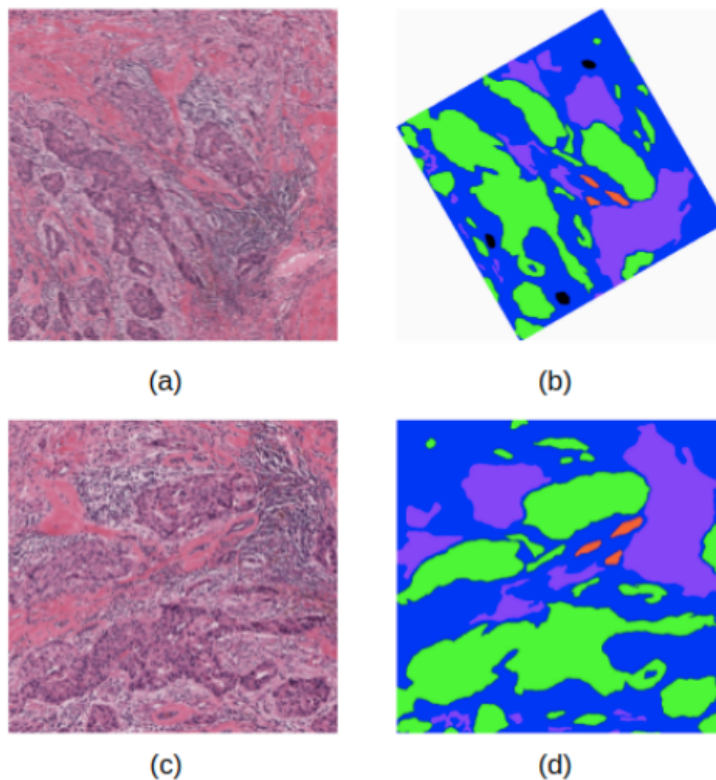


Figure S1. Examples of rotated images and masks from the tissue-bcss dataset within WSIROIS: (a) raw image, (b) raw mask, (c) rotated and cropped image, (d) corresponding annotation mask.

Table S2 provides basic information on the large unlabeled datasets used for training the pre-trained model in this work. These datasets consist of histopathological tissue images such as breast, colon, bone, lung, and prostate. All datasets are configured with a patch-type image, not a WSI-type.

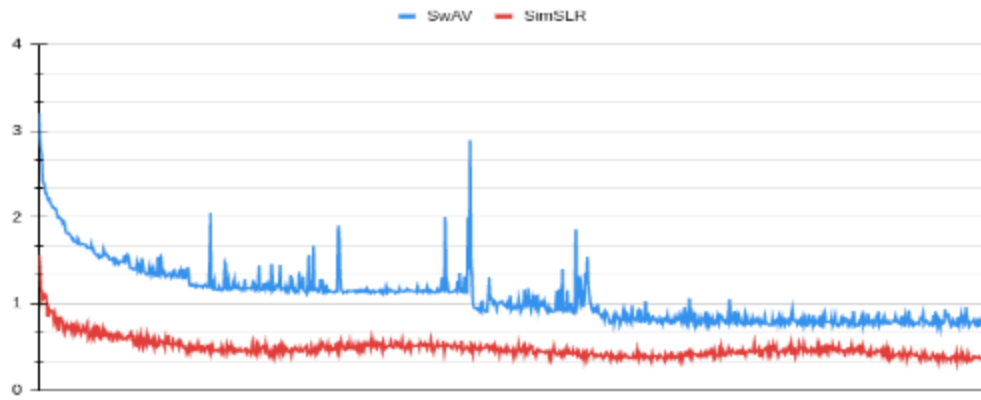
Table S2. Summary of large unlabeled datasets used for pre-training task.

| Dataset                                  | Organ       | Each image size | Number of images |
|--|-------------|-----------------|------------------|
| andrewjanowczyk_epi[22]                  | Breast      | 1000 x 1000     | 125              |
| andrewjanowczyk_mitosis[22]              | Breast      | 2000 x 2000     | 311              |
| andrewjanowczyk_nuclei[22]               | Breast      | 2000 x 2000     | 142              |
| andrewjanowczyk_tubule[22]               | Colon       | 775 x 522       | 85               |
| BACH[45]                                 | Breast      | 2048 x 1536     | 500              |
| breakhis[46]                             | Breast      | 700 x 460       | 9,109            |
| breastpathq[47]                          | Breast      | 512 x 512       | 3,700            |
| CoNSeP[48]                               | Colon       | 1000 x 1000     | 41               |
| Gleason2019[49]                          | Prostate    | 5120 x 5120     | 331              |
| Kather_texture_2016_image_tiles_5000[50] | Colon       | 150 x 150       | 5,000            |
| LC25000[51]                              | Lung, Colon | 768 x 768       | 25,000           |
| Lymph[52]                                | Various     | 1388 x 1040     | 374              |
| MIMM[53]                                 | Bone        | 2560 x 1920     | 85               |
| monuseg_2018_train_data[54]              | Various     | 1000 x 1000     | 37               |
| NCT-CRC-HE-100K[55]                      | Colon       | 224 x 224       | 100,000          |

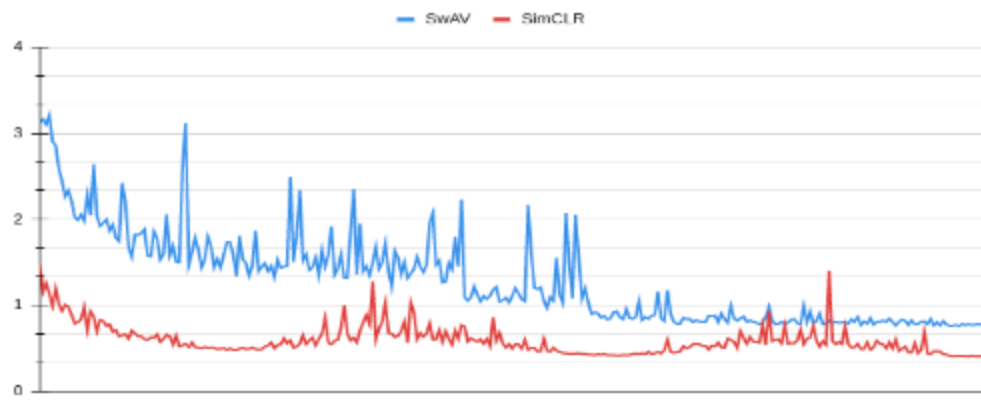
Table S3 details the experimental setup for each self-supervised learning module used for pre-training. Regarding SimCLR, the maximum batch size was set to 1024 due to computation cost or GPU memory issues, and the SwAV batch size was set to 2048. The settings for augmentation methods were as follows: Random Horizontal Flip probability = 0.5, color jitter probability = 0.8, and Random Grayscale probability = 0.2. In our study, we adjusted the default color jitter values ([saturation, contrast, brightness, hue] = 0.8, 0.8, 0.8, 0.4) into lighter ones([0.4, 0.4, 0.4, 0.2]). This modification was made based on insights from the study by Ozan Ciga et al.[11], particularly Appendix C and Figure C7. To multi-crop an image on SwAV, we used the default value (Number of crops: [2, 4], Min scale crop: [0.33, 0.10], Max scale crop: [1, 0.33]).

Table S3. Experiment setup of each self-supervised learning modules.

|                            | SimCLR  | SwAV  |
|----------------------------|---|---|
| Backbone                   | ResNet-18   | ResNet-18   |
| Batch size                 | 1024  | 2048  |
| Epochs                     | 300   | 300   |
| Optimizer                  | Adam  | Adam  |
| Learning rate              | 1.0e-3  | 1.0e-3  |
| LR scheduler               | Cosine  | Lambda  |
| Weight decay               | 1.0e-6  | 1.0e-6  |
| temperature                | 0.1   | 0.5   |
| Epsilon(SwAV)              | -   | 0.05  |
| Sinkhorn iterations(SwAV)  | -   | 3   |
| Number of prototypes(SwAV) | -   | 28  |
| Augmentation               | <ul style="list-style-type: none"> <li>- Color Jitter</li> <li>- Random Grayscale</li> <li>- Random Horizontal Flip</li> <li>- Gaussian blur</li> <li>- Random Resize crop</li> </ul> | <ul style="list-style-type: none"> <li>- Color Jitter</li> <li>- Random Grayscale</li> <li>- Random Horizontal Flip</li> <li>- Gaussian blur</li> <li>- Random Resize crop</li> <li>- Multi crop</li> </ul> |



(a)



(b)

Figure S2. SimCLR and SwAV loss curves obtained during pre-training. The red curve depicts SimCLR, and the blue depicts SwAV during (a) training and (b) validation.

Table S4 details the experimental setup of tissue segmentation and lymphocyte detection tasks. While U-Net's encoder typically comprises general convolutional neural networks, we employed ResNet-18 as an encoder backbone. For tissue segmentation and lymphocyte detection, we performed experiments by sweeping the learning rate [1.0e-3, 1.0e-4, 1.0e-5] and selected the most optimal learning rate for each task. The optimal learning rate was 1.0e-4 for tissue segmentation and 1.0e-3 for lymphocyte detection. Figure S3 presents the validation loss curve according to the learning rate for each downstream task.

Table S4. Experiment setup of each downstream tasks.

|                   | Tissue segmentation task | Lymphocytes detection task |
|-------------------|--------------------------|----------------------------|
| Module            | DeepLabv3                | U-Net                      |
| Backbone          | ResNet-18                | ResNet-18                  |
| Batch size        | 40                       | 15                         |
| Epochs            | 100                      | 25                         |
| Optimizer         | Adam                     | Adam                       |
| Learning rate     | 1.0e-4                   | 1.0e-3                     |
| LR scheduler      | Cosine                   | Cosine                     |
| Weight decay      | 1.0e-6                   | 1.0e-6                     |
| Evaluation metric | Dice score               | FROC score                 |
| Loss function     | Dice BCE loss            | BCE loss                   |

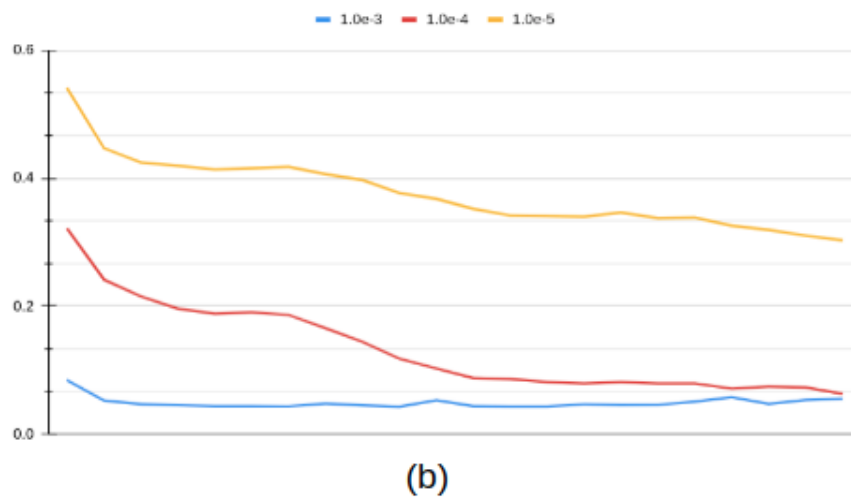
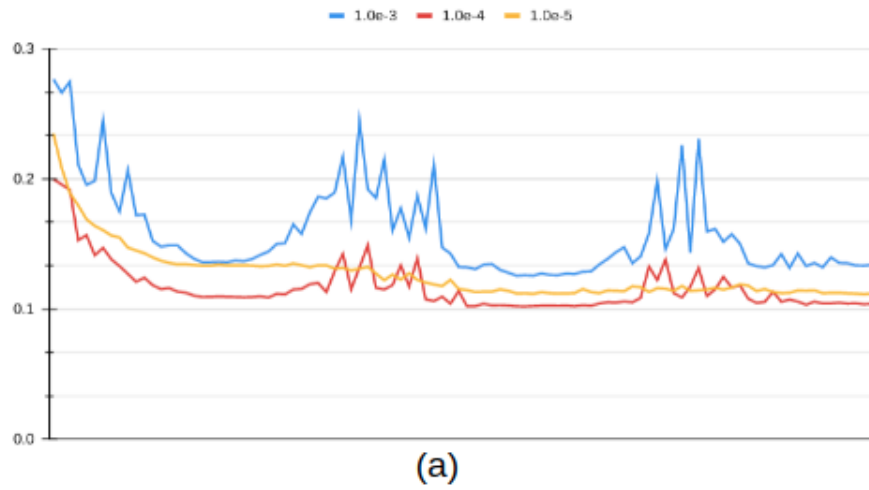


Figure S3. Validation loss curves for each downstream task relative to learning rate: (a) tissue segmentation and (b) lymphocyte detection.

## Reference

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