

# PAI-WSIT: a Comprehensive Curated Resource for Cancerous Pathology With Deep Learning

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## Research Article

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# **PAI-WSIT: a comprehensive curated resource for cancerous pathology with deep learning**

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1 **Abstract**

2 **Background**

3 The possibility of digitizing whole-slide images (WSI) of tissue has led to the advent of  
4 artificial intelligence (AI) in digital pathology. Advances in precision oncology have resulted  
5 in an increasing demand for predictive assays that enable mining of subvisual morphometric  
6 phenotypes and might improve patient care ultimately. Hence, a pathologist-annotated and  
7 artificial intelligence-empowered platform for integration and analysis of WSI data and  
8 molecular detection data in tumors was established, called PAI-WSIT  
9 (<http://www.paiwsit.com>).

10 **Methods**

11 The standardized data collection process was used for data collection in PAI-WSIT, while a  
12 multifunctional annotation tool was developed and a user-friendly search engine and web  
13 interface were integrated for the database access. Furthermore, deep learning frameworks were  
14 applied in two tasks to detect malignant regions and classify phenotypic subtypes in colorectal  
15 cancers (CRCs), respectively.

16 **Results**

17 PAI-WSIT recorded 8633 WSIs of 1772 tumor cases, of which CRC from four regional  
18 hospitals in China and The Cancer Genome Atlas (TCGA) were the main ones, as well as  
19 cancers in breast, lung, prostate, bladder, and kidneys from two Chinese hospitals. A total of  
20 1298 WSIs with high-quality annotations were evaluated by a panel of 8 pathologists. Gene

1 detection reports of 582 tumor cases were collected. Clinical information of all tumor cases  
2 was documented. Besides, we reached overall accuracy of 0.933 in WSI classification for  
3 malignant region detection of CRC, and area under the curves (AUC) of 0.719 on colorectal  
4 subtype dataset.

## 5 **Conclusions**

6 Collectively, the annotation function, data integration and AI function analysis of PAI-WSIT  
7 provide support for AI-assisted tumor diagnosis, all of which have provided a comprehensive  
8 curation of carcinomas pathology.

9 **Keywords** Artificial intelligence, Digital pathology, Database, Whole-slide images,  
10 Annotations

## 11 **Background**

12 Pathology is considered as the “gold standard” of diagnostic medicine and directly related to  
13 the subsequent treatment. Instead of conventional microscopy, digital pathology plays a crucial  
14 role in modern clinical practice in recent years due to its advances in computing power, fast  
15 networks, and large storage [1, 2]. With the digital slide scanners, whole slide images (WSIs)  
16 become a great source of information and complexity in pathology because of their large size  
17 (commonly at a resolution of 100k×100k) [3]. Furthermore, artificial intelligence (AI),  
18 particularly deep learning, is bringing a paradigm shift to many breakthroughs in image  
19 classification, object detection and segmentation [4]. AI algorithms have the potential for  
20 developing an unifying approach in digital pathology [5], including segmentation and

1 classification of various regions in WSIs [6, 7], detection of tumor proliferation [8] and cancer  
2 metastases [9], mitosis detection [10], as well as prediction of patient prognosis [11, 12].  
3 Several pathology datasets with AI, for example, CAMELYON16 challenge for breast cancer  
4 metastasis detection [13], and MoNuSeg2018 challenge for multi-organ nuclei segmentation  
5 [14] have demonstrated that they are highly useful for facilitating disease studies and diagnosis  
6 tool developments in AI [15].

7

8 Rather than being a single, uniform disease type, accumulating evidence suggests that cancer  
9 comprises a group of molecularly heterogeneous diseases that are characterized by a range of  
10 genomic and epigenomic alterations. Pathology diagnosis depends not only on WSI analysis  
11 but also on several other sources of data that need to be included coming from omics, clinical  
12 records, and patient medical information. For example, immunohistochemistry (IHC) staining  
13 has a profound role in diagnosis by helping doctors to determine the biological characteristics  
14 of a wide variety of tumors, to make a prognosis, and to select appropriate systemic therapies  
15 for patients with cancer [16]. As the use of genomic technologies spreading, DNA-level and  
16 transcriptional-level features obtained from tissues will be evaluated for their utility in creating  
17 molecular subtypes of cancer to predict future disease behavior and treatment response [17].  
18 For example, the Pan-Cancer Atlas reclassifies human tumor types based on molecular  
19 similarity [18], indicating that the cell of origin influences but does not fully determine tumor  
20 classification, which informs future clinical trial design and interpretation.

21

22 In 2015, The CRC Subtyping Consortium (CRCSC) was formed to show marked

1 interconnectivity between six independent classification systems coalescing into four  
2 consensus molecular subtypes (CMSs) with distinguishing features: CMS1 (microsatellite  
3 instability immune); CMS2 (canonical); CMS3 (metabolic); and CMS4 (mesenchymal) [19].  
4 Most clinicians consider the CMS groups would be taken forward into routine clinical practice  
5 with the aim of prognostic value [20]. AI is essential to recognize the phenotypic features of  
6 CRC, discover more complicated or subtle connections than a human would and help  
7 pathologists make the best clinical decisions for patients.

8

9 Thus, we have established an artificial intelligence multicenter platform for integration and  
10 analysis in ([www.paiwsit.com](http://www.paiwsit.com)). The standardized data collection process was used for data  
11 collection, a multifunctional annotation tool was developed and a user-friendly search engine  
12 and web interface were integrated for database access. To facilitate data analysis and  
13 interpretation based on PAI-WSIT, a systematic analytical framework was also proposed. A  
14 deep learning model ResNet for malignant regions detection in colorectal WSI with slides and  
15 annotations were provided, meanwhile, we actively explored whether it is possible to classify  
16 four CMSs of CRC only using WSI via deep learning, which lay the foundation for the  
17 deployment of computational decision support systems for CRC in clinical practice.

## 18 **Methods**

### 19 **Data collection and curation**

20 As a multicenter platform, we collected pathological data of cancer patients from four hospitals  
21 (Nanjing First Hospital, the First Affiliated Hospital of Zhejiang University, the First Affiliated

1 Hospital of Soochow University and Nanjing Drum Tower Hospital) and TCGA. With cancer  
2 patients as the basic elements, PAI-WSIT recorded physiological information, clinical and  
3 pathological reports, WSIs and gene mutation data from detection reports.

4  
5 WSIs with hematoxylin-eosin (H&E) and immunohistochemistry staining were stored. Slides  
6 were scanned by Hamatsu NanoZoomer C9600-12 at a magnification of 40x (image resolution:  
7 0.225  $\mu\text{m}/\text{pixel}$ ). The biomarker mutation data were generated based upon the target region  
8 probe capture technology and sequenced by next-generation sequencing (NGS) technology  
9 using Illumina platform and the detection of plasma and tissue samples from cancer patients.  
10 Clinical data such as physiological parameters and pathological diagnosis information of  
11 patients were mostly in unstructured free-text reports. With these metadata, researchers were  
12 able to annotate WSIs and also train deep learning algorithms for more tasks such as lymphoma  
13 type classification. A detailed listing of all the fields of metadata and their descriptions  
14 (Additional file1: Table S1) are provided, meanwhile.

## 15 **Data annotation**

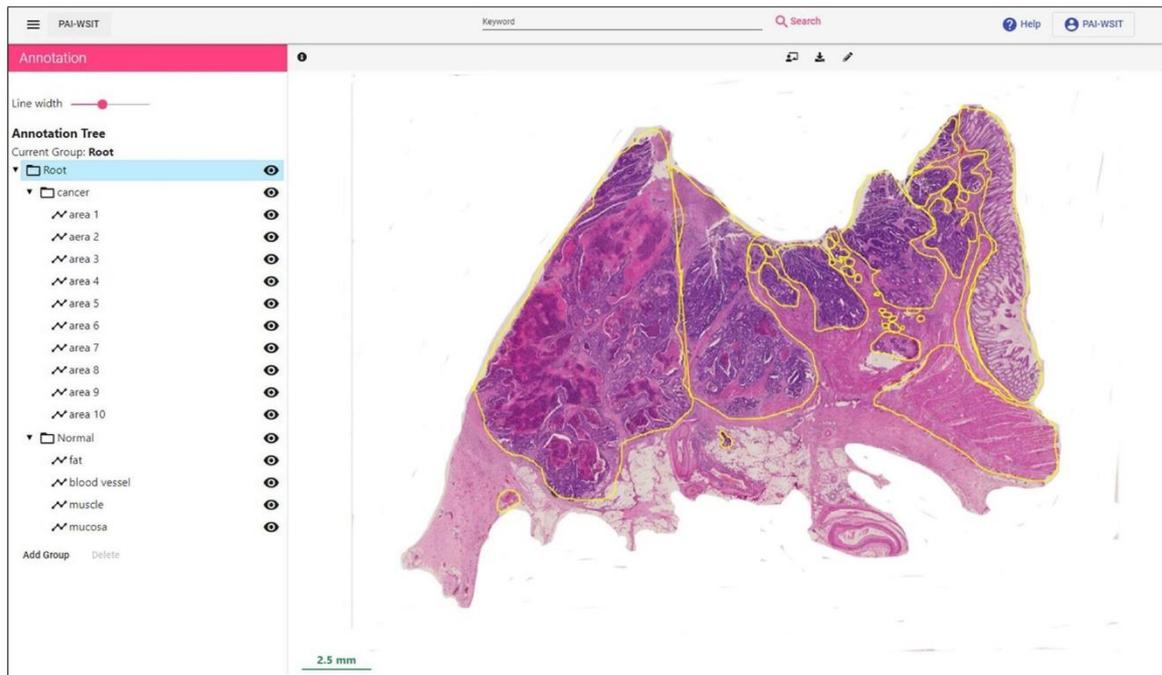
16 Lack of high-quality annotation is one of the biggest challenges for AI in digital pathology [21].  
17 In PAI-WSIT, we developed the annotation tools, including smooth curve tool, polygon tool  
18 and other shaped tools. Using these tools, the users could draw shapes on the WSIs to highlight  
19 various kinds of cells or regions on the slides and thereby enable them to annotate the WSIs in  
20 higher accuracy with less effort. For each user, all annotations for a given WSI were grouped  
21 in one annotation tree (**Fig. 1(a)**). More importantly, PAI-WSIT supported the storing

1 annotations from multiple pathologists for the same WSI. Pathologists or other platform users  
2 could view annotations drawn by other pathologists. Multi-user annotations provided the  
3 possibility and convenience to compare different annotations and to adopt a flexible data  
4 processing strategy for deep learning case studies.

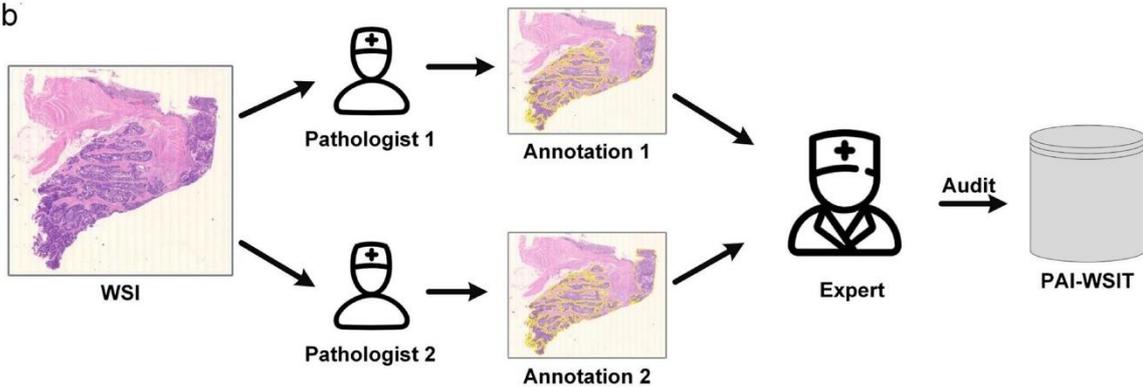
5

6 We invited several experienced pathologists annotated colorectal cancer WSIs at the pixel  
7 levels by using the annotation tools. To control the quality of annotations, each slide was  
8 annotated by two pathologists. An independent expert of pathology further examined the  
9 quality of annotations, and merged the annotations for each slide into a definitive one. The data  
10 were then stored on a dedicated server cluster and a web interface provided the convenient  
11 access of data, which could be referenced by the users of PAI-WSIT. The annotation protocol  
12 was shown in **Fig. 1(b)**.

a



b



1

2 **Fig. 1.** Annotation tool in PAI-WSIT. (a) Annotation tree: the user draws two groups of regions

3 in a WSI, one is cancer areas and the other is normal areas. (b) Annotation protocol: each

4 annotation in PAI-WSIT was annotated by two pathologists and audited by an experienced

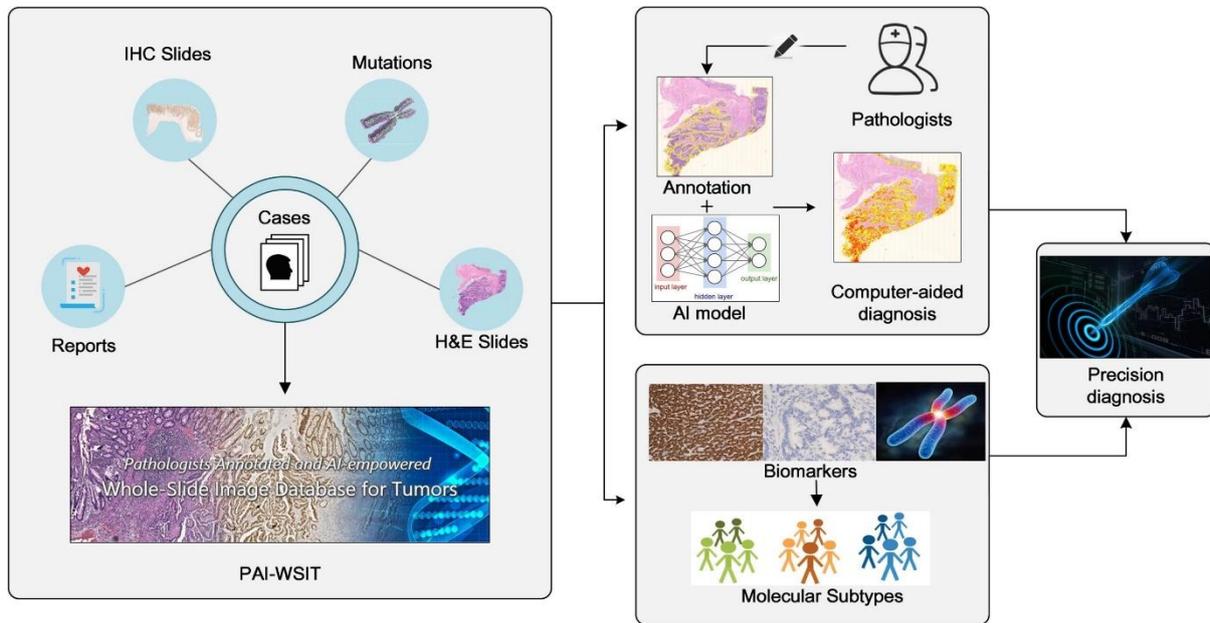
5 expert. *WSI* whole slide image

## 6 Database architecture

7 The overall workflow of PAI-WSIT is summarized in **Fig. 2.** PAI-WSIT collected large

8 pathological data of patients, such as basic information, pathological reports, WSIs and gene

1 detection reports and also integrated annotation tools and deep learning models. Moreover, a  
 2 number of annotations produced by experienced pathologists, which lay the foundation for the  
 3 deployment of computational decision support systems in clinical practice.



4  
 5 **Fig. 2.** The overall workflow of PAI-WSIT. PAI-WSIT contains basic information, pathological  
 6 reports, WSIs and target biomarker results of cancer cases. The integration of annotation tools  
 7 towards WSI makes AI in digital pathology more convenient. Biomarkers in DNA-level and  
 8 transcriptional-level are helpful for molecular subtype research. *IHC* immunohistochemistry,  
 9 *H&E* hematoxylin-eosin, *AI* artificial intelligence

10  
 11 A user-friendly search engine and web interface were incorporated for users to search and  
 12 browse WSIs along with their metadata and annotations. Outstandingly, PAI-WSIT can  
 13 visualize the result generated by AI analysis for colorectal WSIs and relevant studies. PAI-  
 14 WSIT takes advantages of various storage technique, including distributed file system (CephFS  
 15 [22]), a relational database (MySQL) and a document database (MongoDB [23]), as well as a  
 16 search engine (Elasticsearch [24]) providing functionalities of searching data synchronized

1 from MongoDB database. For web browsing, the front page of the retrieval system was based  
 2 on HTML. The web interface is a single page application built using Angular framework to  
 3 provide a user-friendly experience as well as to support sophisticated features such as  
 4 annotation management and various annotation tools.

5 **Framework for malignant regions detection (in colorectal WSIs)**

6 We trained a deep learning model ResNet for malignant region detection in colorectal WSI  
 7 with slides and annotations from PAI-WSIT. Both training sets and test sets were H&E slides  
 8 from Nanjing First Hospital and validation set were slides from Nanjing Drum Tower Hospital.  
 9 The summary of patient information in this study and the distribution of WSIs are represented  
 10 in Table 1.

12 **Table 1 Summary of patient information and the distribution of WSIs**

<b>Data set</b>	<b>Training set</b>	<b>Test set</b>	<b>Validation set</b>
<b>Sex</b>			
(MALE/FEMALE)	73/57		28/22
<b>Age</b>	62.5 ± 12.1		64.2 ± 13.2
<b>Normal</b>	40/40	13/13	21/21
(patients/WSIs)			
<b>Cancer</b>	60/60	17/17	29/29
(patients/WSIs)			

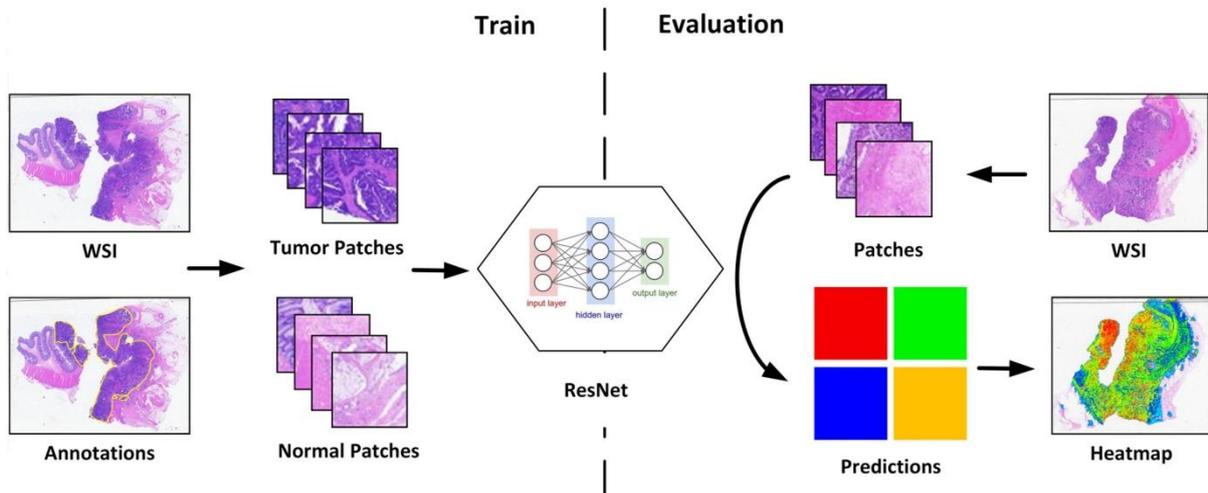
13 *WSI* whole slide image

1 Several efforts were put in the technical validation of PAI-WSIT. First, regions of interest (ROIs)  
 2 are calculated for the requested WSI to avoid processing the white background of the WSI.  
 3 Next, the images of the ROIs were cropped with 256\*256 patches with pathologists'  
 4 annotations (positive samples for cancer regions and negative samples for tumor regions) as  
 5 that of in the original model input. There was an unbalance between positive and negative  
 6 samples, so cancer samples were augmented by extracting the rectangle until the number of  
 7 normal and cancer samples approximately equal finally.

8  
 9 ResNet utilizes shortcut connections to significantly reduce the difficulty of training, which  
 10 achieves competitive performances in classification compared with other kinds of networks.  
 11 Therefore, ResNet is used in our case. It starts a stochastic gradient descent (SGD) at a learning  
 12 rate of 0.001. we chose cross-entropy as loss function:

$$H_{y'}(y) = - \sum_i y_i' \log(y_i) \quad (1)$$

13 Where  $y_i$  denotes prediction and  $y_i'$  denotes the ground truth. We generated probability maps  
 14 using the trained model and drew heatmap for visualization, with which even can achieve the  
 15 location of the tumor area. The whole process is shown in **Fig. 3**.



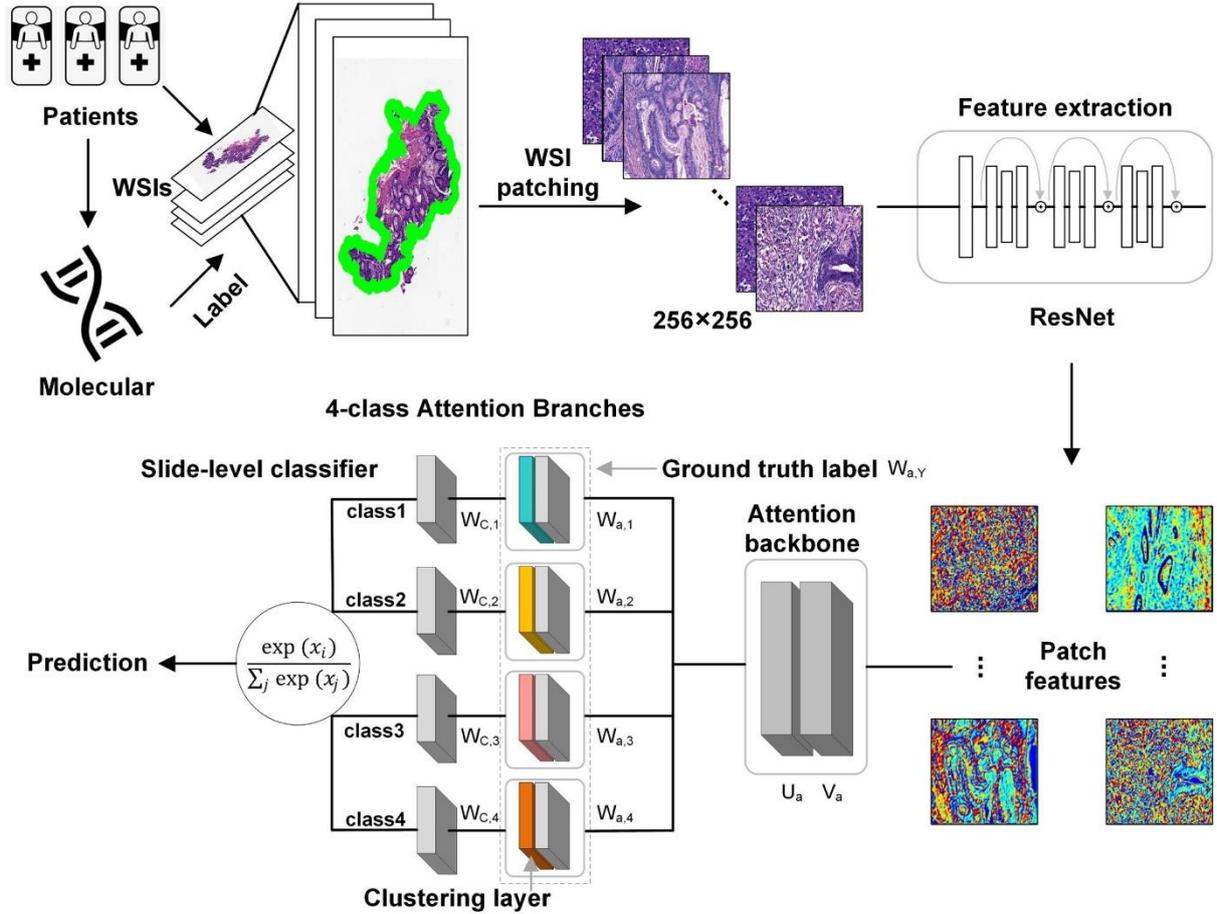
1 **Fig. 3.** AI workflow. Patches were extracted by WSIs in training set, and label as positive or  
2 negative samples by annotation. After training, WSIs in validation set were predicted and  
3 visualized as heatmaps. *WSI* whole slide image

#### 4 **AI in molecular subtypes of CRC**

5 Molecular subtypes of CRC can be characterized by genomic and phenotypic features. Given  
6 that different subtypes have different outcomes, the ability to subtype tumors in the clinical  
7 practice would be highly favorable, enabling optimal treatment for individual patients [20]. In  
8 PAI-WSIT, the data of molecular biomarkers and IHC results from patients were recorded,  
9 which were helpful for researchers to explore the molecular subtypes of cancer.

10

11 Given that WSI contains a wealth of histological features about CRC, and would present a  
12 more readily translatable method for subtyping CRC tumors. Therefore, one of the purposes of  
13 this study was to investigate whether we can classify CMS of CRC using WSI by deep learning,  
14 since WSI is more easily acquired in the routine clinical pathology laboratory. The whole  
15 process is shown in **Fig. 4.**



1

2

**Fig. 4.** Pipeline of CMS classification. The WSIs of CMS were labeled by gene expression data, all patches are extracted from tissue regions of a WSI. Patches are encoded once by a pretrained ResNet into a descriptive feature representation. Attention-pooling weighs patches and summarizes patch-level features into slide-level representations to make final prediction.

3

*WSI* whole slide image

4

5

For each digitized slide, the corresponding label was lied on the gene expression data of each patient. After segmentation,  $256 \times 256$  patches were generated to be encoded by a pretrained ResNet. Based on the clustering-constrained attention multiple instance learning model [25],

6

attention-based learning was applied for aggregating patch-level features into slide-level representations for classification. Following features extraction, both training and inference

7

1 can be carried out in the low-dimensional feature space. In instance-level clustering, for each  
2 of 4 classes, we place a clustering layer with 512 hidden units after the first fully-connected  
3 layer,  $W_1$ .  $W_1 \in \mathbb{R}^{512 \times 1024}$  further compress each fixed 1024-dimensional patch-level  
4 representation  $z_k$  to a 512-dimensional vector  $h_k = W_1 z_k^T$ . In the 4-class classification task,  
5 the first two layers of the attention network  $U_a \in \mathbb{R}^{256 \times 512}$  and  $V_a \in \mathbb{R}^{256 \times 512}$  collectively  
6 as the attention backbone shared by all classes, the attention network splits into 4 parallel  
7 attention branches  $W_{a,1}, \dots, W_{a,4} \in \mathbb{R}^{1 \times 256}$ . Similarly, 4 parallel independent classifiers,  
8  $W_{c,1}, \dots, W_{c,4}$  are built to score each class-specific slide-level representation. Accordingly, the  
9 attention score of the  $k^{th}$  patch for the 4 classes, denoted  $a_{k,4}$ , is given by Eq2 and the slide-  
10 level representation aggregated per the attention score distribution for the 4 classes, denoted  
11  $h_{slide,4} \in \mathbb{R}^{1 \times 512}$ , is given by Eq3:

$$a_{k,4} = \tag{2}$$

$$\frac{\exp\{W_{a,4}(\tanh(V_a h_k^T) \odot \text{sigm}(U_a h_k^T))\}}{\sum_{j=1}^4 \exp\{W_{a,j}(\tanh(V_a h_k^T) \odot \text{sigm}(U_a h_k^T))\}}$$

12

$$h_{slide,4} = \sum_{k=1}^N a_{k,4} h_k \tag{3}$$

13 The corresponding unnormalized slide-level score  $s_{slide,4}$  is given via the classifier layer  
14  $W_{c,4} \in \mathbb{R}^{1 \times 256}$  by  $s_{slide,4} = W_{c,4} h_{slide,4}^T$ . For inference, the predicted probability  
15 distribution over each class is computed by applying a softmax function to the slide-level  
16 prediction scores.  $s_{slide}$ .

17

18 Our data set was derived from TCGA, including 391 cases, 731 WSIs. The CMS slides with  
19 annotated ROIs from gene expression data were cropped with  $256 \times 256$  patches as input to the

1 original model. Finally, we evaluated the slide-level classification performance using 10-fold  
 2 monte carlo cross-validation. For each cross-validate fold, we randomly partitioned WSI  
 3 dataset into a training set (80% of cases), a validation set (10% of cases) and test set (10% of  
 4 cases). The distribution of WSIs is represented in Table 2.

6 **Table 2 Distribution of WSIs Dataset**

	<b>CMS1</b>	<b>CMS2</b>	<b>CMS3</b>	<b>CMS4</b>
Cases	63	176	57	95
WSIs	124	330	101	176
Patches	606520	1682444	509845	1174840

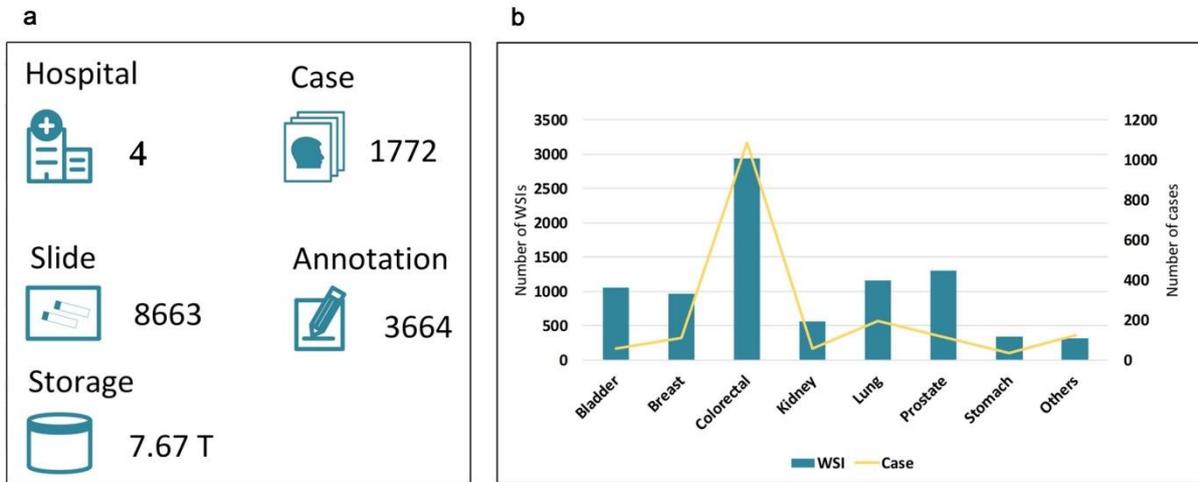
7 *CMS* consensus molecular subtyping, *WSI* whole slide image

## 8 **Results**

### 9 **Data statistics in PAI-WSIT**

10 PAI-WSIT collected 1772 cases, including colorectal cancer, breast cancer, prostate cancer,  
 11 lung cancer, kidney cancer and bladder cancer from four hospitals in China and TCGA. The  
 12 metadata of all cases such as basic information, pathological diagnosis reports were recorded.  
 13 Furthermore, 8663 WSIs, including H&E slides and IHC slides and 3664 high-quality  
 14 annotations generated by 8 experienced pathologists H&E slides, were also collected. Currently,  
 15 PAI-WSIT occupies 7.67 terabytes of disk space of the storage cluster, and the summary and  
 16 distribution of data are shown in **Fig. 5**. All information on the cases including basic

1 information, pathological diagnosis reports, H&E slides, IHC slides and high-quality  
2 annotations, are available at [www.paiwsit.com](http://www.paiwsit.com).



3  
4 **Fig. 5.** An overview of the data PAI-WSIT has recorded. (a) Data summary in PAI-WSIT. (b)  
5 Cases and slides by major primary site in PAI-WSIT. *WSI* whole slide image

## 6 **Web interfaces in PAI-WSIT**

7 A user-friendly web interface and search engine were incorporated for researchers in PAI-WSIT  
8 ([www.paiwsit.com](http://www.paiwsit.com)), which allows you to store your digital pathology images into the cloud  
9 platform so that you can search and view the images in the browser. PAI-WSIT also provides  
10 a feature-rich online tool for annotating your digital slides. Also, you can view the annotations  
11 drawn by other pathologists. For colorectal cancer, PAI-WSIT leverages AI technology to  
12 detect the abnormal regions in whole slide images. Results can be achieved and visualized in  
13 the form of heatmaps. The usage documentary (Additional file2: Figure S1) of PAI-WSIT is  
14 provided in a detailed description. Moreover, several help documents, including account  
15 management, WSI collection management, patient case management, WSI viewer usage and  
16 search engine usage are listed on (<http://www.paiwsit.com/help>), which may instruct you how

1 to use the platform.

## 2 **Application for Binary Positive vs. Negative Classification (in colorectal WSIs)**

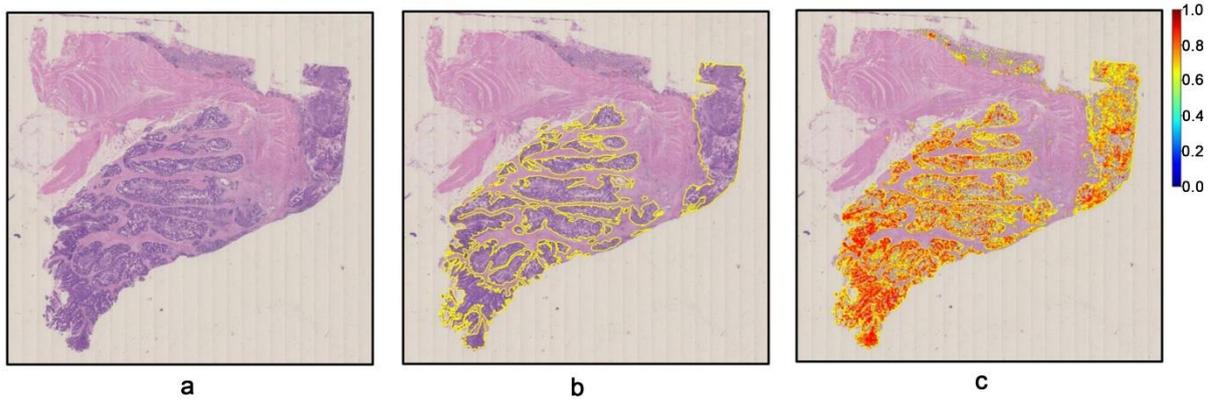
3 The classification results of test and validation sets in patch-level and image-level are listed in  
4 Table 3. Benchmark metrics of prediction in patch-levels are better than the image-levels,  
5 especially in accuracy. Although all benchmark metrics in validation are little worse than them  
6 in testing set, the performance is satisfactory and suggests that the deep learning-based  
7 approaches can be broadly applied in histopathology image field to assist pathologists in  
8 dealing with clinical tasks. With the help of heatmap, it even can map the location of the tumor  
9 area, and the results are shown in **Fig. 6**.

10

11 **Table 3 The results of ResNet in both testing and validation sets at patch-level and image-**  
12 **level**

<b>Dataset</b>	<b>Level</b>	<b>Accuracy</b>	<b>Recall</b>	<b>F1 score</b>
Testing	Patch	0.967	0.947	0.951
	Image	0.933	0.941	0.941
Validation	Patch	0.953	0.978	0.939
	Image	0.920	0.966	0.933

13



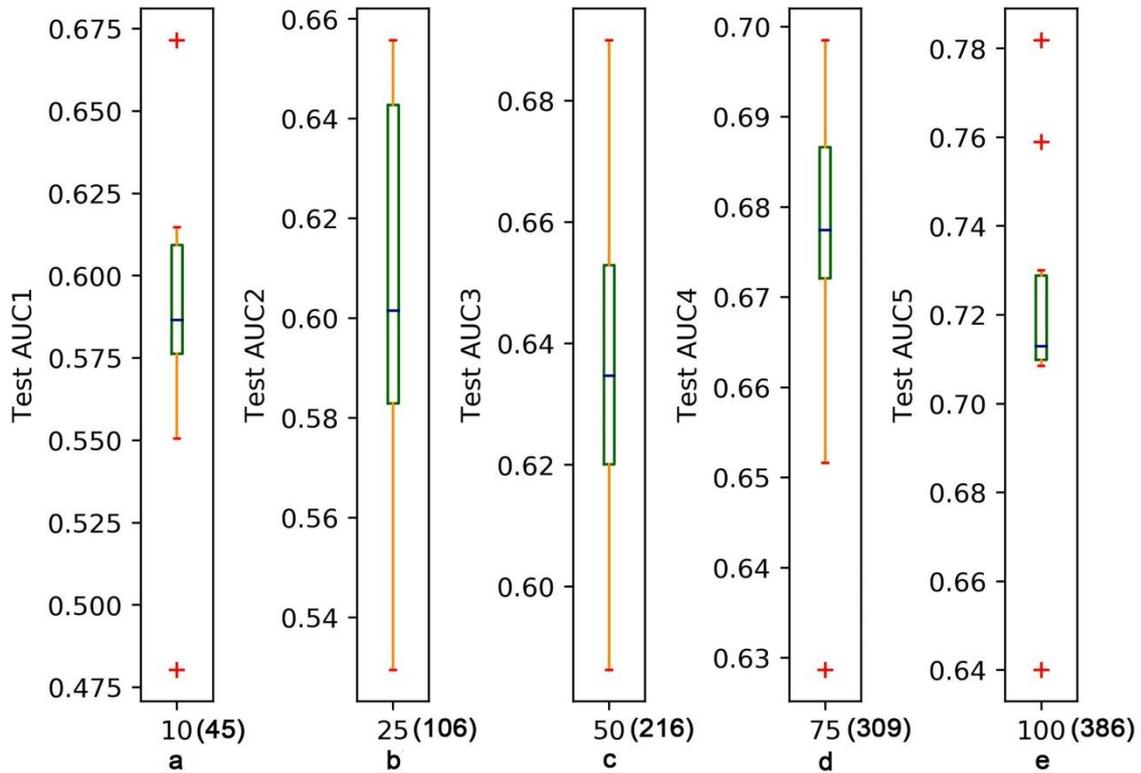
1  
2 **Fig. 6.** Prediction of location of tumor regions in ResNet. (a) Raw WSI;(b) Annotation; (c)  
3 Prediction. For each annotated slide, the whole slide attention heatmap is generated by their  
4 tumor probability. *WSI* whole slide image

#### 6 **AI for Subtyping Problem (4-class CRC Subtyping)**

7 We evaluated the slide-level classification performance using 10-fold monte carlo cross-  
8 validation. For each cross-validate fold, we randomly partitioned WSI dataset into a training  
9 set (80% of cases), a validation set (10% of cases) and test set (10% of cases). To investigate  
10 the dependency of the model's performance on the amount of training data available, for each  
11 cross-validated fold created, we sequentially sampled subsets of training data equal to  
12 75%,50%,25%,10% of the total number of cases in the training set, while keeping the  
13 validation and test set the same.

14  
15 We observed that the model is more confident in its correct predictions than in its incorrect  
16 predictions and becomes less and less confident as the size of the training set is reduced  
17 **(Fig.7(a-d))**. When testing on the test cohort, the 10-fold cross-validated model trained using

1 100% of the training set achieved an average one-vs-rest AUC (macro-averages) of 0.719 on  
 2 colorectal subtype dataset (**Fig.7(e)**), which reflects the shortcomings of quality and number of  
 3 the dataset.



4  
 5 **Fig. 7.** AUC of test set. (a-e) were % of Training set used (Number of WSIs). *AUC* area under  
 6 the curve, *WSI* whole slide image

7 **Discussion**

8 There is increasing evidence that AI will be essential to integrate disparate sources of  
 9 information, discover more complicated or subtle connections than a human would and help  
 10 pathologists make the best clinical decisions for patients [17, 26, 27]. To address the data  
 11 integration and analysis for computational pathology mainly in colorectal cancer, we developed  
 12 a pathologist-annotated for WSI database. We also proposed frameworks for binary task and

1 subtyping problem with standard annotated WSIs. Therefore, the platform of PAI-WSIT may  
2 serve as an excellent source for both clinical and research settings in tumors precision diagnosis,  
3 and create the collaboration among clinical pathologists to further develop the computer-aided  
4 prognosis as well.

5  
6 The aim of present study was to provide data for artificial intelligent researches to fuel the  
7 development of algorithms and tools in cancer research and clinical diagnosis. To achieve this  
8 goal, as a multicenter platform, PAI-WSIT collected pathological data of cancer patients from  
9 four regional hospitals in China and TCGA. With cancer patients as the basic elements, PAI-  
10 WSIT recorded physiological information, clinical and pathological reports, WSIs and gene  
11 mutation data from detection reports. More importantly, we integrated annotation tools and  
12 deep learning models for malignant regions detection and molecular subtype classification of  
13 CRCs.

14  
15 Accurate detection of malignant regions in colorectal WSIs is a perfect combination between  
16 AI and histopathology, while phenotypic subtyping could be the first step toward precision  
17 medicine for CRC. Routine subtyping for CRC tumors could revolutionize the treatment of  
18 patients, with each subtype receiving a different therapeutic regime. For example, it is already  
19 known that the EGFR monoclonal antibody, cetuximab may not be useful for patients with the  
20 CMS1 or CMS3 subtypes [28]. Nevertheless, CMS1 appears to be the only subtype sensitive  
21 to Src family kinase inhibitors such as Dasatinib [29]. The study result has also been shown  
22 that CMS4 is resistant to chemotherapy [30]. Though the results of AI models in the

1 performance of CRC molecular subtypes were unsatisfactory, it has laid the foundation for  
2 future work improvement.

3  
4 Annotating the 1298 colorectal slides with high-quality is a valuable effort, being comparable  
5 to an earlier breast cancer dataset [13], though those do not contain functionality for reading  
6 annotations or storing image analysis results. Given that the sizes of datasets in recent studies  
7 focusing on a specific disease are exceeding the 10000 WSI mark [31] and digital pathology is  
8 moving towards a more epidemiological scale [32-34], we are working with hospitals and  
9 pathologists to further improve and popularize PAI-WSIT with more WSIs and annotations  
10 which makes it a valuable resource in computational pathology in the very near future.

11  
12 There are two limitations of this study. First, the prediction results of AI in the molecular  
13 subtypes of CRCs are slightly unsatisfactory. In future work, artificial subjective bias caused  
14 by slide's quality should be avoided, post-processing methods should be improved, and better  
15 models such as U-NET [35] should be tried. Second, and more importantly, it should be more  
16 than just WSI analysis to increase physicians' understanding of AI outcomes. Thus, we will  
17 integrate other omics data, including proteomics and genomics, in future research.

## 18 **Conclusions**

19 PAI-WSIT (<https://www.paiwsit.com>) contains histopathology, immunohistochemistry, gene  
20 mutations and clinical data of tumor patients, forming pathological big data. The platform's  
21 annotation function and deep learning models provide support for AI-assisted tumor diagnosis,

1 and can serve as a valuable resource for use by the community of researchers in the WSI  
2 analysis and tissue diagnostics domains.

### 3 **Supplementary information**

4 Supplementary data are available at Journal of Translational Medicine online.

### 5 **Abbreviations**

6 AI: Artificial intelligence; WSI: Whole slide image; CMS: Consensus molecular subtyping;  
7 CRCs: Colorectal cancers; IHC: Immunohistochemistry; H&E: Hematoxylin-eosin; NGS:  
8 Next-generation sequencing; ROIs: Regions of interest; SGD: Stochastic gradient descent;  
9 CRCSC: The Colorectal Cancer Subtyping Consortium; TCGA: The Cancer Genome Atlas;  
10 AUC: area under the curve.

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13 University.

### 14 **Authors' contributions**

15 C.Z. carried out the main research. C.Z. and X.F. wrote the manuscript. Y.J. designed the Web  
16 application. H.F.G. polished the manuscript. X.F., Y.Z., L.G. and X.T. collected and annotated  
17 the data. J.J., S.J., Y.X. and X.F. interpreted the data. J.L. contributed to method development  
18 and reviewed the manuscript.

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## 5 **Availability of data and materials**

6 The curated patience cases along with WSIs were stored in a MySQL database cluster and a  
7 distributed file system deployed on a group of on-premises servers. A feature-rich web  
8 application was developed to provide public access to the data. The backend of the application  
9 is developed using ASP.NET Core, while the frontend is developed using Angular, which  
10 communicates with the backend using REST APIs. To help researches fetch patient information  
11 (including WSIs and their annotations) programmatically from the platform, a library written  
12 in C# is available on our GitHub repository (<https://github.com/yigolden/paiwsit-client-csharp>).

## 13 **Ethics approval and consent to participate**

14 The study was approved by the Ethical Committee of Nanjing First Hospital, the First Affiliated  
15 Hospital of Zhejiang University, the First Affiliated Hospital of Soochow University and  
16 Nanjing Drum Tower Hospital. Due to the retrospective nature of the study, written informed  
17 consent for participation in the study was waived.

1 **Consent for publication**

2 All the authors in this paper consent to publication of the work.

3 **Competing interests**

4 The author declares that they have no competing interests.

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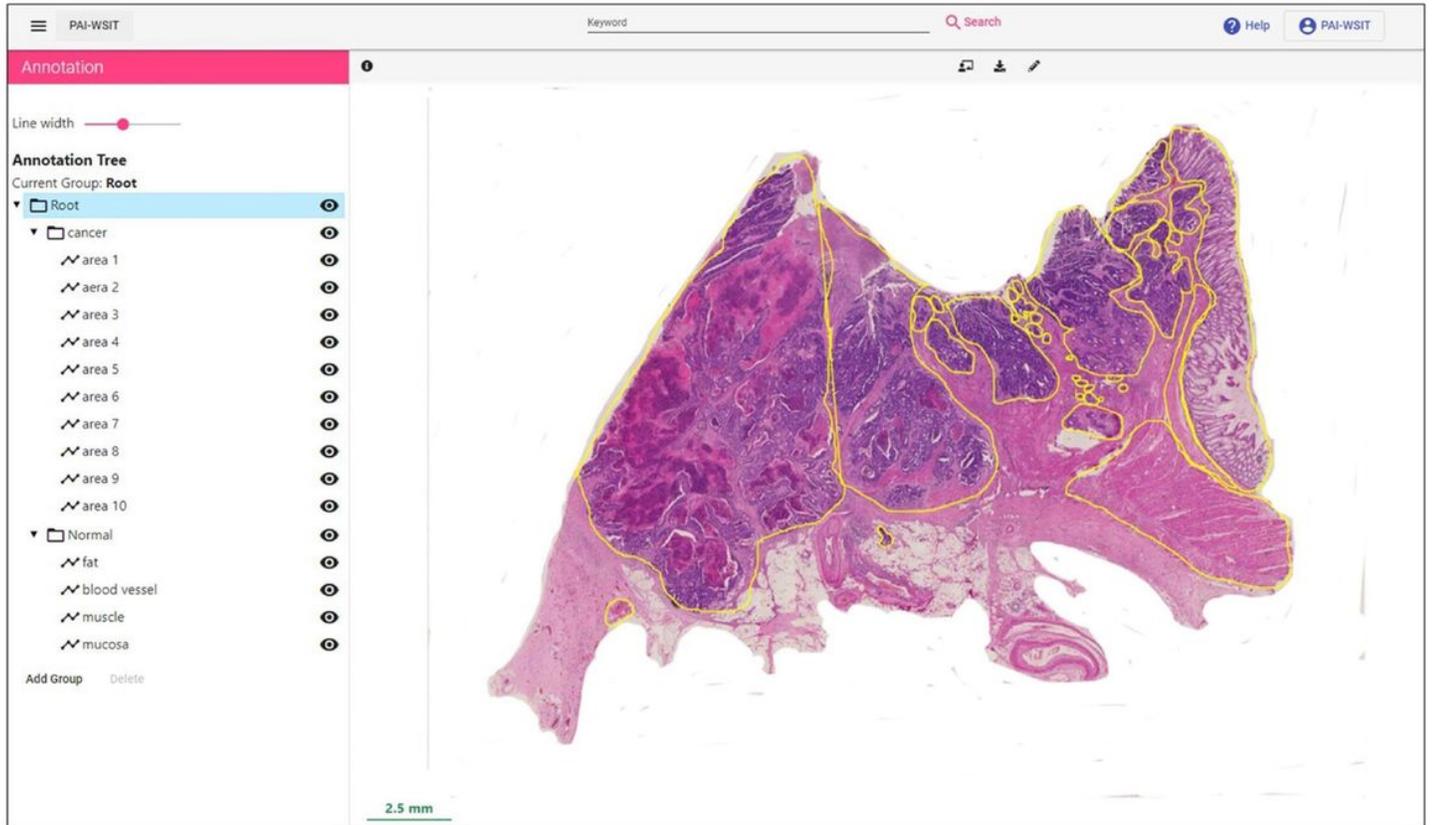
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10

# Figures

a



b

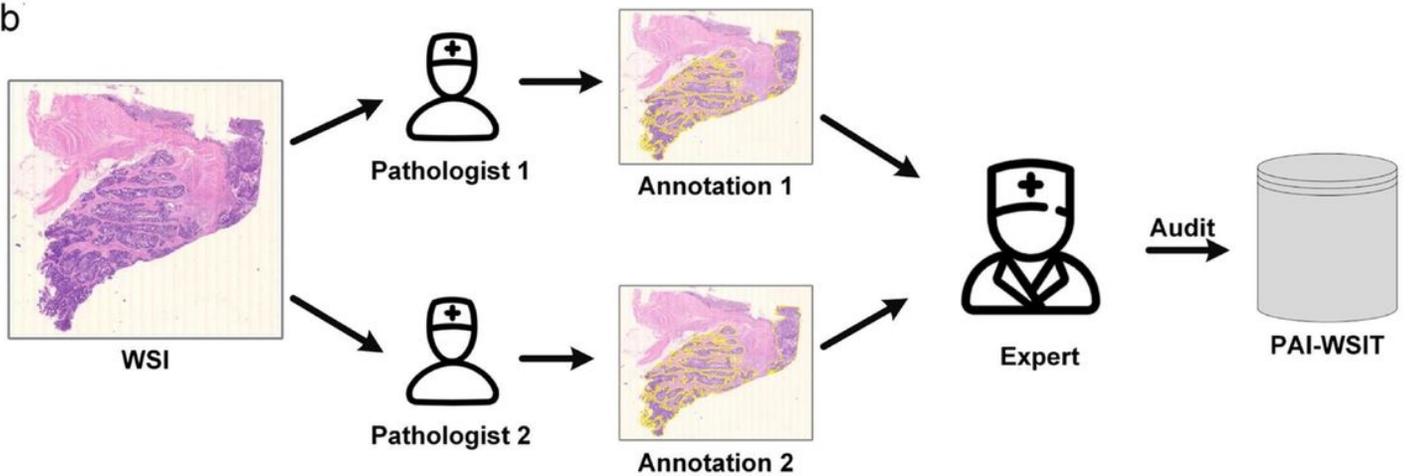


Figure 1

Annotation tool in PAI-WSIT. (a) Annotation tree: the user draws two groups of regions in a WSI, one is cancer areas and the other is normal areas. (b) Annotation protocol: each annotation in PAI-WSIT was annotated by two pathologists and audited by an experienced expert. WSI whole slide image

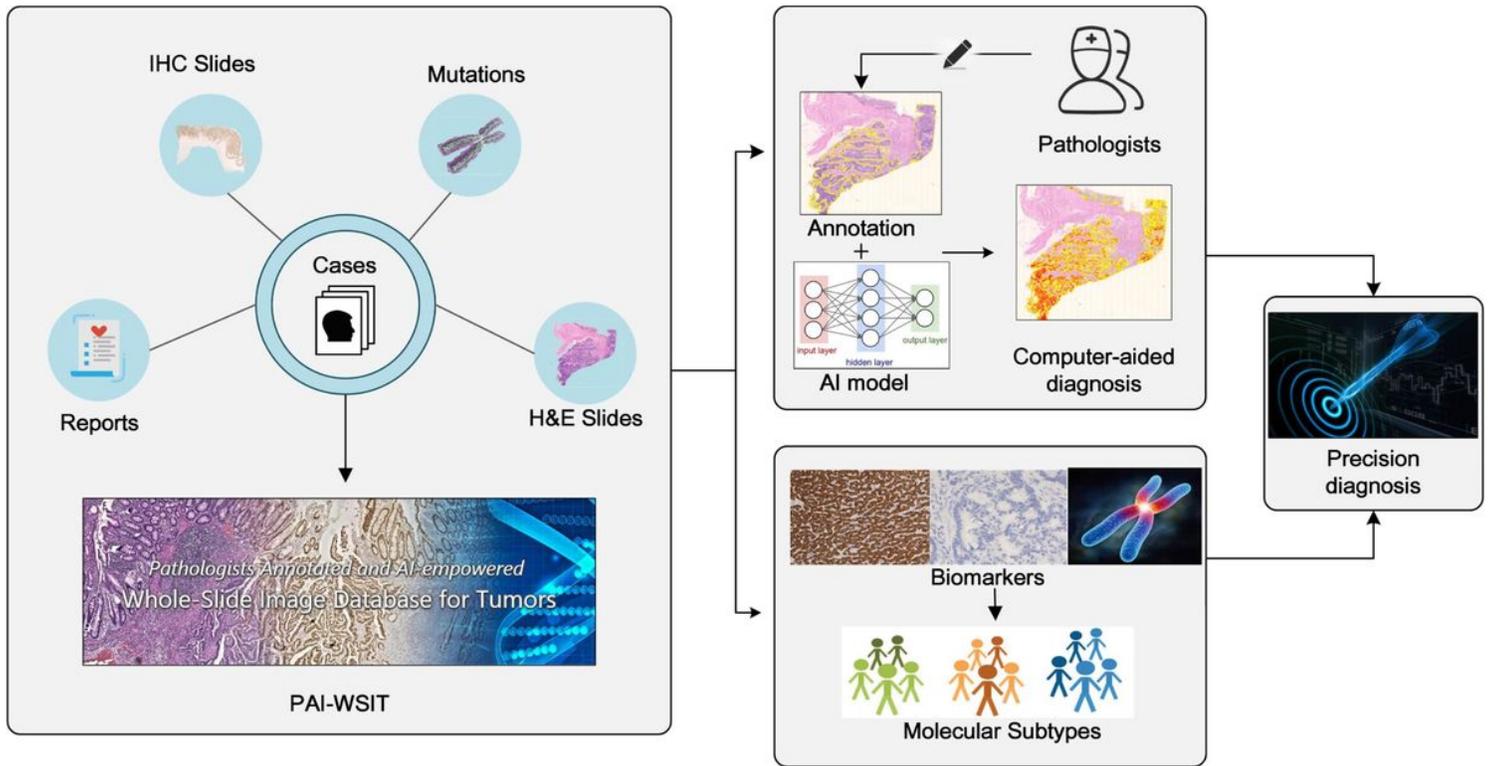


Figure 2

The overall workflow of PAI-WSIT. PAI-WSIT contains basic information, pathological reports, WSIs and target biomarker results of cancer cases. The integration of annotation tools towards WSI makes AI in digital pathology more convenient. Biomarkers in DNA-level and transcriptional-level are helpful for molecular subtype research. IHC immunohistochemistry, H&E hematoxylin-eosin, AI artificial intelligence

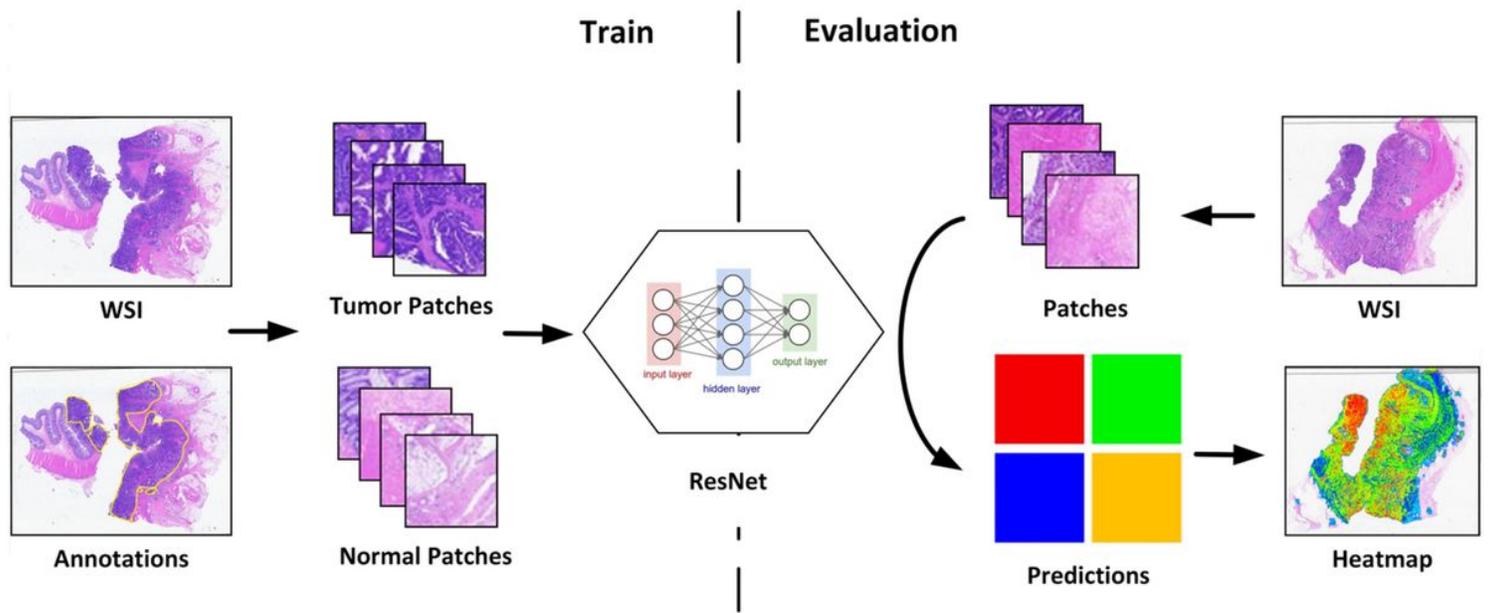


Figure 3

AI workflow. Patches were extracted by WSIs in training set, and label as positive or negative samples by annotation. After training, WSIs in validation set were predicted and visualized as heatmaps. WSI whole slide image

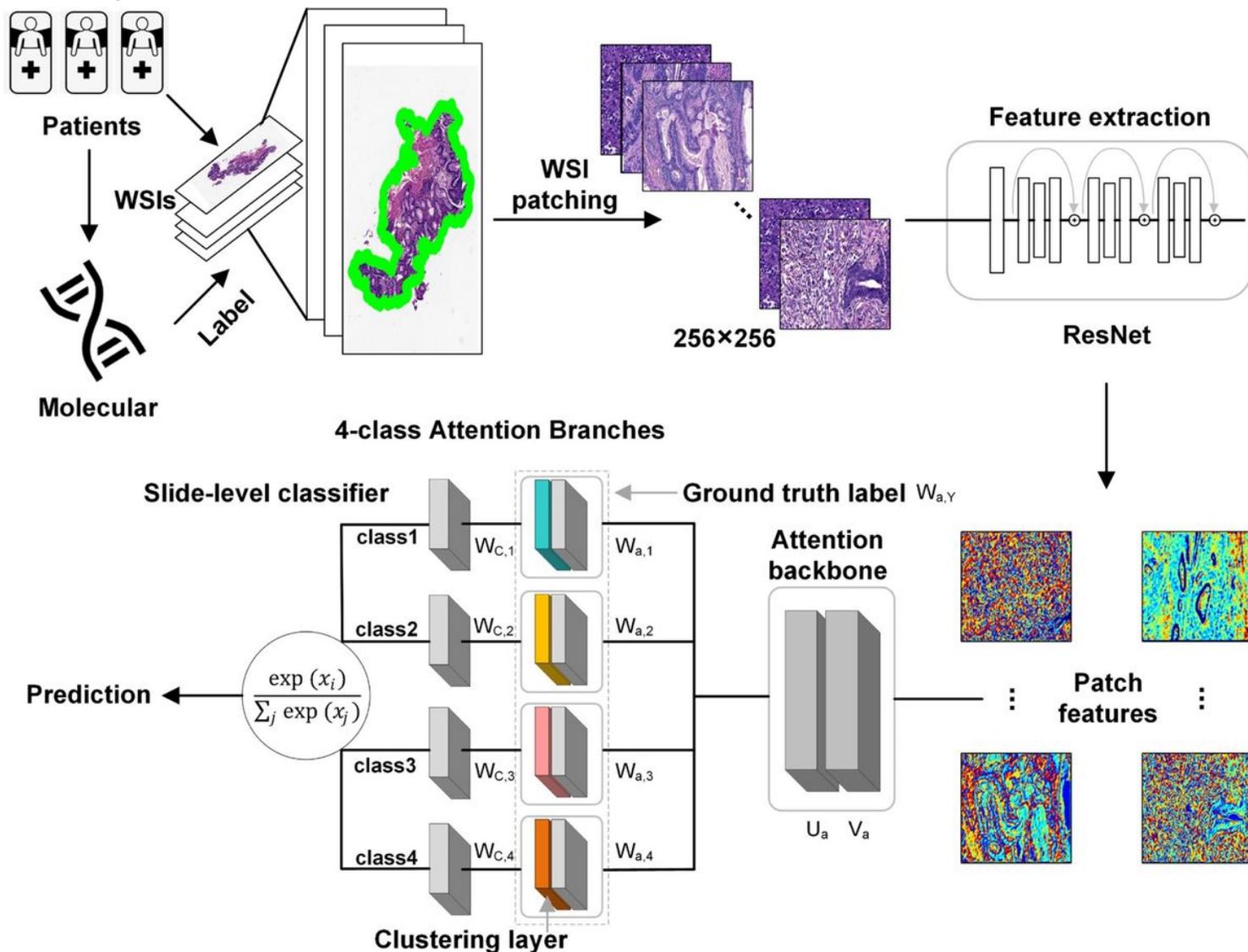
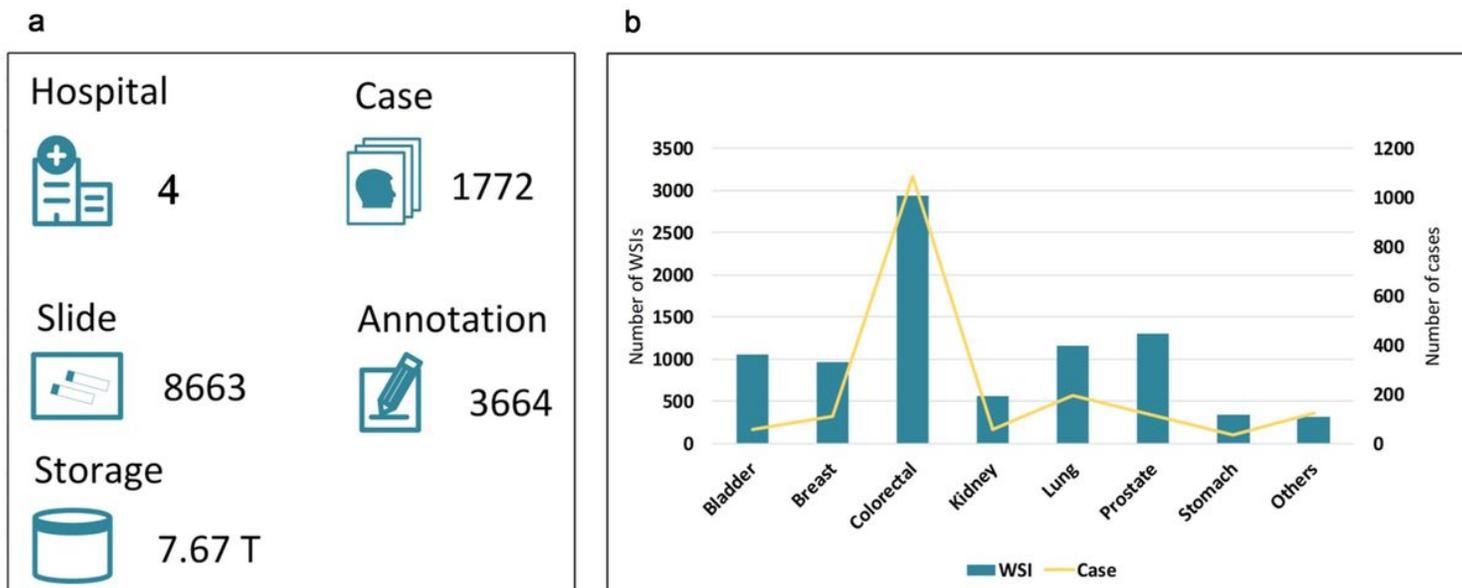


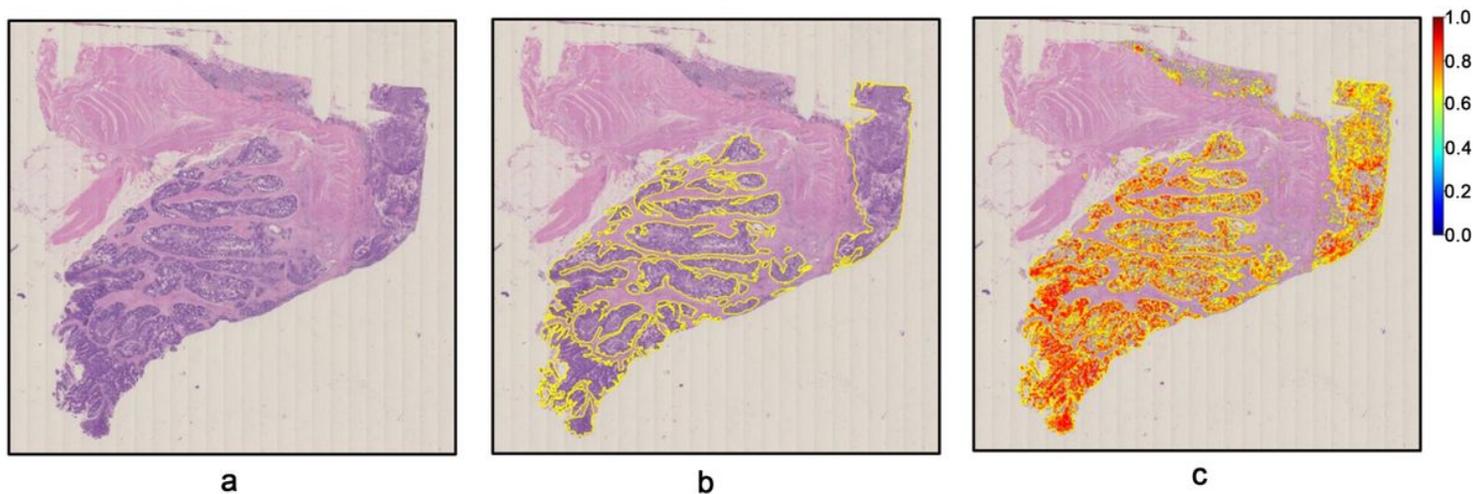
Figure 4

Pipeline of CMS classification. The WSIs of CMS were labeled by gene expression data, all patches are extracted from tissue regions of a WSI. Patches are encoded once by a pretrained ResNet into a descriptive feature representation. Attention-pooling weighs patches and summarizes patch-level features into slide-level representations to make final prediction. WSI whole slide image



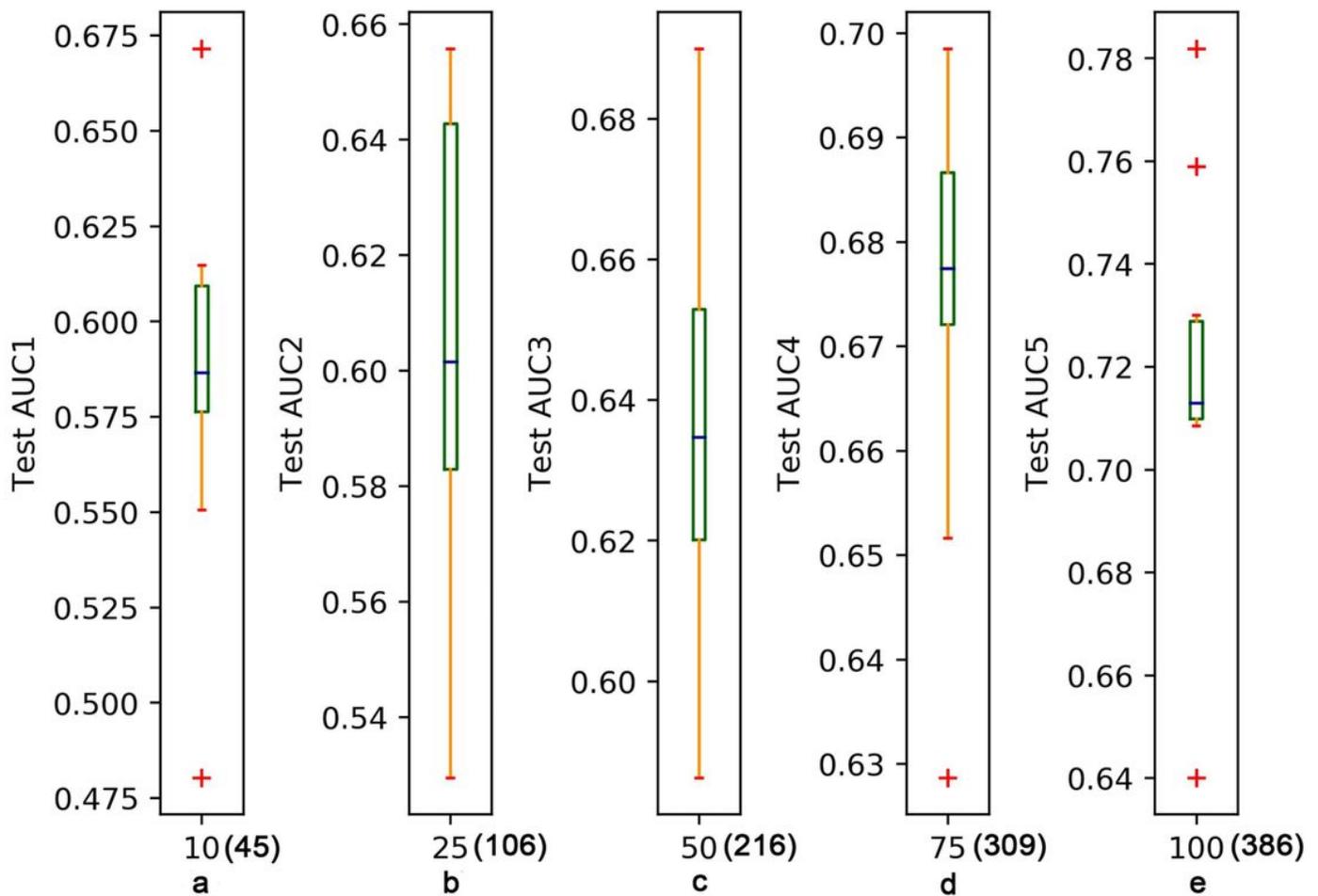
**Figure 5**

An overview of the data PAI-WSIT has recorded. (a) Data summary in PAI-WSIT. (b) Cases and slides by major primary site in PAI-WSIT. WSI whole slide image



**Figure 6**

Prediction of location of tumor regions in ResNet. (a) Raw WSI;(b) Annotation; (c) Prediction. For each annotated slide, the whole slide attention heatmap is generated by their tumor probability. WSI whole slide image



**Figure 7**

AUC of test set. (a-e) were % of Training set used (Number of WSIs). AUC area under the curve, WSI whole slide image

## Supplementary Files

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