

Rotation-Agnostic Image Representation Learning for Digital Pathology

(Supplementary File)

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Algorithms

1. Algorithm **S1**: HistoRotate: 360° Rotation Augmentation Method.

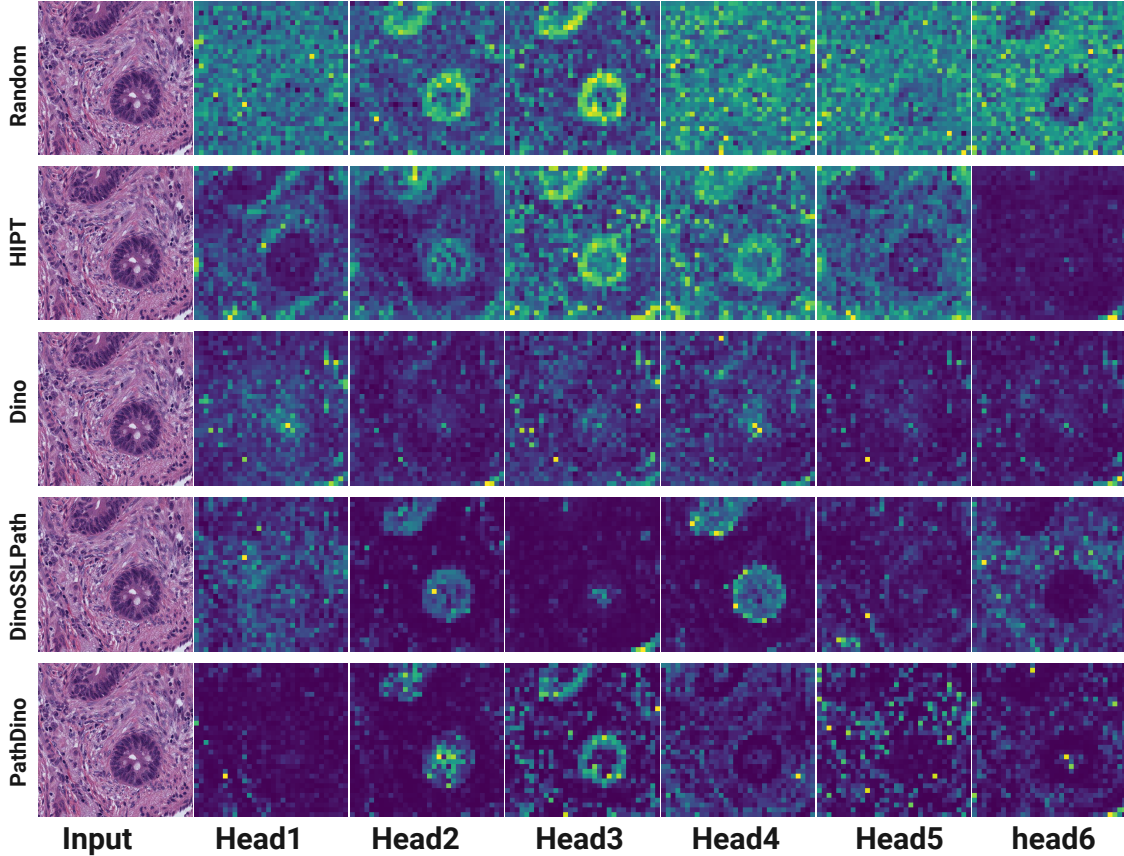


Figure S1. Attention visualization of the proposed PathDino as compared to other ViT-samll models.

Table S1. Summary of Model Attributes. It is worth noting that DinoV2, CLIP, and DinoSSLPath also trained with CNN-based backbones such as ResNet50, however, we only employ the Transformer-based backbones in our comparisons. Floating Point Operations Per Second (FLOPs) are used to quantify the computational complexity of models. Note that we specified the data size used for the exact pre-trained models in our study rather than the general mentioned in the corresponding papers. For example, DinoSSLPath [1] was trained on 32.6M patches (19M from TCGA and 13.6M from a TULIP, which is a private dataset), however, the publically available pre-trained models are trained only on TCGA. Thus, we report 19M for pretraining DinoSSLPath, SwAV-ResNet50, MoCoV2-ResNet50, and Barlow-Twins-ResNet50. PubMed consists of a total of 15, 282, 336, however, the training set is 13.9M.

	Model	Pretrained On	Pretraining Domain	Modality	Training Data Size	Learning Paradigm	Input Dim.	Output Embedding	Model Size	FLOPs	
CNN	ResNet50 - [2]	ImageNet-1k	Natural Images	Image	1, 200, 000	Supervised	224 × 224	2048	23, 527, 264	4, 374, 897, 664	
	DenseNet121 - [3]	ImageNet-1k	Natural Images	Image	1, 200, 000	Supervised	224 × 224	1024	6, 870, 208	2, 833, 364, 480	
	EfficientNet-b3-288 - [4]	ImageNet-1k	Natural Images	Image	1, 200, 000	Supervised	288 × 288	1536	10, 608, 936	1, 587, 788, 048	
	EfficientNet-b5 - [4]	ImageNet-1k	Natural Images	Image	1, 200, 000	Supervised	448 × 448	2048	28, 168, 048	9, 402, 729, 536	
	ConvNext-B [5]	ImageNet-21k	Natural Images	Image	14, 000, 000	Supervised	224 × 224	1024	87, 510, 272	15, 353, 709, 568	
	ConvNext-xlarge - [5]	ImageNet-21k	Natural Images	Image	14, 000, 000	Supervised	224 × 224	2048	348, 035, 584	60, 918, 990, 848	
	SwAV-ResNet50 - [1]	TCGA	Histopathology Images	Image	19, 000, 000	Self-supervised	1024 × 768	2048	23, 508, 032	64, 757, 958, 656	
	MoCoV2-ResNet50 - [1]	TCGA	Histopathology Images	Image	19, 000, 000	Self-supervised	1024 × 768	2048	23, 508, 032	64, 757, 958, 656	
	MuDiPath-ResNet50 - [6]	TCGA	Histopathology Images	Image	882, 800	Supervised	224 × 224	2048	25, 557, 032	4, 131, 592, 192	
	MuDiPath-DenseNet-101 - [6]	TCGA	Histopathology Images	Image	882, 800	Supervised	224 × 224	1024	6, 953, 856	2, 895, 983, 104	
	KimiaNet - [7]	TCGA	Histopathology Images	Image	240, 000	Supervised	1000 × 1000	1024	6, 953, 856	57, 471, 584, 640	
	Barlow-Twins-ResNet50 - [1]	TCGA	Histopathology Images	Image	19, 000, 000	Self-supervised	1024 × 768	2048	23, 508, 032	64, 757, 958, 656	
	Transformers	ViT-B16 [8]	ImageNet-1k	Natural Images	Image	1, 200, 000	Supervised	224 × 224	768	85, 646, 592	16, 862, 862, 336
		DinoV1-ViT-s16 - [9]	ImageNet-1k	Natural Images	Image	1, 200, 000	Self-supervised	224 × 224	384	21, 589, 632	4, 248, 399, 360
DinoV1-ViT-b16 - [9]		ImageNet-1k	Natural Images	Image	1, 200, 000	Self-supervised	224 × 224	768	85, 646, 592	16, 862, 862, 336	
DinoV2-ViT-b14 - [10]		Internet	Natural Images	Image	142, 000, 000	Self-Supervised	224 × 224	768	85, 508, 352	21, 963, 549, 696	
DinoV2 - ViT-B16 - [11]		Internet	Natural Image-Text	Image-Text	400, 000, 000	Contrastive Learning	224 × 224	512	85, 646, 592	16, 862, 862, 336	
BiomedCLIP - [12]		PMC-15M	Medical (PubMed)	Image-Text	13, 900, 000	Contrastive Learning	224 × 224	512	85, 646, 592	16, 862, 862, 336	
HIPT-ViT-s16 [13]		TCGA	Histopathology Images	Image	104, 000, 000	Self-supervised	256 × 256	384	21, 589, 632	5, 542, 417, 920	
PLIP [14]		OpenPath	Histopathology (Twitter)	Image-Text	208, 414	Contrastive Learning	224 × 224	512	85, 646, 592	16, 862, 862, 336	
iBOT-Path [15]		TCGA	Histopathology Images	Image	40, 000, 000	Self-supervised	224 × 224	768	85, 646, 592	16, 862, 862, 336	
DinoSSLPathology-8 [1]		TCGA	Histopathology Images	Image	19, 000, 000	Self-supervised	224 × 224	384	21, 368, 448	16, 756, 372, 992	
PathDino-224 (ours)		TCGA	Histopathology Images	Image	2, 118, 068	Self-supervised	224 × 224	384	9, 168, 384	1, 804, 061, 184	
PathDino-512 (ours)		TCGA	Histopathology Images	Image	6, 087, 558	Self-supervised	512 × 512	384	9, 168, 384	9, 387, 852, 288	

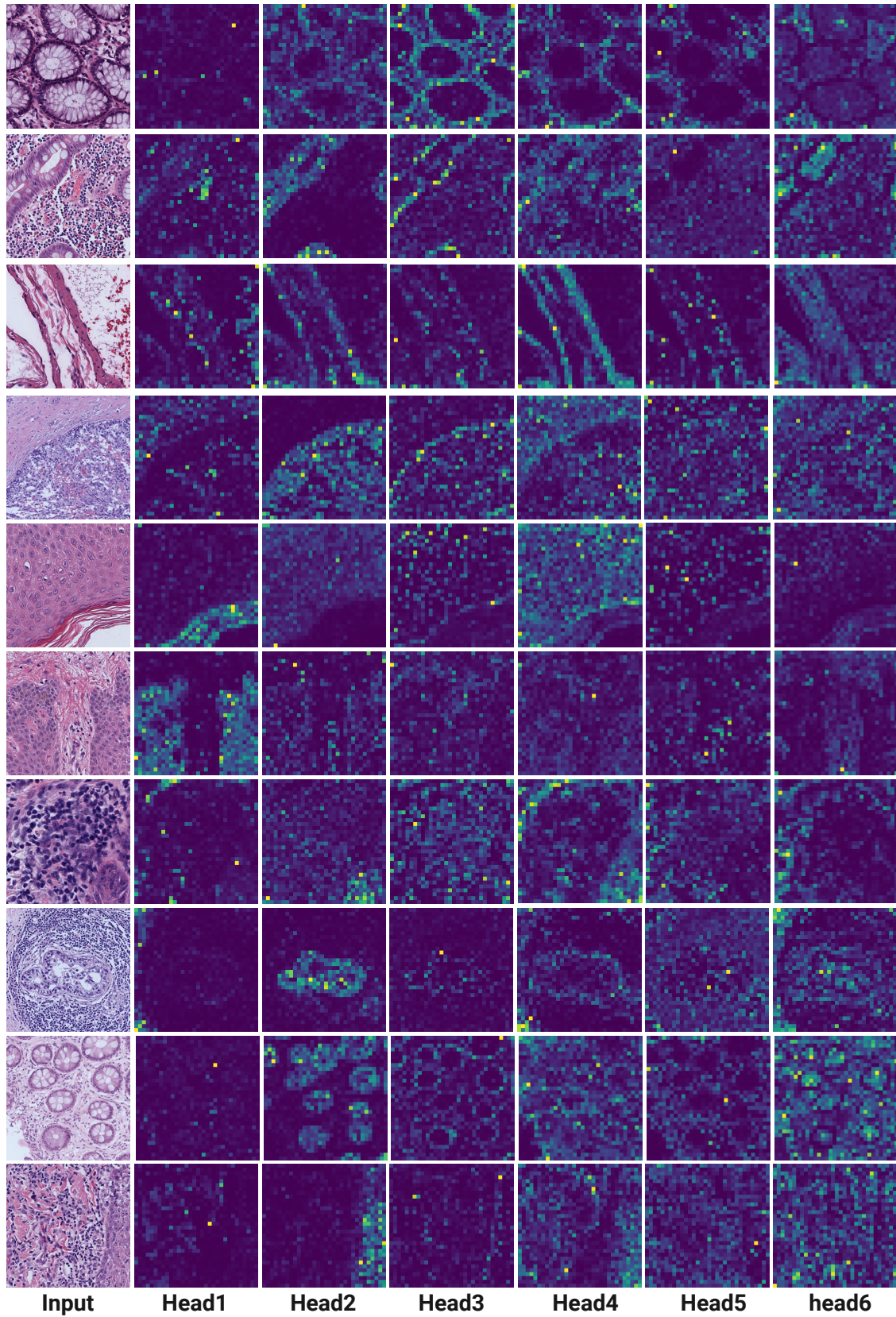
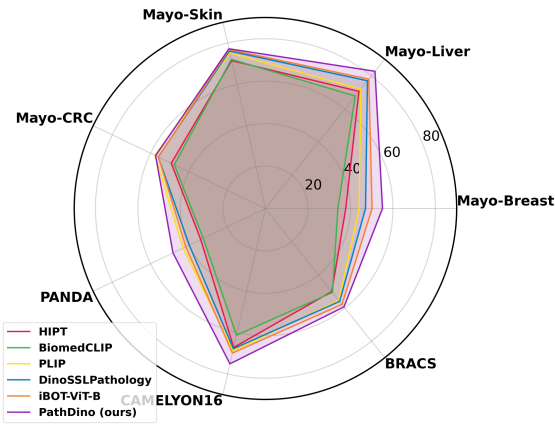
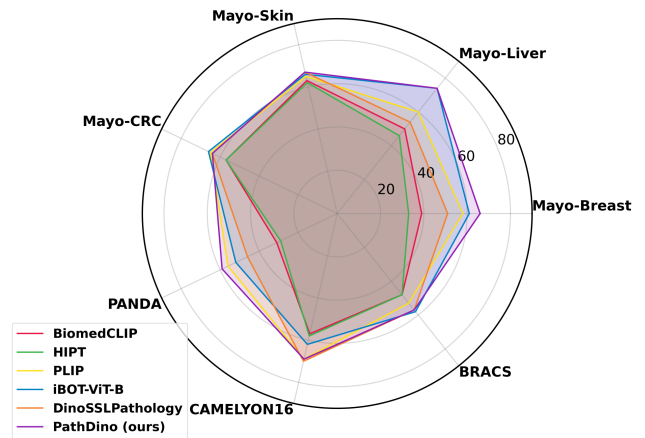


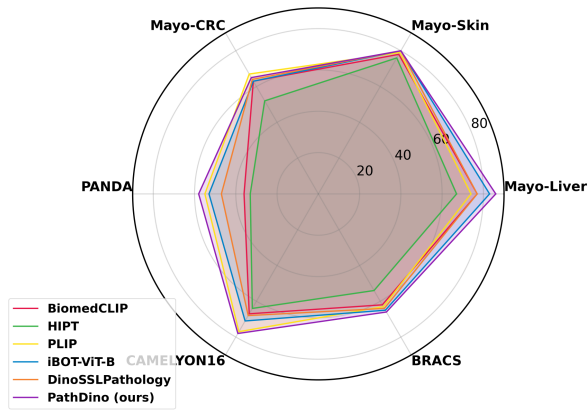
Figure S2. Attention visualization of the proposed PathDino transformer heads.



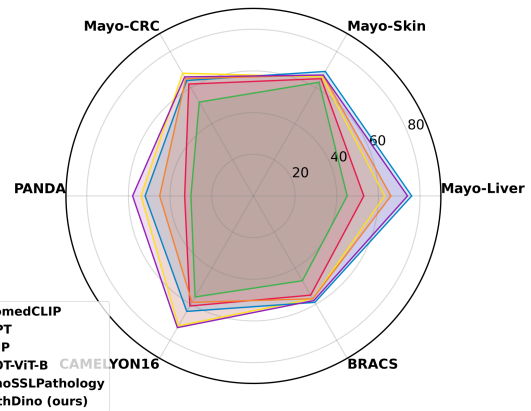
(A) Patch-Level Retrieval MV@5 Accuracy



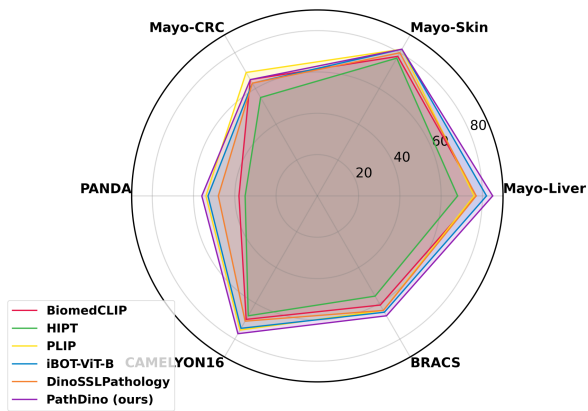
(B) WSI-Level Retrieval Top-1 Accuracy



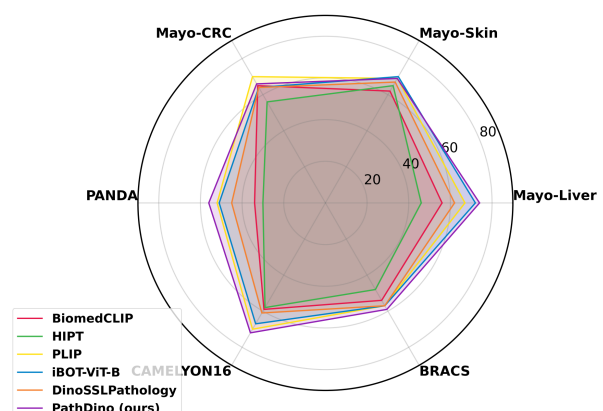
(C) WSI-Level Retrieval MV@3 Accuracy



(D) WSI-Level Retrieval MV@3 Macro Avg



(E) WSI-Level Retrieval MV@5 Accuracy



(F) WSI-Level Retrieval MV@5 Macro Avg

Figure S3. Performance of selected Transformer-based histopathology feature extractors including HIPT, BiomedCLIP, PLIP, DinoSSLPath, iBOT, and PathDino. The performance is represented as the macro average of the F_1 score for the MV@5 in the patch-level retrieval settings.

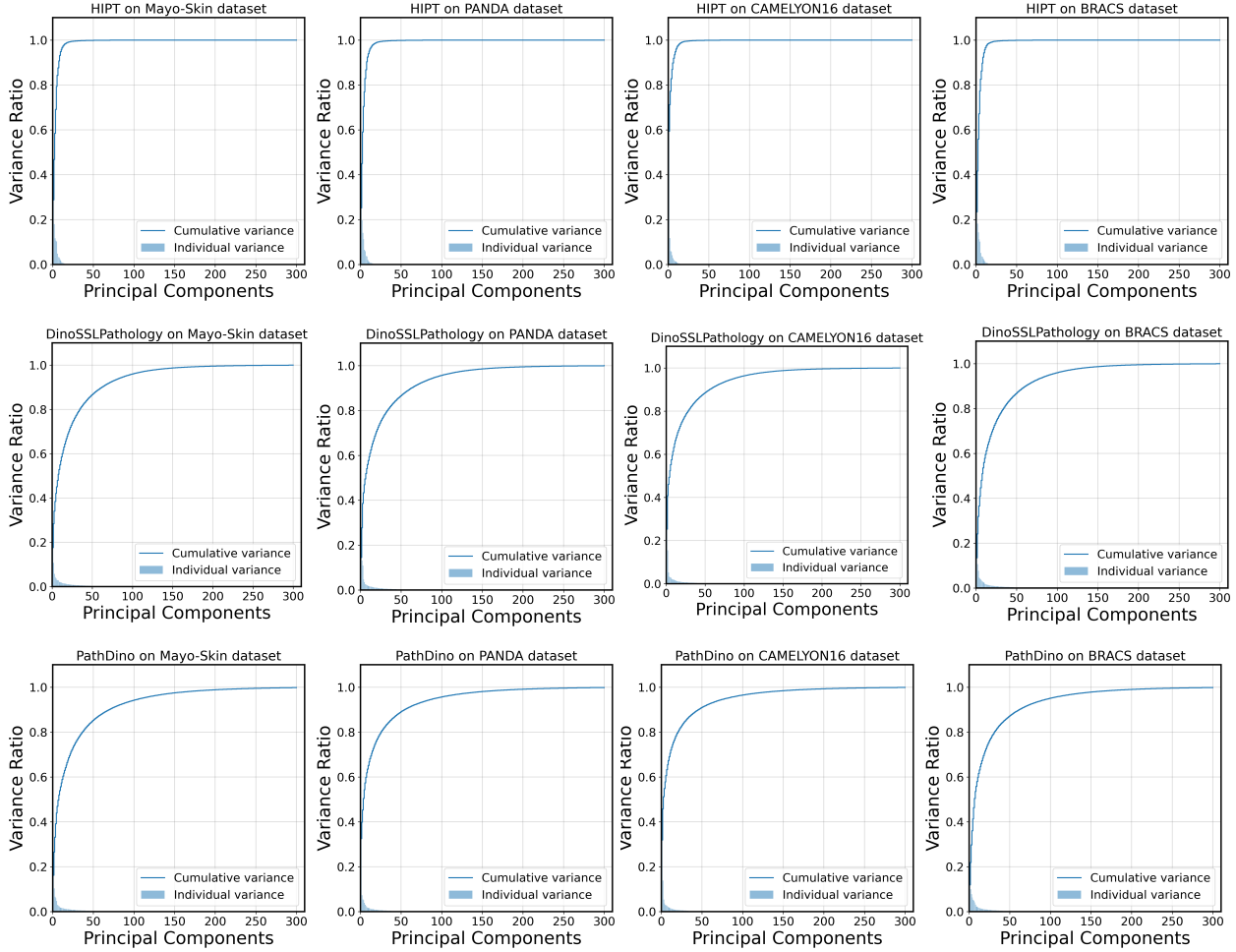


Figure S4. Embedding variance analysis of three selected Transformer-based histopathology feature extractors which have output vector size of 384 including HIPT, DinoSSLPath, and our PathDino.

Table S2. (accuracy) Patient matching outcomes across four internal and three public datasets for classification, subtyping, and grading tasks, utilizing the Yottixel framework and leave-one-patient-out method.

Dataset		DinoV2 [10]		CLIP [11]		BiomedCLIP [12]		PLIP [14]		KimiaNet [7]		DinoSSLPath [1]		PathDino		
		Yottixel	FPS	Yottixel	FPS	Yottixel	FPS	Yottixel	FPS	Yottixel	FPS	Yottixel	FPS	Yottixel	FPS	
Internal Data	Private-Breast	Top 1	36	53	45	49	47	47	55	58	56	51	59	58	63	68
		MV@3	71	71	63	67	70	74	70	73	76	78	75	74	81	83
	Private-Liver	MV@3	73	74	69	69	75	77	76	74	79	80	77	77	86	86
		MV@5	70	72	72	71	74	77	73	76	80	78	81	77	87	85
	Private-Skin	Top 1	59	72	68	75	68	75	72	75	78	75	79	78	79	78
		MV@3	66	77	73	79	73	78	77	79	81	81	80	80	81	80
	Private-CRC	MV@5	68	87	77	80	76	78	80	82	82	82	80	80	81	82
		Top 1	52	56	57	56	55	58	60	64	60	64	60	63	57	63
	Private-CRC	MV@3	52	59	59	58	60	63	61	67	60	65	61	64	60	65
		MV@5	55	59	56	60	59	65	62	69	60	62	63	63	61	65
Public Data	PANDA [16]	Top 1	35	31	35	36	33	34	53	56	58	57	48	47	59	58
		MV@3	33	32	37	38	36	36	53	55	58	56	50	47	58	58
		MV@5	35	35	39	40	38	38	53	54	56	54	51	48	58	56
	CAMELYON16 [17]	Top 1	57	61	66	67	60	61	70	73	75	76	75	74	76	73
		MV@3	58	58	66	67	58	67	71	77	72	78	74	68	77	78
		MV@5	57	63	64	69	64	69	70	75	79	81	75	70	78	77
	BRACS [18]	Top 1	53	51	53	58	56	55	62	60	66	62	61	65	64	64
		MV@3	55	53	58	60	58	62	64	63	66	64	61	64	65	66
		MV@5	58	56	59	61	59	61	66	64	67	66	62	64	66	67

Table S3. (Macro Avg) Patient matching outcomes across four internal and three public datasets for retrieval, subtyping, and grading tasks, utilizing the FPS vs Yottixel framework and leave-one-patient-out method on Macro Average $F-1$ score.

Dataset		DinoV2 [10]		CLIP [11]		BiomedCLIP [12]		PLIP [14]		KimiaNet [7]		DinoSSLPath [1]		PathDino			
		Yottixel	FPS	Yottixel	FPS	Yottixel	FPS	Yottixel	FPS	Yottixel	FPS	Yottixel	FPS	Yottixel	FPS		
Internal Data	Private-Breast	Top 1	24	46	33	39	39	39	45	58	56	47	55	51	60	66	
		Top 1	61	49	52	46	59	50	60	60	62	66	65	54	76	74	
	Private-Liver	MV@3	59	42	50	47	68	53	68	63	67	62	69	66	83	74	
		MV@5	54	53	56	52	64	56	59	67	65	61	74	62	81	74	
	Private-Skin	Top 1	54	65	62	66	61	63	63	65	70	65	71	67	68	67	
		MV@3	58	66	65	66	62	65	65	66	70	71	68	67	69	67	
	Private-CRC	MV@5	58	66	67	67	65	62	67	69	70	69	66	67	68	69	
		Top 1	51	56	54	56	54	57	59	65	60	64	60	64	58	64	
	Public Data	PANDA [16]	MV@3	49	59	55	58	58	62	60	68	61	66	61	65	60	66
			MV@5	51	59	50	60	57	65	61	70	60	63	63	64	60	66
		CAMELYON16 [17]	Top 1	56	57	65	61	59	57	68	69	72	74	57	70	73	69
			MV@3	56	50	64	58	55	61	68	72	68	74	69	59	74	73
BRACS [18]		MV@5	54	54	62	61	61	59	65	70	75	77	70	61	73	72	
		Top 1	48	45	47	52	48	48	56	53	59	57	54	57	59	57	
BRACS [18]		MV@3	48	46	51	54	49	55	59	57	59	57	53	57	58	58	
		MV@5	50	49	53	55	49	54	60	57	58	59	53	57	57	59	

Table S4. Quantitative Assessment via 5-Fold Cross-Validation: Accuracy in Patch-Level Classification in Histopathological Image Analysis.

		Internal Datasets						Public Datasets					
		Private-Breast	Private-Liver	Private-Skin	Private-CRC	PANDA [16]	CAMELYON16 [17]	BRACS [18]	DigestPath [19]	Kather [20]	PanNuke [21]	WSSS4LUD [22]	
Pret. on Natural Data	CNN-based	ResNet50 [2]	62.86±2.68	71.77±3.06	74.88±1.23	53.84±2.63	37.22±0.76	66.30±1.88	54.97±0.21	92.18±2.79	98.82±0.56	77.75±1.80	81.79±0.65
		DenseNet121 [3]	57.75±1.44	72.24±2.06	72.71±5.13	51.22±2.38	34.66±1.61	65.79±4.86	47.92±4.48	91.85±3.12	98.06±0.24	61.27±1.92	82.35±0.92
		EfficientNet-b3-288 [4]	57.99±2.12	74.00±1.13	74.76±0.80	57.52±1.34	37.19±0.59	63.88±2.11	56.51±0.63	91.25±2.58	98.04±0.33	72.49±2.60	83.78±0.45
		EfficientNet-b5 [4]	75.31±0.74	78.94±4.34	78.67±2.78	63.73±3.06	40.00±0.81	70.16±5.25	61.48±0.76	92.79±2.68	99.03±0.20	80.29±1.51	84.44±3.05
		ConvNext-b-224 [5]	73.24±1.54	78.02±1.20	77.09±0.91	57.33±2.93	38.69±0.97	69.46±2.11	57.87±1.59	93.88±1.98	99.35±0.11	82.68±1.56	85.18±0.58
	Transformer	ConvNext-large [5]	76.88±1.23	79.22±0.99	79.96±0.86	60.53±1.98	38.91±1.95	70.13±3.64	57.85±1.10	94.84±2.16	99.72±0.12	87.53±1.76	87.54±0.93
		ViT-b16-224 [8]	53.27±3.03	76.17±1.82	75.79±1.15	51.58±4.03	35.08±1.06	64.99±3.41	52.03±1.13	90.76±2.56	99.04±0.36	79.09±1.82	78.26±8.70
		DinoV1-ViT-s16 [9]	66.85±2.62	76.67±2.60	70.49±6.51	54.00±2.24	33.24±1.40	69.66±3.69	52.91±2.00	95.47±1.59	99.35±0.22	82.08±2.19	83.87±2.88
		DinoV1-ViT-b16 [9]	67.54±1.67	79.86±1.83	73.11±3.10	57.93±2.38	31.65±3.64	69.17±4.00	54.70±4.22	94.75±1.99	99.35±0.18	85.25±2.45	86.63±1.48
		DinoV2-ViT-b14 [10]	59.91±2.90	74.97±5.76	71.59±5.64	55.18±2.15	34.51±2.55	64.60±6.80	50.75±4.31	89.88±6.30	98.22±0.72	70.74±3.08	73.19±8.17
Pret. on Histopathology Data	CNN-based	CLIP - ViT-B/16 [11]	55.04±2.89	80.55±1.29	78.65±1.87	59.43±5.62	40.44±0.77	71.16±3.47	59.46±2.21	88.75±3.24	98.65±0.29	72.03±2.77	82.95±1.30
		Barlow-Twins-ResNet50 [11]	76.15±3.96	85.92±6.54	82.80±1.46	71.54±5.05	45.50±1.87	76.77±5.48	66.58±2.36	89.11±6.83	99.53±0.25	78.14±3.66	89.16±0.96
		MoCoV2-ResNet50 [11]	79.59±1.81	84.37±0.62	79.77±0.49	69.40±0.54	44.10±0.35	74.94±3.01	63.83±0.57	95.88±1.63	96.60±0.75	61.68±2.81	83.07±1.08
		MuDiPath-ResNet50 [6]	53.08±6.68	77.32±1.80	74.38±2.08	55.29±2.59	37.40±1.00	65.32±6.19	50.87±3.07	90.49±1.25	98.97±0.21	79.24±1.32	83.47±1.01
		MuDiPath-DenseNet-101 [6]	54.06±6.78	74.58±1.43	73.97±2.35	54.07±3.09	34.32±2.26	64.65±3.33	51.13±5.84	91.86±1.75	98.80±0.26	75.87±1.28	81.39±2.15
	Transformer	KimiaNet [7]	77.03±4.13	89.25±1.46	83.45±2.00	69.58±3.74	38.74±5.74	79.48±3.34	64.75±3.70	94.58±2.40	99.26±0.21	85.42±1.68	82.48±2.41
		BiomedCLIP [12]	50.76±3.93	73.50±1.34	75.62±0.59	56.13±2.23	37.41±0.31	67.44±1.62	56.53±0.83	93.79±1.48	96.09±0.67	64.14±2.01	84.39±1.11
		HIPT-ViT-s16 [13]	53.07±6.57	74.93±3.75	74.36±2.37	50.53±2.93	33.70±3.27	65.63±5.92	52.05±5.54	88.27±4.73	97.58±0.50	65.52±3.86	83.49±1.10
		TransPath [23]	20.12±10.81	61.89±4.59	65.22±1.48	42.68±2.57	29.95±1.46	56.80±10.84	52.51±4.60	71.78±10.28	78.82±4.92	30.49±11.68	73.65±1.93
		PLIP [14]	56.66±2.72	77.03±1.45	78.81±0.56	64.14±2.18	42.16±0.26	74.16±1.04	61.18±0.42	93.63±2.33	92.52±1.29	60.86±2.26	77.77±1.25
DinoSSLPathology-8 [1]	iBOT-Path [15]	86.92±1.97	86.66±0.60	81.51±0.73	68.33±0.59	40.22±1.03	74.96±1.71	61.66±2.85	96.73±1.13	99.83±0.12	98.13±0.57	90.04±0.97	
	DinoSSLPathology-8 [1]	81.06±1.31	80.45±4.27	78.56±0.85	59.28±3.96	36.82±0.53	74.21±2.95	58.48±2.02	95.53±1.27	99.74±0.06	92.50±1.35	89.31±0.68	
	PathDino-224 (ours)	79.24±3.84	81.85±0.37	77.32±1.36	60.83±1.98	33.30±1.38	70.03±5.43	53.73±3.72	95.39±2.25	99.72±0.14	89.63±1.30	88.34±1.61	
	PathDino-512 (ours)	89.92±2.65	89.16±2.29	82.01±0.90	70.68±2.36	38.47±2.66	81.42±1.04	63.05±4.44	96.52±1.82	99.67±0.08	91.76±2.05	88.83±0.67	

Table S5. Quantitative Assessment via 5-Fold Cross-Validation: Macro-Averaged F_1 Score for Patch-Level Classification in Histopathological Image Analysis.

		Internal Datasets				Public Datasets							
		Private-Breast	Private-Liver	Private-Skin	Private-CRC	PANDA [16]	CAMELYON16 [17]	BRACS [18]	DigestPath [19]	Kather [20]	PanNuke [21]	WSSS4LUDAD [22]	
Pret. on Natural Data	CNN-based	ResNet50 [2]	55.80 ± 2.19	54.77 ± 4.96	61.31 ± 0.76	53.69 ± 2.98	27.90 ± 1.17	64.10 ± 1.81	45.96 ± 1.80	90.13 ± 2.86	98.54 ± 0.49	61.37 ± 2.16	65.30 ± 6.95
		DenseNet121 [3]	51.84 ± 3.32	54.63 ± 5.78	58.42 ± 1.49	50.54 ± 2.78	26.14 ± 1.47	62.19 ± 3.57	40.48 ± 1.90	90.31 ± 4.10	97.43 ± 0.34	54.56 ± 1.68	69.54 ± 8.54
		EfficientNet-b3-288 [4]	51.17 ± 3.01	61.43 ± 2.78	63.73 ± 0.68	57.58 ± 1.35	27.60 ± 0.81	61.04 ± 1.50	47.85 ± 0.88	89.35 ± 3.74	97.63 ± 0.24	53.60 ± 2.94	70.04 ± 8.42
		EfficientNet-b5 [4]	70.41 ± 2.86	72.91 ± 4.75	68.18 ± 2.76	63.12 ± 3.57	30.56 ± 2.27	66.52 ± 3.83	53.19 ± 0.86	91.20 ± 3.88	98.86 ± 0.30	65.45 ± 2.07	71.69 ± 9.74
		ConvNext-b-224 [5]	65.02 ± 4.39	67.42 ± 1.35	67.65 ± 0.88	56.41 ± 3.70	27.65 ± 0.76	65.96 ± 1.76	48.52 ± 1.80	92.69 ± 2.50	99.24 ± 0.09	69.52 ± 2.37	68.24 ± 6.55
	ConvNext-xtlarge [5]	70.72 ± 1.75	70.88 ± 5.03	69.23 ± 2.60	60.48 ± 1.81	30.31 ± 1.12	68.01 ± 2.61	49.44 ± 3.14	93.72 ± 2.82	99.69 ± 0.15	76.40 ± 1.80	74.33 ± 8.44	
	ViT-b16-224 [8]	43.44 ± 2.92	66.79 ± 2.21	62.84 ± 1.52	50.37 ± 5.81	25.88 ± 2.93	63.11 ± 2.14	43.64 ± 2.95	82.81 ± 7.25	98.79 ± 0.46	64.73 ± 2.94	58.76 ± 19.83	
	DinoV1-ViT-s16 [9]	60.57 ± 2.90	65.24 ± 7.94	58.52 ± 2.51	51.82 ± 4.24	23.62 ± 6.60	66.32 ± 3.93	39.70 ± 4.32	94.06 ± 2.12	99.16 ± 0.23	68.40 ± 2.28	67.65 ± 7.25	
	DinoV1-ViT-b16 [9]	62.80 ± 3.65	71.58 ± 2.77	62.23 ± 2.33	57.44 ± 2.85	24.35 ± 2.21	65.89 ± 4.27	47.74 ± 2.11	93.18 ± 2.88	99.18 ± 0.20	72.70 ± 2.52	73.69 ± 8.64	
	DinoV2-ViT-b14 [10]	51.16 ± 4.28	63.08 ± 6.31	60.34 ± 3.60	53.99 ± 3.26	25.20 ± 3.77	60.70 ± 6.66	41.46 ± 4.62	86.34 ± 9.14	97.61 ± 1.17	50.50 ± 3.99	69.20 ± 8.31	
CLIP - ViT-B/16 [11]	48.56 ± 1.72	61.76 ± 8.24	66.91 ± 2.59	57.13 ± 8.27	40.44 ± 0.77	63.52 ± 7.99	51.87 ± 3.84	86.58 ± 3.12	98.36 ± 0.32	50.72 ± 3.62	68.04 ± 8.32		
Pret. on Histopathology Data	CNN-based	Barlow-Twins-ResNet50 [1]	70.94 ± 6.64	77.81 ± 4.48	71.87 ± 4.22	70.55 ± 5.79	37.77 ± 3.03	70.64 ± 9.57	59.54 ± 2.34	86.53 ± 8.46	99.47 ± 0.25	63.77 ± 4.32	72.56 ± 8.62
		SwAV-ResNet50 [11]	78.23 ± 5.79	84.78 ± 5.13	78.91 ± 1.06	74.65 ± 2.62	40.39 ± 1.85	78.35 ± 5.18	58.17 ± 4.98	95.87 ± 1.34	98.51 ± 0.42	62.85 ± 3.56	71.43 ± 7.35
		MoCoV2-ResNet50 [11]	73.11 ± 2.02	66.87 ± 6.62	65.51 ± 0.93	69.76 ± 0.56	33.52 ± 0.41	69.47 ± 6.53	52.28 ± 1.76	94.81 ± 2.11	95.61 ± 0.84	34.22 ± 2.72	65.55 ± 6.66
		MuDiPath-ResNet50 [6]	45.79 ± 7.27	61.64 ± 5.17	64.42 ± 0.77	54.42 ± 3.25	28.44 ± 1.92	63.42 ± 4.56	46.83 ± 4.10	87.30 ± 4.20	98.77 ± 0.28	65.47 ± 2.10	69.75 ± 8.82
		MuDiPath-DenseNet-101 [6]	52.62 ± 4.34	58.31 ± 3.31	59.57 ± 3.28	52.94 ± 4.08	26.62 ± 2.21	62.14 ± 3.29	42.14 ± 3.97	89.34 ± 2.90	98.47 ± 0.33	59.79 ± 2.45	66.46 ± 9.08
	KimiaNet [7]	76.01 ± 1.76	85.77 ± 4.22	76.78 ± 1.95	69.56 ± 4.00	34.09 ± 5.32	77.90 ± 2.77	58.35 ± 1.35	93.22 ± 3.66	99.14 ± 0.25	72.57 ± 3.21	65.93 ± 10.00	
	BiomedCLIP [12]	38.82 ± 1.64	48.44 ± 1.15	56.62 ± 0.61	55.89 ± 2.57	25.97 ± 0.34	58.19 ± 4.99	41.89 ± 0.93	92.07 ± 2.33	94.89 ± 0.84	37.81 ± 2.12	69.98 ± 8.12	
	HiPT-ViT-s16 [13]	43.08 ± 6.27	59.31 ± 5.08	59.47 ± 2.85	48.69 ± 4.62	25.65 ± 1.38	61.56 ± 4.25	42.02 ± 8.82	84.66 ± 7.17	96.81 ± 0.69	42.17 ± 3.80	64.26 ± 7.50	
	TransPath [23]	10.17 ± 5.14	39.78 ± 5.56	43.79 ± 2.94	34.81 ± 2.74	14.69 ± 2.14	39.23 ± 8.06	38.49 ± 0.96	58.28 ± 12.80	72.46 ± 4.98	12.16 ± 2.73	50.16 ± 10.75	
	PLIP [14]	46.07 ± 3.20	50.78 ± 1.48	62.48 ± 1.11	64.11 ± 2.70	31.53 ± 0.47	69.67 ± 1.45	46.72 ± 1.05	92.07 ± 2.91	90.90 ± 1.63	27.77 ± 2.54	61.51 ± 7.19	
iBOT-Path [15]	85.12 ± 1.74	84.37 ± 1.31	73.09 ± 0.39	68.38 ± 0.52	32.95 ± 0.86	73.76 ± 1.67	56.52 ± 1.96	95.67 ± 2.17	99.81 ± 0.17	95.76 ± 1.78	73.31 ± 5.91		
DinoSSL.Pathology-8 [1]	77.59 ± 2.17	74.25 ± 4.56	66.98 ± 1.00	58.17 ± 4.77	28.75 ± 2.31	70.61 ± 1.81	46.42 ± 5.59	94.50 ± 1.91	99.68 ± 0.11	86.17 ± 2.61	76.30 ± 9.60		
PathDino-224 (ours)	78.06 ± 4.03	74.34 ± 4.98	64.89 ± 2.14	60.65 ± 2.23	27.74 ± 2.44	69.26 ± 4.94	46.58 ± 3.78	94.03 ± 3.06	99.66 ± 0.19	81.03 ± 2.51	74.47 ± 9.05		
PathDino-512 (ours)	88.57 ± 3.08	86.35 ± 5.33	71.36 ± 1.64	70.47 ± 2.47	32.08 ± 2.57	79.61 ± 1.00	52.59 ± 3.21	95.82 ± 2.26	99.65 ± 0.11	84.79 ± 3.14	72.69 ± 7.60		

Table S6. Internal histopathology image datasets. Four different datasets were collected at a hospital for four sites including Liver, Skin, Breast, and colon sites.

Dataset	#Class	#WSI	#Patches	Diagnosis
CRC	3	209	4,619	Cancer Adjacent polyp Non-recurrent polyp Recurrent polyp
Liver	3	324	2,976	Alcoholic Steatohepatitis Non-alcoholic Steatohepatitis Normal tissue
Skin	4	660	8,390	Well differentiated Moderately differentiated Poorly differentiated Normal tissue
Breast	16	73	1,141	Adenoid Cystic Carcinoma Adenomyoepithelioma Ductal Carcinoma In Situ Ductal Carcinoma In Situ, Columnar Cell Lesions Including Flat Epithelial Atypia, Atypical Ductal Hyperplasia Intraductal Papilloma, Columnar Cell Lesions Invasive Breast Carcinoma of No Special Type Invasive lobular carcinoma Lobular Carcinoma In Situ + Atypical Lobular Hyperplasia Lobular Carcinoma In Situ, Flat Epithelial Atypia, Atypical Lobular Hyperplasia Malignant Adenomyoepithelioma Metaplastic Carcinoma Microglandular Adenosis Microinvasive carcinoma Mucinous Cystadenocarcinoma Radial scar complex sclerosing lesion Normal tissue

Table S7. Public histopathology image datasets including PANDA, CAMELYON16, BRACS, DigestPath, Kather, PanNuke, and WSSS4LUAD. Number of images represents the total images (patches) used in the evaluation regardless of their training/testing split, since we used the leave-one-out evaluation method for the search task and k-fold cross-validation for the classification task.

Dataset	Analysis Scale	#Class	#WSI	#Image	Diagnosis
PANDA	WSI/Patch	6	10,349	87,451	background (non tissue) or unknown benign tissue (stroma and epithelium combined) cancerous tissue, not specified cancerous epithelium (Gleason 3) cancerous epithelium (Gleason 4) cancerous epithelium (Gleason 5)
CAMELYON16	WSI/Patch	2	128	2,864	Tumor Normal
BRACS	WSI/Patch	3	523	10,984	Benign Atypical Malignant
DigestPath	Patch-Level	2	-	1,103	Benign Malignant
Kather	Patch-Level	9	-	7,180	ADIPOSE BACKGROUND DEBRIS LYMPHO MUCUS Smooth Muscle Normal Colon Mucosa Cancer-Associated Stroma Colorectal Adenocarcinoma Epithelium
PanNuke	Patch-Level	19	-	2,656 2,523 2,722	Breast Colon Bile-duct Esophagus Uterus Lung Cervix Head Neck Skin Adrenal_gland kidney Stomach Prostate testis Liver Thyroid Pancreatic Overin Bladder
WSSS4LUAD	Patch-Level	7	-	10,091	Normal Stroma Stroma-Normal Tumor Tumor-Normal Tumor-Stroma Tumor-Stroma-Normal

Table S8. WSI-level Top-1 Accuracy using the proposed FPS patching method and minimum of medium proposed in Yottixel [24]

		Internal Datasets				Public Datasets			
		Private-Breast	Private-Liver	Private-Skin	Private-CRC	PANDA [16]	CAMELYON16 [17]	BRACS [18]	
Pret. on Natural	CNN-based	ResNet50 [2]	0.48	0.67	0.73	0.58	0.32	0.54	0.53
		DenseNet121 [3]	0.48	0.64	0.69	0.49	0.3	0.67	0.52
		EfficientNet-b3-288 [4]	0.41	0.66	0.73	0.6	0.32	0.59	0.55
		EfficientNet-b5 [4]	0.51	0.71	0.71	0.63	0.37	0.57	0.54
		ConvNext-b-224 [5]	0.56	0.75	0.74	0.6	0.34	0.62	0.58
	ConvNext-xlarge [5]	0.56	0.76	0.74	0.58	0.35	0.61	0.58	
	Transformer	ViT-b16-224 [8]	0.41	0.7	0.72	0.5	0.31	0.6	0.54
		DinoV1-ViT-s16 [9]	0.48	0.71	0.74	0.55	0.36	0.67	0.6
		DinoV1-ViT-b16 [9]	0.55	0.72	0.73	0.61	0.37	0.63	0.59
		DinoV2-ViT-b14 [10]	0.53	0.71	0.72	0.56	0.31	0.61	0.51
CLIP - ViT-B/16 [11]		0.49	0.67	0.75	0.56	0.36	0.67	0.58	
Pret. on Histopathology	CNN-based	Barlow-Twins-ResNet50 [1]	0.58	0.77	0.77	0.64	0.61	0.67	0.61
		MoCoV2-ResNet50 [1]	0.62	0.79	0.74	0.64	0.62	0.67	0.6
		MuDiPath-ResNet50 [6]	0.44	0.7	0.72	0.58	0.35	0.63	0.51
		MuDiPath-DenseNet-101 [6]	0.51	0.68	0.74	0.66	0.36	0.65	0.56
		KimiaNet [7]	0.51	0.78	0.75	0.64	0.57	0.76	0.62
	Transformer	BiomedCLIP - [12]	0.47	0.74	0.75	0.58	0.34	0.61	0.55
		HIPT-ViT-s16 [13]	0.44	0.68	0.73	0.57	0.32	0.62	0.52
		PLIP [14]	0.58	0.73	0.75	0.64	0.56	0.73	0.6
		iBOT-Path [15]	0.64	0.79	0.76	0.65	0.53	0.67	0.64
		DinoSSLPathology-8 [1]	0.58	0.74	0.78	0.63	0.47	0.74	0.61
PathDino-224 (ours)	0.53	0.75	0.74	0.61	0.46	0.72	0.61		
PathDino-512 (ours)	0.68	0.83	0.78	0.63	0.58	0.73	0.64		

Table S9. WSI-level Top-1 Macro avg $F-1$ score

		Internal Datasets				Public Datasets			
		Private-Breast	Private-Liver	Private-Skin	Private-CRC	PANDA [16]	CAMELYON16 [17]	BRACS [18]	
Pret. on Natural	CNN-based	ResNet50 [2]	0.43	0.49	0.63	0.58	0.29	0.48	0.48
		DenseNet121 [3]	0.37	0.44	0.61	0.48	0.27	0.65	0.47
		EfficientNet-b3-288 [4]	0.35	0.49	0.64	0.6	0.29	0.55	0.5
		EfficientNet-b5 [4]	0.41	0.52	0.6	0.63	0.35	0.54	0.49
		ConvNext-b-224 [5]	0.47	0.61	0.64	0.6	0.31	0.6	0.53
	ConvNext-xlarge [5]	0.51	0.52	0.64	0.58	0.33	0.57	0.52	
	Transformer	ViT-b16-224 [8]	0.3	0.51	0.62	0.5	0.28	0.54	0.49
		DinoV1-ViT-s16 [9]	0.41	0.52	0.64	0.55	0.34	0.63	0.55
		DinoV1-ViT-b16 [9]	0.49	0.59	0.62	0.61	0.35	0.6	0.54
		DinoV2-ViT-b14 [10]	0.46	0.49	0.65	0.56	0.28	0.57	0.45
CLIP - ViT-B/16 [11]		0.39	0.46	0.66	0.56	0.34	0.61	0.52	
Pret. on Histopathology	CNN-based	Barlow-Twins-ResNet50 [1]	0.49	0.56	0.65	0.65	0.62	0.63	0.56
		MoCoV2-ResNet50 [1]	0.49	0.63	0.63	0.64	0.64	0.64	0.53
		MuDiPath-ResNet50 [6]	0.41	0.57	0.61	0.58	0.33	0.59	0.45
		MuDiPath-DenseNet-101 [6]	0.47	0.5	0.63	0.66	0.33	0.63	0.5
		KimiaNet [7]	0.47	0.66	0.65	0.64	0.58	0.74	0.57
	Transformer	BiomedCLIP - [12]	0.39	0.5	0.63	0.57	0.31	0.57	0.48
		HIPT-ViT-s16 [13]	0.33	0.46	0.62	0.57	0.29	0.58	0.48
		PLIP [14]	0.58	0.6	0.65	0.65	0.56	0.69	0.53
		iBOT-Path [15]	0.61	0.74	0.66	0.66	0.52	0.62	0.58
		DinoSSLPathology-8 [1]	0.51	0.54	0.67	0.64	0.46	0.7	0.57
PathDino-224 (ours)	0.56	0.6	0.63	0.61	0.45	0.69	0.56		
PathDino-512 (ours)	0.66	0.74	0.67	0.64	0.59	0.69	0.57		

Table S10. WSI-level MV@3 Accuracy

		Internal Datasets			Public Datasets			
		Private-Liver	Private-Skin	Private-CRC	PANDA [16]	CAMELYON16 [17]	BRACS [18]	
Pret. on Natural	CNN-based	ResNet50 [2]	0.72	0.76	0.64	0.34	0.6	0.58
		DenseNet121 [3]	0.72	0.74	0.51	0.32	0.67	0.54
		EfficientNet-b3-288 [4]	0.69	0.76	0.61	0.33	0.6	0.58
		EfficientNet-b5 [4]	0.71	0.75	0.64	0.38	0.62	0.57
		ConvNext-b-224 [5]	0.75	0.78	0.62	0.37	0.68	0.6
	ConvNext-xlarge [5]	0.76	0.79	0.61	0.37	0.65	0.62	
	Transformer	ViT-b16-224 [8]	0.71	0.76	0.55	0.33	0.67	0.57
		DinoV1-ViT-s16 [9]	0.74	0.77	0.61	0.38	0.67	0.59
		DinoV1-ViT-b16 [9]	0.77	0.77	0.62	0.39	0.69	0.63
		DinoV2-ViT-b14 [10]	0.74	0.77	0.59	0.32	0.58	0.53
CLIP - ViT-B/16 [11]		0.69	0.79	0.58	0.38	0.67	0.6	
Pret. on Histopathology	CNN-based	Barlow-Twins-ResNet50 [1]	0.79	0.77	0.66	0.58	0.7	0.64
		MoCoV2-ResNet50 [1]	0.83	0.78	0.65	0.6	0.69	0.61
		MuDiPath-ResNet50 [6]	0.73	0.78	0.58	0.37	0.67	0.56
		MuDiPath-DenseNet-101 [6]	0.72	0.77	0.63	0.37	0.68	0.58
		KimiaNet [7]6	0.8	0.81	0.65	0.56	0.78	0.64
	Transformer	BiomedCLIP - [12]	0.77	0.78	0.63	0.36	0.67	0.62
		HIPT-ViT-s16 [13]	0.67	0.76	0.52	0.33	0.64	0.54
		PLIP [14]	0.74	0.79	0.67	0.55	0.77	0.63
		iBOT-Path [15]	0.83	0.8	0.63	0.53	0.71	0.65
		DinoSSLPathology-8 [1]	0.77	0.8	0.64	0.47	0.68	0.64
		PathDino-224 (ours)	0.79	0.8	0.59	0.48	0.74	0.61
		PathDino-512 (ours)	0.86	0.8	0.65	0.58	0.78	0.66

Table S11. WSI-level MV@3 Macro Avg $F-1$ score

		Internal Datasets			Public Datasets			
		Private-Liver	Private-Skin	Private-CRC	PANDA [16]	CAMELYON16 [17]	BRACS [18]	
Pret. on Natural	CNN-based	ResNet50 [2]	0.49	0.65	0.64	0.3	0.52	0.53
		DenseNet121 [3]	0.49	0.62	0.5	0.28	0.62	0.48
		EfficientNet-b3-288 [4]	0.5	0.65	0.6	0.3	0.52	0.52
		EfficientNet-b5 [4]	0.55	0.61	0.64	0.35	0.56	0.53
		ConvNext-b-224 [5]	0.6	0.67	0.61	0.33	0.63	0.53
	ConvNext-xlarge [5]	0.56	0.66	0.61	0.34	0.6	0.54	
	Transformer	ViT-b16-224 [8]	0.48	0.64	0.54	0.29	0.61	0.51
		DinoV1-ViT-s16 [9]	0.54	0.65	0.61	0.34	0.6	0.53
		DinoV1-ViT-b16 [9]	0.66	0.65	0.62	0.35	0.64	0.58
		DinoV2-ViT-b14 [10]	0.54	0.66	0.59	0.29	0.5	0.46
CLIP - ViT-B/16 [11]		0.47	0.66	0.58	0.35	0.58	0.54	
Pret. on Histopathology	CNN-based	Barlow-Twins-ResNet50 [1]	0.63	0.62	0.67	0.59	0.64	0.57
		MoCoV2-ResNet50 [1]	0.71	0.64	0.65	0.6	0.65	0.54
		MuDiPath-ResNet50 [6]	0.5	0.64	0.58	0.33	0.62	0.49
		MuDiPath-DenseNet-101 [6]	0.53	0.63	0.63	0.34	0.64	0.52
		KimiaNet [7]	0.62	0.71	0.66	0.56	0.74	0.57
	Transformer	BiomedCLIP - [12]	0.53	0.65	0.62	0.33	0.61	0.55
		HIPT-ViT-s16 [13]	0.45	0.63	0.52	0.3	0.56	0.47
		PLIP [14]	0.63	0.66	0.68	0.54	0.72	0.57
		iBOT-Path [15]	0.76	0.69	0.64	0.52	0.64	0.59
		DinoSSLPathology-8 [1]	0.66	0.67	0.65	0.45	0.59	0.57
		PathDino-224 (ours)	0.6	0.68	0.59	0.46	0.69	0.53
		PathDino-512 (ours)	0.74	0.67	0.66	0.58	0.73	0.58

Table S12. WSI-level MV@5 Accuracy

		Internal Datasets			Public Datasets			
		Private-Liver	Private-Skin	Private-CRC	PANDA [16]	CAMELYON16 [17]	BRACS [18]	
Pret. on Natural	CNN-based	ResNet50 [2]	0.71	0.78	0.63	0.36	0.64	0.6
		DenseNet121 [3]	0.7	0.78	0.49	0.34	0.7	0.58
		EfficientNet-b3-288 [4]	0.68	0.78	0.59	0.36	0.61	0.57
		EfficientNet-b5 [4]	0.7	0.77	0.64	0.4	0.66	0.61
		ConvNext-b-224 [5]	0.73	0.79	0.58	0.38	0.71	0.62
	ConvNext-xlarge [5]	0.78	0.8	0.63	0.39	0.67	0.64	
	Transformer	ViT-b16-224 [8]	0.72	0.78	0.54	0.35	0.69	0.58
		DinoV1-ViT-s16 [9]	0.76	0.78	0.6	0.39	0.67	0.63
		DinoV1-ViT-b16 [9]	0.78	0.79	0.62	0.41	0.71	0.64
		DinoV2-ViT-b14 [10]	0.72	0.78	0.59	0.35	0.63	0.56
CLIP - ViT-B/16 [11]		0.71	0.8	0.6	0.4	0.69	0.61	
Pret. on Histopathology	CNN-based	Barlow-Twins-ResNet50 [1]	0.79	0.79	0.64	0.57	0.74	0.66
		MoCoV2-ResNet50 [1]	0.82	0.78	0.65	0.58	0.71	0.64
		MuDiPath-ResNet50 [6]	0.73	0.79	0.57	0.39	0.7	0.56
		MuDiPath-DenseNet-101 [6]	0.72	0.78	0.66	0.39	0.71	0.6
		KimiaNet [7]	0.78	0.82	0.62	0.54	0.81	0.66
	Transformer	BiomedCLIP - [12]	0.77	0.78	0.65	0.38	0.69	0.61
		HIPT-ViT-s16 [13]	0.68	0.77	0.55	0.35	0.67	0.56
		PLIP [14]	0.76	0.82	0.69	0.54	0.75	0.64
		iBOT-Path [15]	0.82	0.82	0.63	0.53	0.74	0.65
		DinoSSLPathology-8 [1]	0.77	0.8	0.63	0.48	0.7	0.64
		PathDino-224 (ours)	0.76	0.8	0.57	0.48	0.71	0.64
		PathDino-512 (ours)	0.85	0.82	0.65	0.56	0.77	0.67

Table S13. WSI-level MV@5 Macro Avg $F-1$ score

		Internal Datasets			Public Datasets			
		Private-Liver	Private-Skin	Private-CRC	PANDA [16]	CAMELYON16 [17]	BRACS [18]	
Pret. on Natural	CNN-based	ResNet50 [2]	0.48	0.66	0.63	0.32	0.55	0.54
		DenseNet121 [3]	0.47	0.65	0.49	0.3	0.64	0.52
		EfficientNet-b3-288 [4]	0.5	0.65	0.59	0.31	0.49	0.51
		EfficientNet-b5 [4]	0.47	0.63	0.64	0.36	0.58	0.56
		ConvNext-b-224 [5]	0.5	0.65	0.57	0.33	0.65	0.55
	ConvNext-xlarge [5]	0.53	0.66	0.63	0.35	0.57	0.56	
	Transformer	ViT-b16-224 [8]	0.49	0.65	0.53	0.31	0.59	0.5
		DinoV1-ViT-s16 [9]	0.52	0.65	0.61	0.36	0.57	0.56
		DinoV1-ViT-b16 [9]	0.57	0.66	0.61	0.37	0.65	0.57
		DinoV2-ViT-b14 [10]	0.53	0.66	0.59	0.3	0.54	0.49
CLIP - ViT-B/16 [11]		0.52	0.67	0.6	0.35	0.61	0.55	
Pret. on Histopathology	CNN-based	Barlow-Twins-ResNet50 [1]	0.67	0.63	0.65	0.56	0.69	0.57
		MoCoV2-ResNet50 [1]	0.66	0.61	0.66	0.57	0.65	0.56
		MuDiPath-ResNet50 [6]	0.49	0.64	0.57	0.35	0.62	0.49
		MuDiPath-DenseNet-101 [6]	0.49	0.63	0.66	0.35	0.66	0.52
		KimiaNet [7]	0.61	0.69	0.63	0.54	0.77	0.59
	Transformer	BiomedCLIP - [12]	0.56	0.62	0.65	0.34	0.59	0.54
		HIPT-ViT-s16 [13]	0.46	0.65	0.56	0.3	0.58	0.48
		PLIP [14]	0.67	0.69	0.7	0.52	0.7	0.57
		iBOT-Path [15]	0.72	0.70	0.64	0.51	0.67	0.57
		DinoSSLPathology-8 [1]	0.62	0.67	0.64	0.45	0.61	0.57
		PathDino-224 (ours)	0.65	0.67	0.58	0.45	0.64	0.56
		PathDino-512 (ours)	0.74	0.69	0.66	0.56	0.72	0.59

Algorithm S1 HistoRotate, Image Augmentation in a Self-Supervised Manner (DINO Framework)

Require: Input image I , Global crop scales $[a, b]$, Local crop scales $[c, d]$, Number of local crops n , Set of discrete angles Θ

```
1: function EXACTROTATION( $I, \Theta$ )
2:    $\theta \leftarrow \text{random.choice}(\Theta)$ 
3:    $I' \leftarrow \text{rotate}(I, \theta)$ 
4:   return  $I'$ 
5: function HISTOROTATE( $I, [a, b], [c, d], n, \Theta$ )
6:   Initialize empty list  $crops$ 
7:   if  $\text{size}(I)[0] = 1024$  then
8:      $crops.append(\text{global-transfo1-1024}(I))$  ▷ Include Random 360° Rotation
9:      $crops.append(\text{global-transfo2-1024}(I))$  ▷ Include Random 360° Rotation
10:    for  $i = 1, n$  do
11:       $crops.append(\text{local-transfo}(I))$  ▷ Always Include Random 360° Rotation
12:    else
13:       $crops.append(\text{global-transfo1}_{512}(I))$  ▷ Include Random Rotation from  $\Theta = \{90, 180, 270, 360\}$ 
14:       $crops.append(\text{global-transfo2}_{512}(I))$  ▷ Include Random Rotation from  $\Theta = \{90, 180, 270, 360\}$ 
15:      for  $i = 1, n$  do
16:         $crops.append(\text{local-transfo}(I))$  ▷ Always Include Random 360° Rotation
17:    return  $crops$ 
```

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