
A multimodal whole-slide foundation model for pathology

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Brand	Scanner	MPP ($\mu\text{m}/\text{pixel}$)	Count
Leica	Aperio GT450	0.26	96,257
	Aperio AT2	0.50	21,249
Hamamatsu	S210	0.22	20,445
	S60	0.22	416
	NanoZoomer-2.0 HT	0.23	83
	NanoZoomer-XR	0.45	17
	S360	0.46	5
Motic	EasyScan Pro 6	0.52	87,937
	EasyScan Pro 6	0.26	20,606
3D Histech	Pannoramic 250	0.24	18,381
	Pannoramic 1000	0.24	9,020
	Pannoramic 250	0.12	2,752
	Pannoramic 1000	0.12	276
Philips	Ultra Fast Scanner	0.25	33,394
Roche	Ventana iScan HT	0.25	19
Zeiss	MIRAX MIDI	0.32	6
GTE consortium	Aperio	0.49	24,782

Supplementary Table 1: Scanner specifications for WSIs within Mass-340K. No scanner information is provided for GTE consortium dataset [lonsdale2013genotype].

Hyperparameter	Value
Image size	448×448
Automatic mixed precision	FP16
Batch size	256
Gradient accumulation steps	3
Learning rate scheduler	Cosine
Warmup steps	250
Peak learning rate	$1\text{e-}4$
AdamW β	(0.9, 0.999)
AdamW ϵ	$1\text{e-}8$
Weight decay	0.2
Softmax temperature	Learned
Epochs	20

Supplementary Table 2: Hyperparameters used in CONCH v1.5 training. $8 \times 80\text{GB}$ NVIDIA GPUs were used for training CONCH v1.5. We initialized vision backbone with UNI [chen2024towards], while keeping the text tower configuration of CONCH v1 unchanged. Effective batch size used for optimization is batch size $\times$ gradient accumulation steps. The maximum sequence length for captions is set to 128.

Hyperparameter	Value
Layers	6
Heads	12
Head activation	GELU
Embedding dimension	768
Drop path rate	0.1
Global crop size	14
Global crop number	2
Local crop size	6
Local crop number	10
Partial prediction shape	Block
Partial prediction ratio	0.3
Partial prediction variance	0.2
Gradient clipping max norm	3.0
Normalize last layer	False
Shared head	True
AdamW β	(0.9, 0.999)
Batch size	1024
Freeze last layer epochs	3
Warmup epochs	30
Warmup teacher temperature epochs	90
Max epochs	300
Learning rate schedule	Cosine
Learning rate (start)	0
Learning rate (post warmup)	5e-4
Learning rate (final)	1e-6
Teacher temperature (start)	0.04
Teacher temperature (final)	0.07
Teacher momentum (start)	0.996
Teacher momentum (final)	1.000
Weight decay (start)	0.04
Weight decay (end)	0.4
Automatic mixed precision	bf16

Supplementary Table 3: Hyperparameters used in pretraining the unimodal vision model. $4 \times 80\text{GB}$ NVIDIA A100 GPUs were used for training. Batch size refers to the total batch size across GPUs.

Example pathchat prompt	Provided are H&E-stained images from a {tissue site} tissue region. The first image shows the microview of the region for you to have an overview of what this region looks like, and the following images are the representative features in this region at higher resolution for you to check the morphologies more clearly. Your task is to write a short morphological caption that describes the unique microscopic findings (cellular and tissue characteristics) in this region as a whole. 1. Do not describe each image individually. 2. Do not list your findings one by one. You must summarize all observed microscopic findings in a single paragraph and answer holistically. 3. Pretend you are a busy pathologist writing microscopic findings for this tissue region. Make your description as short as possible and only include the most important findings. 4. Format your reply like a pathology report. Title is not needed.
Example synthetic caption	Microscopic examination of the bladder tissue region reveals a complex histological landscape. The region is characterized by a mixture of squamous and glandular components, indicative of adenosquamous carcinoma. The squamous component is evident by the presence of keratinizing cells, while the glandular component is identified by the formation of gland-like structures. Additionally, there are areas of necrosis and inflammation, suggesting an aggressive tumor behavior. The stroma surrounding the tumor is fibrotic, and there is a notable presence of desmoplasia, which is a reactive fibrous tissue response to the tumor. The tumor cells exhibit pleomorphism, with some cells showing prominent nucleoli, indicative of high-grade malignancy.

Supplementary Table 4: PathChat prompts for synthetic caption generation for 8192×8192 pixels ROIs at $20\times$ magnification.

System prompt	You are assisting me summarizing detailed pathology descriptions into concise, clear, and holistic reports suitable for a busy pathologist. The summaries should focus on the key diagnostic features and findings, avoiding unnecessary details while maintaining accuracy. Instructions: 1. Read the detailed description and identify the key diagnostic features, such as growth patterns, cellular characteristics, presence or absence of malignant features, and any significant findings. 2. Write a summary that captures the essential information in a clear and concise manner. Aim to keep the summary brief and to the point, using incomplete sentences if needed for brevity. It should provide a holistic view of the pathology findings. 3. You can choose the formats from a) concise summarization in one paragraph; b) summarization using keywords and incomplete sentences similar to a busy and lazy pathologist; and c) formatted similar to a pathologic report. 4. Ignore "grade -" in the description.
Example rewritten caption	Microscopic examination of the bladder tissue shows a complex mix of squamous and glandular elements, characteristic of adenosquamous carcinoma. The presence of keratinized cells identifies the squamous component, while gland-like structures signify the glandular aspect. Necrosis and inflammation indicate an invasive tumor. The surrounding stroma is fibrotic, with marked desmoplasia. Tumor cells display pleomorphism, including cells with large nuclei, suggesting high malignancy grade.

Supplementary Table 5: Prompts for synthetic caption rewriting using Qwen-2-7b instruct.

System prompt	You are assisting me extracting slide description from patient-level pathology reports. The slides of the patient are named by block ids such "A". Each block represents a tissue taken from the patient. You'll be given the entire pathology report of a patient which contains descriptions of multiple blocks, and the specific block we are interested in. Your task to extract the block description from the pathology report, summarizing the morphological details and diagnoses. Instructions: 1. Locate the block description in the report. 2. Record Metadata: Identify and record the organ and diagnosis for each slide.
Example user prompt	block: A report: A. SPECIMEN LABELED "SUBGALEAL COLLECTION": Fibrous tissue with florid acute and chronic inflammation and Gram-positive bacilli (highlighted by Gram, MSS, and Warthin-Starry Stains; FITE stain is negative for microorganisms). B. SPECIMEN LABELED "RIGHT FRONTAL BONE": Bone with no significant pathologic change. C. SPECIMEN LABELED "RIGHT FRONTAL LESION": Meninges and brain parenchyma with necrosis, florid acute and chronic inflammation and Gram-positive microorganisms (highlighted by Gram, MSS, and Warthin-Starry Stains; FITE stain is negative for microorganisms). NOTE: Concurrent cultures are positive for Cutibacterium acnes. Correlation with final culture results and other laboratory and clinical findings is recommended.
Example LLM response	Fibrous tissue with florid acute and chronic inflammation.

Supplementary Table 6: Prompts for parsing slide description from patient-level reports.

System prompt	You are assisting me cleaning noisy pathologic reports for H&E stained slides. You should remove the following information from the report if they are present: 1. sensitive patient information including name, age, and address; 2. hospital name; 3. Results of immunohistochemical stain / Immuno stain / other stainings and molecular test; 4. patient clinical history; 5. date. Rewrite the report if it's incomplete or has grammatical mistakes. If the report does not have any sensitive information, just reply the original report. Do not reply "The report does not contain any sensitive information". Along with the original noisy report, you'll be provided diagnosis and tissue site for your information. Reply the cleaned report only. Do not include any explanation.
Example user prompt	ANUS BIOPSY: Diagnosis of Extramammary Paget disease supported by immunohistochemical stains showing positivity for CK7, CEA, EMA and negativity for SOX-10 and CK20. Mucicarmine stain highlights intracytoplasmic mucin in the tumor cells. Slides were reviewed by Dr. {Doctor Name} from the section of dermatopathology.
Example LLM response	The biopsy from the anus shows features consistent with Extramammary Paget disease.

Supplementary Table 7: Prompts for removing sensitive information and information that is not directly visible from the slides.

System prompt	You are assisting me enhancing the diversity of pathology reports while maintaining a formal and professional tone. Reply the diversified report only.
Example user prompt	The biopsy from the kidney shows poorly differentiated carcinoma, consistent with renal cell carcinoma, subtype not determined.
Example rewritten report	Kidney biopsy reveals a poorly differentiated carcinoma, suggestive of renal cell carcinoma, with the subtype yet to be identified.

Supplementary Table 8: Prompts for rewriting parsed slide-level reports.

Hyperparameter	Value
Automatic mixed precision	fp16
Batch size	1568
Gradient accumulation	2
Vision weight decay	1e-6
Other weight decay	5e-5
Vision peak learning rate	5e-6
Other peak learning rate	5e-5
Vision warmup steps	600
Other warmup steps	200
AdamW β	(0.9, 0.999)
Temperature	Learned
Learning rate schedule	Cosine
Epochs	10

Supplementary Table 9: Hyperparameters used in visual-caption pretraining. 8 $\times$ 80GB NVIDIA A100 GPUs were used for training. Effective batch size used for optimization is batch size $\times$ gradient accumulation steps. The maximum sequence length for captions is set to 128.

Hyperparameter	Value
Automatic mixed precision	fp16
Batch size	128
Gradient accumulation	2
Vision weight decay	1e-5
Other weight decay	5e-5
Vision peak learning rate	5e-5
Other peak learning rate	5e-5
Vision warmup steps	1800
Other warmup steps	200
AdamW β	(0.9, 0.999)
Temperature	Learned
Learning rate schedule	Cosine
Epochs	5

Supplementary Table 10: Hyperparameters used in visual-report pretraining. 8 $\times$ 80GB NVIDIA A100 GPUs were used for training. Effective batch size used for optimization is batch size $\times$ gradient accumulation steps. The maximum sequence length for captions is set to 128.

Tissue site	Class	OncoTree code	#samples (train:val:test)
Adrenal gland	Adrenocortical carcinoma	ACC	493 (371:74:48)
Biliary tract	Cholangiocarcinoma	CHOL	90 (57:3:30)
Bladder	Bladder urothelial carcinoma	BLCA	943 (535:103:305)
Bowel	Colon adenocarcinoma	COAD	798 (623:120:55)
Brain	Glioblastoma multiforme	GBM	2283 (1223:342:718)
	Lower grade glioma	–	2098 (1113:278:707)
Breast	Invasive carcinoma	BRCA	2196 (1086:261:849)
Cervix	Squamous cell carcinoma and endocervical adenocarcinoma	CESC, ECAD	591 (340:78:173)
Esophagus	Esophageal carcinoma	–	294 (117:27:150)
Eye	Uveal melanoma	UM	147 (65:16:66)
Head and neck	Head and neck squamous cell carcinoma	HNSC	1159 (555:158:446)
Kidney	Renal clear cell carcinoma	CCRCC	798 (406:100:292)
	Papillary renal cell carcinoma	PRCC	443 (249:43:151)
	Chromophobe Renal Cell Carcinoma	CHRC	180 (103:33:44)
Liver	Hepatocellular carcinoma	HCC	841 (565:128:148)
Lung	Lung adenocarcinoma	LUAD	1217 (676:144:397)
	Lung squamous cell carcinoma	LUSC	1213 (606:195:412)
Lymph	Diffuse large B-cell lymphoma	–	72 (37:12:23)
–	Mesothelioma	–	163 (75:31:57)
Ovary	Serous Cystadenocarcinoma	–	220 (95:24:101)
Pancreas	Pancreatic adenocarcinoma	PAAD	341 (190:42:109)
–	Pheochromocytoma and paraganglioma	PHC, PGNG	128 (81:17:30)
Prostate	Prostate adenocarcinoma	PRAD	815 (411:117:287)
Rectum	Rectum adenocarcinoma	READ	150 (93:29:28)
Soft tissue	Sarcoma	–	1270 (850:186:234)
Skin	Cutaneous Melanoma	SKCM	931 (313:94:524)
Stomach	Stomach adenocarcinoma	STAD	2306 (1482:335:489)
Testis	Testicular germ cell tumor	–	551 (375:79:97)
Thymus	Thymoma	THYM	328 (138:34:156)
Thyroid	Thyroid carcinoma	–	1063 (528:166:369)
Uterus	Uterine corpus endometrial carcinoma	UCEC	1172 (424:144:604)
	Uterine carcinosarcoma	UCS	201 (71:21:109)

Supplementary Table 11: Overview of the dataset TCGA-UniformTumor-8K with 32 classes grouped by tissue site and sorted by largest class. This dataset is exclusively curated for ROIs (8,192×8,192 pixels) subtyping task. Not every class has a one-to-one mapping to a tissue site or a single OncoTree code.

Tissue site	OncoTree code	#samples (train:val:test)
Adrenal gland	ACC	227 (158:50:19)
	PHC	163 (118:27:18)
Bladder	BLCA	457 (376:49:32)
Bowel	COAD	375 (278:49:48)
	READ	156 (113:25:18)
	MACR	63 (48:11:4)
Brain	GBM	858 (798:50:10)
	OAST	217 (165:45:7)
	ODG	203 (152:46:5)
	AASTR	164 (113:39:12)
	AOAST	155 (112:41:2)
	ASTR	104 (64:33:7)
Breast	IDC	838 (743:49:46)
	ILC	211 (154:36:21)
Cervix	CESC	229 (134:40:55)
Eye	UM	79 (34:10:35)
Head and neck	HNSC	472 (338:47:87)
Kidney	CCRCC	519 (455:49:15)
	PRCC	297 (197:46:54)
	CHRC	109 (65:19:25)
Liver	HCC	362 (303:46:13)
Lung	LUAD	531 (305:48:178)
	LUSC	512 (364:48:100)
Melanoma	MEL	393 (347:31:15)
Ovary	HGSOC	107 (75:23:9)
Pancreas	PAAD	194 (135:32:27)
Pleura	PLEMESO	62 (43:17:2)
Prostate	PRAD	449 (382:44:23)
Skin	SKCM	75 (36:29:10)
Soft tissue	MFH	165 (119:40:6)
	LMS	155 (108:37:10)
	MFS	141 (91:41:9)
	DDLS	87 (56:29:2)
	THYM	34 (18:6:10)
Stomach	STAD	193 (114:46:33)
	ESCC	92 (60:12:20)
	TSTAD	87 (45:14:28)
	DSTAD	74 (57:14:3)
	ESCA	66 (44:10:12)
Testis	NSGCT	128 (78:43:7)
	SEM	91 (55:32:4)
Thymus	THYM	146 (68:35:43)
Thyroid	THPA	408 (253:45:110)
	THFO	109 (41:11:57)
Uterus	UEC	422 (308:44:70)
	USC	120 (64:40:16)
	UCS	87 (42:34:11)

Supplementary Table 12: Overview of the dataset TCGA-OT with 46 OncoTree codes grouped by tissue site and sorted by largest classes. This dataset is used for slide-level evaluations. Some cancer types can occur at multiple tissue sites and are listed in the tissue sites with the most samples, e.g., Leiomyosarcoma (LMS) contains samples from the uterus, stomach, bone, ovary, and head and neck. Additionally, all melanomas (MEL) are listed as a separate site with samples from skin (241), lymph (110), soft tissue (21), bowel (8), spleen (2), adrengal gland, brain, head and neck, thorax, and vulva (each 1). For every OncoTree code, we list the total number of samples and the number of samples contained in train, val, and test folds.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (12.5)	0.803±0.0061	0.862±0.0039	0.784±0.0061	0.829±0.0043	0.791±0.0058	0.826±0.0041
TITAN _V (25)	0.810±0.0059	0.860±0.0040	0.791±0.0063	0.841±0.0042	0.809±0.0057	0.837±0.0041
TITAN _V (50)	<u>0.818±0.0057</u>	<u>0.865±0.0039</u>	<u>0.802±0.0058</u>	<u>0.850±0.0040</u>	0.816±0.0050	<u>0.839±0.0041</u>
TITAN _V	0.820±0.0055	0.870±0.0037	0.818±0.0053	0.864±0.0039	<u>0.812±0.0050</u>	0.842±0.0038

Supplementary Table 13: Ablation study of dataset size. Linear probing results for tumor subtype ($C = 32$) prediction on TCGA-UT-8K. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (12.5)	0.656±0.0184	0.741±0.0123	0.610±0.0173	0.700±0.0132	<u>0.684±0.0187</u>	0.759±0.0118
TITAN _V (25)	0.655±0.0194	0.726±0.0126	0.626±0.0174	0.706±0.0130	0.674±0.0197	0.755±0.0120
TITAN _V (50)	<u>0.678±0.0179</u>	<u>0.743±0.0119</u>	0.644±0.0178	<u>0.735±0.0125</u>	0.706±0.0198	0.783±0.0113
TITAN _V	0.690±0.0196	0.758±0.0123	<u>0.639±0.0149</u>	0.744±0.0124	0.706±0.0183	<u>0.775±0.0116</u>

Supplementary Table 14: Ablation study of dataset size. Linear probing results for OncoTree code ($C = 46$) prediction on TCGA-OT. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (12.5)	0.520±0.0111	0.502±0.0134	0.448±0.0098	0.415±0.0123	0.511±0.0112	0.511±0.0131
TITAN _V (25)	0.526±0.0109	0.507±0.0130	0.452±0.0102	0.421±0.0129	0.515±0.0110	0.514±0.0127
TITAN _V (50)	<u>0.537±0.0102</u>	<u>0.515±0.0127</u>	0.468±0.0101	0.435±0.0123	0.537±0.0109	0.532±0.0127
TITAN _V	0.558±0.0104	0.536±0.0127	0.464±0.0105	<u>0.430±0.0128</u>	<u>0.524±0.0106</u>	<u>0.517±0.0129</u>

Supplementary Table 15: Ablation study of dataset size. Linear probing results for OncoTree code ($C = 108$) prediction on OT108. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (12.5)	0.723±0.0209	0.773±0.0177	<u>0.630±0.0216</u>	<u>0.690±0.0207</u>	0.708±0.0211	0.714±0.0186
TITAN _V (25)	0.721±0.0204	0.774±0.0191	0.620±0.0203	0.689±0.0202	<u>0.725±0.0208</u>	<u>0.724±0.0184</u>
TITAN _V (50)	0.733±0.0206	<u>0.784±0.0180</u>	0.618±0.0207	0.684±0.0207	0.719±0.0202	0.727±0.0184
TITAN _V	<u>0.732±0.0208</u>	0.785±0.0175	0.656±0.0187	0.709±0.0199	0.742±0.0192	0.727±0.0182

Supplementary Table 16: Ablation study of dataset size. Linear probing results for tumor type ($C = 30$) prediction on EBRAINS. The best result is marked in bold and the second best is underlined.

Dataset	Link
TCGA	https://portal.gdc.cancer.gov/
CPTAC	https://proteomic.datacommons.cancer.gov/pdc
EBRAINS	https://doi.org/10.25493/WQ48-ZGX
DHMC-RCC	https://bmirds.github.io/KidneyCancer
DHMC-LUAD	https://bmirds.github.io/LungCancer/
BRACS	https://www.bracs.icar.cnr.it/
PANDA	https://panda.grand-challenge.org
PD-L1	https://www.synapse.org/!Synapse:syn26642505
IMP	https://rdm.inesctec.pt/dataset/nis-2023-008
BCNB	https://bupt-ai-cz.github.io/BCNB/
MUT-HET-RCC	https://aacrjournals.org/cancerres/article/82/15/2792/707325/Intratumoral-Resolution-of-Driver-Gene-Mutation

Supplementary Table 17: Summary of publicly available datasets.

Dataset	Tissue site	Target	Label-level	# Classes	# Patients	# WSIs	Metric	External test
OT108	Pan-cancer	OncoTree	WSI	108	5,510	5,564	Bal. acc.	
TCGA-OT	Pan-cancer	OncoTree	WSI	46	9,149	11,186	Bal. acc.	
TCGA-UT-8K	Pan-cancer	Subtype	WSI	32	7,784	24,392	Bal. acc.	
EBRAINS	Brain	Diagnosis	WSI	30	2,147	2,319	Bal. acc.	
BRACS	Breast	Subtype	WSI	7	189	547	Bal. acc.	
BRACS	Breast	Subtype (coarse)	WSI	3	189	547	Bal. acc.	
TCGA-BRCA	Breast	Subtype	WSI	2	984	1,049	AUROC	
CRANE	Heart	Cellular	Patient	2	1,688	5,021	AUROC	
TCGA-RCC	Kidney	OncoTree	WSI	3	895	922	Bal. acc.	
CPTAC-DHMC	Kidney	OncoTree	WSI	3	673	872	Bal. acc.	✓
Renal allograft rejection	Kidney	AMR	Patient	2	1,118	4,847	AUROC	
Renal allograft rejection	Kidney	Cellular rejection	Patient	2	1,118	4,847	AUROC	
TCGA-NSCLC	Lung	Subtype	WSI	2	946	1,043	AUROC	
CPTAC-NSCLC	Lung	Subtype	WSI	2	422	1,091	AUROC	✓

Supplementary Table 18: Overview of the morphological tasks sorted by organ.

Dataset	Tissue site	Target	Label-level	# Classes	# Patients	# WSIs	Metric
IMP	Colorectal	Dysplasia grading	WSI	3	5,333	5,333	Cohen's κ
Renal allograft rejection	Kidney	IFTA status	Patient	3	1,118	4,847	Cohen's κ
PANDA	Prostate	Gleason grading	WSI	6	9,555	9,555	Cohen's κ

Supplementary Table 19: Overview of the grading tasks sorted by organ. The metric Cohen's κ is quadratic weighted.

Dataset	Tissue Site	Target	Label-level	# Patients	# WSIs
TCGA-BRCA	Breast	Survival	Patient	1,022	1,092
TCGA-BLCA	Bladder	Survival	Patient	360	424
TCGA-CRC	Colorectal	Survival	Patient	545	554
TCGA-KIRC	Kidney	Survival	Patient	502	508
TCGA-UCEC	Uterus	Survival	Patient	504	564
TCGA-NSCLC	Lung	Survival	Patient	844	920

Supplementary Table 20: Overview of the survival prediction tasks for measuring disease-specific survival (DSS) with c-index sorted by organ. All tasks are evaluated in five-fold site-preserving cross-validation splits.

Dataset	Tissue Site	Target	Label-level	# Classes	# Patients	# WSIs	Metric	External test
TCGA-GBM	Brain	<i>EGFR</i>	Patient	2	228	560	AUROC	
CPTAC-GBM	Brain	<i>EGFR</i>	Patient	2	99	243	AUROC	✓
TCGA-GBM	Brain	<i>TP53</i>	Patient	2	228	560	AUROC	
CPTAC-GBM	Brain	<i>TP53</i>	Patient	2	99	243	AUROC	✓
TCGA-GBMLGG	Brain	IDH	WSI	2	558	1,123	AUROC	
EBRAINS	Brain	IDH	WSI	2	795	873	AUROC	✓
BCNB	Breast	ER	Patient	2	1,058	1,058	AUROC	
BCNB	Breast	PR	Patient	2	1,058	1,058	AUROC	
BCNB	Breast	HER2	Patient	2	1,058	1,058	AUROC	
MGB-BRCA	Breast	ER	Patient	2	874	874	AUROC	
MGB-BRCA	Breast	PR	Patient	2	874	874	AUROC	
MGB-BRCA	Breast	HER2	Patient	2	816	816	AUROC	
MGH-BRCA (IHC)	Breast	ER level	Patient	6	962	962	Cohen's κ	
MGH-BRCA (IHC)	Breast	PR level	Patient	6	1,070	1,070	Cohen's κ	
PDL1-LUAD (IHC)	Lung	PD-L1 level	Patient	3	217	234	Cohen's κ	
TCGA-BRCA	Breast	ER	Patient	2	937	996	AUROC	
CPTAC-BRCA	Breast	ER	Patient	2	102	111	AUROC	✓
TCGA-BRCA	Breast	PR	Patient	2	934	993	AUROC	
CPTAC-BRCA	Breast	PR	Patient	2	97	106	AUROC	✓
TCGA-BRCA	Breast	HER2	Patient	2	647	693	AUROC	
CPTAC-BRCA	Breast	HER2	Patient	2	103	112	AUROC	✓
TCGA-BRCA	Breast	<i>PIK3CA</i>	Patient	2	970	1,034	AUROC	
CPTAC-BRCA	Breast	<i>PIK3CA</i>	Patient	2	103	112	AUROC	✓
TCGA-CRC	Colorectal	MSI	Patient	2	414	419	AUROC	
CPTAC-COAD	Colorectal	MSI	Patient	2	103	107	AUROC	✓
TCGA-CRC	Colorectal	<i>BRAF</i>	Patient	2	487	492	AUROC	
CPTAC-COAD	Colorectal	<i>BRAF</i>	Patient	2	103	107	AUROC	✓
MUT-HET-RCC	Kidney	<i>BAP1</i>	Patient	2	1,292	1,292	AUROC	
MUT-HET-RCC	Kidney	<i>PBRM1</i>	Patient	2	1,292	1,292	AUROC	
MUT-HET-RCC	Kidney	<i>SETD2</i>	Patient	2	1,292	1,292	AUROC	
MGB-LUAD	Lung	CDX-2	Patient	2	79	79	AUROC	
MGB-LUAD	Lung	CK-5&6	Patient	2	58	58	AUROC	
MGB-LUAD	Lung	Napsin A	Patient	2	126	126	AUROC	
MGB-LUAD	Lung	P40	Patient	2	185	185	AUROC	
MGB-LUAD	Lung	P63	Patient	2	153	153	AUROC	
TCGA-NSCLC	Lung	<i>EGFR</i>	Patient	2	462	524	AUROC	
CPTAC-LUAD	Lung	<i>EGFR</i>	Patient	2	108	324	AUROC	✓
TCGA-NSCLC	Lung	<i>TP53</i>	Patient	2	462	524	AUROC	
CPTAC-LUAD	Lung	<i>TP53</i>	Patient	2	108	324	AUROC	✓

Supplementary Table 21: Overview of the molecular tasks sorted by organ. The metric Cohen's κ is quadratic weighted.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.711±0.0069	0.791±0.0046	0.606±0.0073	0.674±0.0050	0.563±0.0071	0.639±0.0052
GigaPath	0.700±0.0069	0.782±0.0046	0.591±0.0074	0.668±0.0051	0.564±0.0070	0.644±0.0051
Mean pool (Virchow)	0.691±0.0072	0.771±0.0047	0.524±0.0079	0.579±0.0055	0.523±0.0070	0.615±0.0054
PRISM	0.774±0.0062	0.824±0.0042	0.708±0.0063	0.737±0.0049	0.702±0.0068	0.777±0.0048
Mean pool (CHIEF)	0.627±0.0077	0.729±0.0050	0.477±0.0076	0.560±0.0054	0.495±0.0072	0.581±0.0056
CHIEF	0.625±0.0079	0.723±0.0051	0.503±0.0072	0.567±0.0053	0.506±0.0071	0.594±0.0054
Mean pool (CONCHv1.5)	0.779±0.0064	0.833±0.0043	0.757±0.0062	0.785±0.0045	0.743±0.0067	0.796±0.0045
TITAN _v	<u>0.820</u> ±0.0055	<u>0.870</u> ±0.0037	<u>0.812</u> ±0.0050	<u>0.842</u> ±0.0038	<u>0.818</u> ±0.0053	<u>0.864</u> ±0.0039
TITAN	0.832 ±0.0056	0.881 ±0.0036	0.843 ±0.0056	0.865 ±0.0037	0.828 ±0.0052	0.875 ±0.0037

Supplementary Table 22: Linear probing results for tumor subtype ($C = 32$) prediction on TCGA-UT-8K. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.568±0.0167	0.662±0.0132	0.479±0.0146	0.562±0.0137	0.419±0.0138	0.521±0.0142
GigaPath	0.543±0.0178	0.659±0.0134	0.477±0.0149	0.538±0.0138	0.402±0.0132	0.516±0.0145
Mean pool (Virchow)	0.564±0.0165	0.656±0.0135	0.379±0.0141	0.454±0.0150	0.371±0.0109	0.479±0.0148
PRISM	0.643±0.0181	0.732±0.0129	0.617±0.0201	0.703±0.0130	0.606±0.0166	0.710±0.0133
Mean pool (CHIEF)	0.526±0.0188	0.643±0.0141	0.416±0.0195	0.493±0.0136	0.381±0.0143	0.496±0.0146
CHIEF	0.528±0.0205	0.640±0.0142	0.442±0.0207	0.478±0.0138	0.403±0.0146	0.504±0.0145
Mean pool (CONCHv1.5)	0.624±0.0169	0.700±0.0131	0.615±0.0171	0.680±0.0130	0.573±0.0153	0.666±0.0132
TITAN _v	<u>0.690</u> ±0.0196	<u>0.758</u> ±0.0123	<u>0.706</u> ±0.0183	<u>0.775</u> ±0.0116	<u>0.639</u> ±0.0149	<u>0.744</u> ±0.0124
TITAN	0.704 ±0.0192	0.764 ±0.0116	0.744 ±0.0152	0.802 ±0.0108	0.685 ±0.0183	0.774 ±0.0119

Supplementary Table 23: Linear probing results for OncoTree code ($C = 46$) prediction on TCGA-OT. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.450±0.0111	0.436±0.0127	0.365±0.0107	0.353±0.0123	0.318±0.0098	0.293±0.0114
GigaPath	0.437±0.0110	0.423±0.0124	0.354±0.0107	0.344±0.0125	0.308±0.0097	0.283±0.0116
Mean pool (Virchow)	0.454±0.0111	0.439±0.0127	0.315±0.0102	0.304±0.0121	0.283±0.0096	0.255±0.0117
PRISM	0.508±0.0110	0.481±0.0133	0.483±0.0119	0.469±0.0131	0.434±0.0102	0.384±0.0129
Mean pool (CHIEF)	0.356±0.0112	0.340±0.0125	0.226±0.0097	0.206±0.0114	0.210±0.0095	0.185±0.0103
CHIEF	0.413±0.0109	0.394±0.0130	0.295±0.0108	0.282±0.0120	0.262±0.0093	0.231±0.0108
Mean pool (CONCHv1.5)	0.476±0.0112	0.459±0.0129	0.411±0.0107	0.404±0.0127	0.368±0.0103	0.341±0.0122
TITAN _V	<u>0.558</u> ±0.0104	<u>0.536</u> ±0.0127	<u>0.524</u> ±0.0106	<u>0.517</u> ±0.0129	<u>0.464</u> ±0.0105	<u>0.430</u> ±0.0128
TITAN	0.587 ±0.0103	0.563 ±0.0130	0.580 ±0.0103	0.567 ±0.0129	0.527 ±0.0101	0.489 ±0.0132

Supplementary Table 24: Linear probing results for OncoTree code ($C = 108$) prediction on OT108. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.712±0.0215	0.766±0.0193	0.626±0.0238	0.627±0.0197	0.543±0.0221	0.633±0.0221
GigaPath	0.680±0.0217	0.746±0.0197	0.626±0.0235	0.610±0.0201	0.530±0.0213	0.621±0.0219
Mean pool (Virchow)	0.665±0.0220	0.735±0.0189	0.559±0.0236	0.553±0.0207	0.481±0.0200	0.573±0.0220
PRISM	0.674±0.0200	0.732±0.0191	0.625±0.0223	0.583±0.0204	0.609±0.0198	0.660±0.0201
Mean pool (CHIEF)	0.594±0.0240	0.663±0.0205	0.487±0.0242	0.463±0.0214	0.368±0.0193	0.443±0.0217
CHIEF	0.598±0.0237	0.670±0.0206	0.478±0.0239	0.453±0.0213	0.415±0.0198	0.498±0.0219
Mean pool (CONCHv1.5)	0.644±0.0215	0.715±0.0200	0.550±0.0221	0.480±0.0217	0.551±0.0221	0.631±0.0211
TITAN _V	<u>0.732</u> ±0.0208	<u>0.785</u> ±0.0175	<u>0.742</u> ±0.0192	<u>0.727</u> ±0.0182	<u>0.656</u> ±0.0187	<u>0.709</u> ±0.0199
TITAN	0.735 ±0.0204	0.786 ±0.0182	0.754 ±0.0203	0.748 ±0.0182	0.695 ±0.0196	0.746 ±0.0200

Supplementary Table 25: Linear probing results for tumor type ($C = 30$) prediction on EBRAINS. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.938±0.0204	0.780±0.0358	0.792±0.0354	0.799±0.0428	0.639±0.0460	0.812±0.0346
GigaPath	0.935±0.0243	0.780±0.0463	0.776±0.0542	0.783±0.0493	0.607±0.0247	0.794±0.0208
Mean pool (Virchow)	0.904±0.0178	0.749±0.0431	0.718±0.0583	0.725±0.0804	0.540±0.0200	0.744±0.0255
PRISM	0.944±0.0241	0.850 ±0.0398	0.877±0.0412	0.906 ±0.0197	<u>0.879</u> ±0.0400	0.919±0.0195
Mean pool (CHIEF)	0.930±0.0137	0.786±0.0593	0.733±0.0702	0.741±0.0863	0.621±0.0375	0.801±0.0297
CHIEF	0.935±0.0219	0.843±0.0534	0.822±0.0261	0.836±0.0269	0.775±0.0708	0.879±0.0378
Mean pool (CONCHv1.5)	0.927±0.0229	0.776±0.0626	0.803±0.0443	0.810±0.0723	0.767±0.0600	0.878±0.0334
TITAN _V	0.948 ±0.0146	<u>0.848</u> ±0.0376	<u>0.885</u> ±0.0290	<u>0.905</u> ±0.0265	0.875±0.0428	<u>0.921</u> ±0.0180
TITAN	<u>0.945</u> ±0.0174	<u>0.848</u> ±0.0293	0.892 ±0.0271	0.903±0.0192	0.902 ±0.0268	0.926 ±0.0162

Supplementary Table 26: Linear probing results for tumor subtype ($C = 2$) prediction on TCGA-BRCA. The best result is marked in bold and the second best is underlined.

Encoder	Cohort	Logistic regression		SimpleShot		20-nearest neighbors	
		AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	TCGA	0.948±0.0129	0.883±0.0278	0.795±0.0636	0.795±0.0656	0.783±0.0109	0.771±0.0125
GigaPath	TCGA	0.934±0.0142	0.869±0.0251	0.759±0.0605	0.758±0.0608	0.744±0.0075	0.727±0.0101
Mean pool (Virchow)	TCGA	0.944±0.0153	0.866±0.0339	0.684±0.0620	0.682±0.0643	0.668±0.0593	0.646±0.0831
PRISM	TCGA	0.977±0.0058	<u>0.934±0.0195</u>	0.914±0.0189	0.915±0.0185	<u>0.927±0.0018</u>	0.928±0.0019
Mean pool (CHIEF)	TCGA	0.947±0.0121	0.881±0.0245	0.765±0.0582	0.764±0.0595	0.803±0.0070	0.793±0.0099
CHIEF	TCGA	0.963±0.0087	0.897±0.0197	0.846±0.0276	0.845±0.0289	0.862±0.0081	0.859±0.0091
Mean pool (CONCHv1.5)	TCGA	0.965±0.0147	0.904±0.0207	0.831±0.0370	0.831±0.0381	0.904±0.0035	0.903±0.0034
TITAN _V	TCGA	<u>0.979±0.0059</u>	0.932±0.0190	<u>0.929±0.0147</u>	<u>0.930±0.0148</u>	0.933±0.0032	<u>0.934±0.0030</u>
TITAN	TCGA	0.982±0.0058	0.941±0.0230	0.944±0.0198	0.944±0.0193	0.933±0.0031	0.935±0.0029
Mean pool (GigaPath)	CPTAC	0.954±0.0105	0.889±0.0166	0.755±0.0367	0.732±0.0432	0.844±0.0086	0.843±0.0087
GigaPath	CPTAC	0.950±0.0105	0.882±0.0165	0.722±0.0310	0.692±0.0396	0.581±0.0097	0.470±0.0188
Mean pool (Virchow)	CPTAC	0.953±0.0151	0.864±0.0208	0.814±0.0300	0.803±0.0364	0.672±0.0118	0.653±0.0159
PRISM	CPTAC	0.973±0.0036	0.932±0.0124	<u>0.941±0.0017</u>	<u>0.941±0.0019</u>	0.922±0.0039	0.921±0.0040
Mean pool (CHIEF)	CPTAC	0.945±0.0130	0.867±0.0186	0.801±0.0226	0.787±0.0266	0.792±0.0149	0.787±0.0159
CHIEF	CPTAC	0.945±0.0116	0.867±0.0175	0.871±0.0115	0.867±0.0125	0.844±0.0092	0.840±0.0107
Mean pool (CONCHv1.5)	CPTAC	0.978±0.0032	0.934±0.0069	0.876±0.0088	0.872±0.0100	0.847±0.0163	0.851±0.0163
TITAN _V	CPTAC	0.986±0.0008	<u>0.939±0.0046</u>	0.940±0.0019	0.940±0.0022	0.939±0.0025	0.939±0.0024
TITAN	CPTAC	<u>0.985±0.0010</u>	0.950±0.0031	0.953±0.0025	0.954±0.0022	<u>0.929±0.0031</u>	<u>0.932±0.0028</u>

Supplementary Table 27: Linear probing results for tumor subtype ($C = 2$) prediction on TCGA-NSCLC and external dataset CPTAC-NSCLC. The best result is marked in bold and the second best is underlined.

Encoder	Cohort	Logistic regression		SimpleShot		20-nearest neighbors	
		Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	TCGA	0.841±0.0470	0.896±0.0334	0.856±0.0561	0.843±0.0425	0.776±0.0262	0.899±0.0304
GigaPath	TCGA	0.823±0.0343	0.892±0.0290	0.859±0.0520	0.863±0.0366	0.745±0.0473	0.905±0.0137
Mean pool (Virchow)	TCGA	0.819±0.0879	0.886±0.0543	0.759±0.1060	0.739±0.1575	0.570±0.0407	0.841±0.0898
PRISM	TCGA	0.866±0.0360	0.915±0.0272	0.859±0.0509	0.855±0.0415	0.713±0.0168	0.917±0.0032
Mean pool (CHIEF)	TCGA	0.900±0.0473	0.921±0.0366	0.897±0.0279	0.881±0.0308	0.832±0.0071	0.910±0.0163
CHIEF	TCGA	0.913±0.0268	0.928±0.0280	0.910±0.0346	0.891±0.0298	0.841±0.0123	0.890±0.0140
Mean pool (CONCHv1.5)	TCGA	0.871±0.0498	0.910±0.0437	0.900±0.0306	<u>0.911±0.0350</u>	0.839±0.0108	0.945±0.0017
TITAN _V	TCGA	<u>0.920±0.0331</u>	<u>0.931±0.0354</u>	<u>0.954±0.0148</u>	0.939±0.0239	<u>0.945±0.0131</u>	0.966±0.0028
TITAN	TCGA	0.942±0.0222	0.941±0.0333	0.955±0.0202	0.939±0.0341	0.971±0.0025	<u>0.965±0.0009</u>
Mean pool (GigaPath)	CPTAC-DHMC	0.854±0.0327	0.919±0.0288	0.840±0.0137	0.835±0.0205	0.841±0.0228	0.950±0.0047
GigaPath	CPTAC-DHMC	0.833±0.0521	0.933±0.0187	0.850±0.0107	0.882±0.0175	0.615±0.0368	0.911±0.0079
Mean pool (Virchow)	CPTAC-DHMC	0.701±0.0716	0.799±0.0827	0.488±0.0135	0.584±0.0332	0.666±0.0884	0.694±0.0091
PRISM	CPTAC-DHMC	0.753±0.0508	0.934±0.0054	0.724±0.0071	0.902±0.0024	0.547±0.0381	0.897±0.0072
Mean pool (CHIEF)	CPTAC-DHMC	0.840±0.0289	0.938±0.0108	0.868±0.0069	0.883±0.0167	0.655±0.0173	0.908±0.0063
CHIEF	CPTAC-DHMC	0.822±0.0143	0.925±0.0115	<u>0.869±0.0059</u>	0.842±0.0123	0.727±0.0091	0.926±0.0047
Mean pool (CONCHv1.5)	CPTAC-DHMC	0.850±0.0238	0.944±0.0089	0.836±0.0033	0.936±0.0025	0.668±0.0079	0.897±0.0026
TITAN _V	CPTAC-DHMC	<u>0.910±0.0169</u>	<u>0.959±0.0063</u>	0.971±0.0011	<u>0.959±0.0029</u>	0.922±0.0067	0.971±0.0021
TITAN	CPTAC-DHMC	0.918±0.0073	0.967±0.0040	0.971±0.0026	0.962±0.0012	<u>0.890±0.0089</u>	<u>0.959±0.0013</u>

Supplementary Table 28: Linear probing results for OncoTree code ($C = 3$) prediction on TCGA-RCC and external dataset CPTAC-CCRCC and DHMC-RCC. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.321±0.0482	0.433±0.0998	0.308±0.0424	0.357±0.0863	0.239±0.0416	0.352±0.0967
GigaPath	0.305±0.0465	0.429±0.1034	0.287±0.0355	0.332±0.0837	0.282±0.0813	0.367±0.1239
Mean pool (Virchow)	0.307±0.0345	0.415±0.1096	0.275±0.0430	0.342±0.0766	0.262±0.0613	0.375±0.0937
PRISM	0.411±0.0569	0.521±0.0584	<u>0.474±0.0594</u>	0.535±0.0760	0.408±0.0524	0.522±0.0662
Mean pool (CHIEF)	0.322±0.0617	0.443±0.1139	0.281±0.0424	0.309±0.0906	0.282±0.0426	0.352±0.0864
CHIEF	<u>0.405±0.0553</u>	<u>0.513±0.0837</u>	0.418±0.0529	0.430±0.1012	<u>0.368±0.0257</u>	0.449±0.0785
Mean pool (CONCHv1.5)	0.332±0.0509	0.450±0.0869	0.336±0.0432	0.396±0.0696	0.313±0.0619	0.412±0.0980
TITAN _V	0.404±0.0409	0.521±0.0836	0.424±0.0554	0.478±0.1046	0.349±0.0375	0.466±0.0884
TITAN	0.400±0.0259	0.511±0.0686	0.483±0.0819	<u>0.491±0.1154</u>	0.367±0.0387	<u>0.479±0.0797</u>

Supplementary Table 29: Linear probing results for subtype ($C = 7$) prediction on BRACS. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.560±0.0906	0.662±0.1228	0.565±0.0755	0.557±0.0847	0.509±0.0904	0.589±0.1080
GigaPath	0.568±0.1028	0.661±0.1221	0.562±0.0620	0.548±0.0766	0.515±0.0774	0.599±0.1054
Mean pool (Virchow)	0.571±0.0792	0.674±0.1144	0.581±0.0863	0.580±0.0946	0.514±0.0633	0.618±0.1045
PRISM	0.658±0.0393	0.759±0.0771	<u>0.726±0.0456</u>	0.761±0.0517	<u>0.672±0.0319</u>	<u>0.766±0.0608</u>
Mean pool (CHIEF)	0.563±0.0811	0.666±0.0884	0.567±0.0566	0.545±0.0834	0.492±0.0530	0.586±0.0793
CHIEF	0.638±0.0547	0.739±0.0695	0.675±0.0985	0.696±0.0844	0.625±0.0738	0.721±0.0897
Mean pool (CONCHv1.5)	0.606±0.0958	0.702±0.1145	0.645±0.0455	0.643±0.0592	0.516±0.0471	0.624±0.0799
TITAN _V	<u>0.679±0.0712</u>	<u>0.780±0.0664</u>	0.739±0.0964	0.738±0.1010	0.630±0.0650	0.737±0.0869
TITAN	0.702±0.0395	0.803±0.0410	0.739±0.0543	<u>0.755±0.0713</u>	0.682±0.0120	0.790±0.0545

Supplementary Table 30: Linear probing results for coarse subtype ($C = 3$) prediction on BRACS. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.882±0.0187	0.811±0.0216	0.692±0.0242	0.690±0.0260	0.513±0.0194	0.354±0.0519
GigaPath	0.865±0.0204	0.801±0.0230	<u>0.721±0.0229</u>	<u>0.717±0.0264</u>	0.528±0.0150	0.489±0.0240
Mean pool (Virchow)	0.872±0.0189	0.805±0.0214	0.706±0.0245	0.706±0.0254	0.499±0.0119	0.308±0.0510
PRISM	0.877±0.0182	0.801±0.0213	0.692±0.0256	0.692±0.0256	<u>0.657±0.0190</u>	0.660±0.0198
Mean pool (CHIEF)	0.887±0.0186	0.817±0.0205	0.654±0.0258	0.654±0.0261	0.562±0.0460	0.565±0.0480
CHIEF	<u>0.893±0.0178</u>	0.822±0.0208	0.667±0.0253	0.667±0.0260	0.504±0.0334	0.465±0.0533
Mean pool (CONCHv1.5)	0.880±0.0196	0.826±0.0212	0.716±0.0235	0.714±0.0253	0.658±0.0419	<u>0.658±0.0413</u>
TITAN _V	0.906±0.0166	0.836±0.0204	0.713±0.0229	0.710±0.0251	0.554±0.0190	0.410±0.0544
TITAN	0.906±0.0162	<u>0.830±0.0207</u>	0.766±0.0222	0.765±0.0237	0.614±0.0343	0.557±0.0500

Supplementary Table 31: Linear probing results for cellular rejection ($C = 2$) prediction on CRANE. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.851±0.0318	0.764±0.0354	0.591±0.0389	0.598±0.0340	0.546±0.0368	0.636±0.0379
GigaPath	0.836±0.0354	0.758±0.0360	0.566±0.0403	0.571±0.0356	0.518±0.0348	0.619±0.0398
Mean pool (Virchow)	0.855±0.0302	0.751±0.0360	0.600±0.0384	0.585±0.0354	0.524±0.0340	0.622±0.0375
PRISM	0.820±0.0350	0.687±0.0351	0.633±0.0383	0.666±0.0327	0.569±0.0363	0.659±0.0358
Mean pool (CHIEF)	0.834±0.0322	0.727±0.0365	0.627±0.0389	0.638±0.0336	0.575±0.0381	0.661±0.0383
CHIEF	0.813±0.0336	0.649±0.0355	0.606±0.0390	0.645±0.0334	0.590±0.0360	0.678±0.0358
Mean pool (CONCHv1.5)	0.817±0.0343	0.594±0.0354	0.644±0.0389	0.668±0.0330	0.541±0.0351	0.642±0.0388
TITAN _V	<u>0.880±0.0293</u>	0.744±0.0356	<u>0.681±0.0370</u>	<u>0.688±0.0319</u>	<u>0.721±0.0371</u>	<u>0.770±0.0303</u>
TITAN	0.915±0.0238	0.807±0.0331	0.709±0.0357	0.704±0.0319	0.802±0.0335	0.844±0.0263

Supplementary Table 32: Linear probing results for antibody-mediated rejection ($C = 2$) prediction on Renal allograft rejection. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.802±0.0331	0.667±0.0344	0.541±0.0384	0.538±0.0373	0.572±0.0361	0.615±0.0359
GigaPath	0.814±0.0331	0.715±0.0364	0.557±0.0389	0.559±0.0371	0.627±0.0356	0.667±0.0347
Mean pool (Virchow)	0.802±0.0323	0.669±0.0347	0.556±0.0386	0.548±0.0371	0.531±0.0376	0.568±0.0366
PRISM	0.840±0.0288	<u>0.736±0.0338</u>	0.692±0.0355	0.713±0.0323	0.670±0.0372	0.687±0.0344
Mean pool (CHIEF)	0.772±0.0360	0.669±0.0346	0.567±0.0387	0.571±0.0368	0.598±0.0371	0.634±0.0355
CHIEF	0.823±0.0307	0.681±0.0347	0.633±0.0384	0.656±0.0356	0.598±0.0374	0.634±0.0356
Mean pool (CONCHv1.5)	0.817±0.0310	0.686±0.0348	<u>0.721±0.0345</u>	<u>0.736±0.0316</u>	0.682±0.0358	<u>0.710±0.0334</u>
TITAN _V	<u>0.860±0.0270</u>	0.716±0.0348	0.719±0.0339	0.718±0.0322	<u>0.691±0.0370</u>	0.708±0.0341
TITAN	0.864±0.0264	0.743±0.0340	0.753±0.0335	0.753±0.0316	0.741±0.0346	0.764±0.0316

Supplementary Table 33: Linear probing results for cellular rejection ($C = 2$) prediction on Renal allograft rejection. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Cohen's κ	Bal. acc.	Cohen's κ	Bal. acc.	Cohen's κ	Bal. acc.
Mean pool (GigaPath)	0.678 $\pm$ 0.0476	0.630 $\pm$ 0.0406	0.317 $\pm$ 0.0604	0.477 $\pm$ 0.0391	0.423 $\pm$ 0.0736	0.516 $\pm$ 0.0383
GigaPath	0.666 $\pm$ 0.0497	0.632 $\pm$ 0.0398	0.396 $\pm$ 0.0584	0.518 $\pm$ 0.0406	0.333 $\pm$ 0.0725	0.449 $\pm$ 0.0369
Mean pool (Virchow)	0.640 $\pm$ 0.0542	0.597 $\pm$ 0.0405	0.309 $\pm$ 0.0596	0.485 $\pm$ 0.0396	0.210 $\pm$ 0.0785	0.416 $\pm$ 0.0364
PRISM	0.603 $\pm$ 0.0528	0.557 $\pm$ 0.0396	0.521 $\pm$ 0.0608	0.554 $\pm$ 0.0413	0.549 $\pm$ 0.0689	<u>0.583</u> $\pm$ 0.0406
Mean pool (CHIEF)	0.673 $\pm$ 0.0495	0.613 $\pm$ 0.0395	0.419 $\pm$ 0.0598	0.529 $\pm$ 0.0366	0.383 $\pm$ 0.0714	0.463 $\pm$ 0.0366
CHIEF	0.665 $\pm$ 0.0527	0.644 $\pm$ 0.0385	0.569 $\pm$ 0.0571	0.638 $\pm$ 0.0355	0.506 $\pm$ 0.0688	0.556 $\pm$ 0.0377
Mean pool (CONCHv1.5)	<u>0.711</u> $\pm$ 0.0482	0.712 $\pm$ 0.0376	<u>0.600</u> $\pm$ 0.0545	0.600 $\pm$ 0.0406	0.411 $\pm$ 0.0756	0.536 $\pm$ 0.0414
TITAN _V	0.685 $\pm$ 0.0519	0.681 $\pm$ 0.0394	0.531 $\pm$ 0.0641	0.613 $\pm$ 0.0416	0.401 $\pm$ 0.0702	0.532 $\pm$ 0.0389
TITAN	0.723 $\pm$ 0.0470	<u>0.688</u> $\pm$ 0.0384	0.627 $\pm$ 0.0506	<u>0.636</u> $\pm$ 0.0392	<u>0.544</u> $\pm$ 0.0645	0.590 $\pm$ 0.0394

Supplementary Table 34: Linear probing results for Interstitial fibrosis and tubular atrophy (IFTA) level ($C = 3$) prediction on Renal allograft rejection. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Cohen's κ	Bal. acc.	Cohen's κ	Bal. acc.	Cohen's κ	Bal. acc.
Mean pool (GigaPath)	0.911 $\pm$ 0.0110	0.923 $\pm$ 0.0085	0.805 $\pm$ 0.0188	0.848 $\pm$ 0.0123	0.841 $\pm$ 0.0162	0.859 $\pm$ 0.0129
GigaPath	0.909 $\pm$ 0.0112	0.919 $\pm$ 0.0092	0.790 $\pm$ 0.0199	0.834 $\pm$ 0.0129	0.852 $\pm$ 0.0151	0.863 $\pm$ 0.0125
Mean pool (Virchow)	0.910 $\pm$ 0.0118	0.917 $\pm$ 0.0100	0.772 $\pm$ 0.0214	0.831 $\pm$ 0.0133	0.838 $\pm$ 0.0169	0.854 $\pm$ 0.0136
PRISM	0.946 $\pm$ 0.0076	<u>0.945</u> $\pm$ 0.0079	0.912 $\pm$ 0.0115	0.929 $\pm$ 0.0081	0.944 $\pm$ 0.0080	0.943 $\pm$ 0.0079
Mean pool (CHIEF)	0.886 $\pm$ 0.0128	<u>0.894</u> $\pm$ 0.0111	0.642 $\pm$ 0.0272	0.767 $\pm$ 0.0150	0.780 $\pm$ 0.0216	0.834 $\pm$ 0.0140
CHIEF	0.909 $\pm$ 0.0129	0.925 $\pm$ 0.0094	0.856 $\pm$ 0.0160	<u>0.886</u> $\pm$ 0.0107	0.895 $\pm$ 0.0139	<u>0.914</u> $\pm$ 0.0098
Mean pool (CONCHv1.5)	0.899 $\pm$ 0.0126	0.907 $\pm$ 0.0104	0.716 $\pm$ 0.0227	0.790 $\pm$ 0.0141	0.831 $\pm$ 0.0165	0.859 $\pm$ 0.0122
TITAN _V	0.935 $\pm$ 0.0097	0.939 $\pm$ 0.0086	0.804 $\pm$ 0.0160	0.820 $\pm$ 0.0138	0.892 $\pm$ 0.0120	0.898 $\pm$ 0.0104
TITAN	<u>0.944</u> $\pm$ 0.0091	0.946 $\pm$ 0.0084	<u>0.857</u> $\pm$ 0.0139	0.859 $\pm$ 0.0124	<u>0.906</u> $\pm$ 0.0111	0.908 $\pm$ 0.0100

Supplementary Table 35: Linear probing results for dysplasia grading ($C = 3$) prediction on IMP-CRC biopsies. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Cohen's κ	Bal. acc.	Cohen's κ	Bal. acc.	Cohen's κ	Bal. acc.
Mean pool (GigaPath)	0.897 $\pm$ 0.0112	0.727 $\pm$ 0.0149	0.477 $\pm$ 0.0289	0.373 $\pm$ 0.0143	0.716 $\pm$ 0.0221	0.526 $\pm$ 0.0169
GigaPath	0.869 $\pm$ 0.0136	0.676 $\pm$ 0.0163	0.461 $\pm$ 0.0287	0.354 $\pm$ 0.0139	0.718 $\pm$ 0.0228	0.532 $\pm$ 0.0169
Mean pool (Virchow)	0.896 $\pm$ 0.0102	<u>0.693</u> $\pm$ 0.0160	0.468 $\pm$ 0.0262	0.326 $\pm$ 0.0131	0.694 $\pm$ 0.0225	0.508 $\pm$ 0.0168
PRISM	0.918 $\pm$ 0.0078	0.663 $\pm$ 0.0157	<u>0.815</u> $\pm$ 0.0171	0.573 $\pm$ 0.0161	0.894 $\pm$ 0.0101	0.652 $\pm$ 0.0155
Mean pool (CHIEF)	0.843 $\pm$ 0.0145	0.625 $\pm$ 0.0165	0.506 $\pm$ 0.0269	0.370 $\pm$ 0.0149	0.722 $\pm$ 0.0222	0.504 $\pm$ 0.0169
CHIEF	<u>0.911</u> $\pm$ 0.0098	0.684 $\pm$ 0.0158	0.712 $\pm$ 0.0209	0.486 $\pm$ 0.0155	0.864 $\pm$ 0.0142	<u>0.639</u> $\pm$ 0.0162
Mean pool (CONCHv1.5)	0.847 $\pm$ 0.0130	0.602 $\pm$ 0.0160	0.703 $\pm$ 0.0192	0.442 $\pm$ 0.0160	0.744 $\pm$ 0.0209	<u>0.538</u> $\pm$ 0.0164
TITAN _V	0.888 $\pm$ 0.0102	0.648 $\pm$ 0.0158	0.704 $\pm$ 0.0199	0.472 $\pm$ 0.0159	0.800 $\pm$ 0.0172	0.571 $\pm$ 0.0166
TITAN	0.899 $\pm$ 0.0097	0.657 $\pm$ 0.0162	0.831 $\pm$ 0.0128	<u>0.533</u> $\pm$ 0.0156	<u>0.867</u> $\pm$ 0.0118	0.622 $\pm$ 0.0158

Supplementary Table 36: Linear probing results for Gleason grading ($C = 6$) prediction on PANDA. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.860 $\pm$ 0.0161	0.643 $\pm$ 0.0277	0.738 $\pm$ 0.0392	0.745 $\pm$ 0.0253	0.532 $\pm$ 0.0060	0.833 $\pm$ 0.0029
GigaPath	0.850 $\pm$ 0.0261	0.564 $\pm$ 0.0243	0.760 $\pm$ 0.0454	0.769 $\pm$ 0.0262	0.527 $\pm$ 0.0146	0.831 $\pm$ 0.0077
Mean pool (Virchow)	<u>0.856</u> $\pm$ 0.0310	<u>0.617</u> $\pm$ 0.0405	0.746 $\pm$ 0.0494	0.746 $\pm$ 0.0297	0.520 $\pm$ 0.0193	0.827 $\pm$ 0.0122
PRISM	0.860 $\pm$ 0.0204	0.560 $\pm$ 0.0428	<u>0.778</u> $\pm$ 0.0615	0.779 $\pm$ 0.0305	0.518 $\pm$ 0.0065	0.826 $\pm$ 0.0038
Mean pool (CHIEF)	0.840 $\pm$ 0.0337	0.552 $\pm$ 0.0295	0.754 $\pm$ 0.0383	0.746 $\pm$ 0.0195	0.515 $\pm$ 0.0170	0.823 $\pm$ 0.0103
CHIEF	0.842 $\pm$ 0.0302	0.577 $\pm$ 0.0484	0.764 $\pm$ 0.0399	0.745 $\pm$ 0.0212	0.522 $\pm$ 0.0096	0.828 $\pm$ 0.0065
Mean pool (CONCHv1.5)	0.842 $\pm$ 0.0386	0.557 $\pm$ 0.0227	0.775 $\pm$ 0.0484	0.796 $\pm$ 0.0230	0.519 $\pm$ 0.0130	0.826 $\pm$ 0.0084
TITAN _V	<u>0.856</u> $\pm$ 0.0194	0.598 $\pm$ 0.0225	0.783 $\pm$ 0.0502	0.796 $\pm$ 0.0214	0.560 $\pm$ 0.0204	0.845 $\pm$ 0.0097
TITAN	0.854 $\pm$ 0.0108	0.580 $\pm$ 0.0107	0.777 $\pm$ 0.0351	<u>0.791</u> $\pm$ 0.0249	<u>0.553</u> $\pm$ 0.0176	<u>0.842</u> $\pm$ 0.0086

Supplementary Table 37: Linear probing results for BAP1 mutation ($C = 2$) prediction on MUT-HET-RCC. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.800 $\pm$ 0.0174	0.728 $\pm$ 0.0199	0.613 $\pm$ 0.0123	0.610 $\pm$ 0.0132	0.649 $\pm$ 0.0252	0.650 $\pm$ 0.0254
GigaPath	0.788 $\pm$ 0.0164	0.722 $\pm$ 0.0227	0.623 $\pm$ 0.0221	0.620 $\pm$ 0.0240	0.654 $\pm$ 0.0208	0.654 $\pm$ 0.0207
Mean pool (Virchow)	<u>0.799</u> $\pm$ 0.0132	<u>0.726</u> $\pm$ 0.0150	0.627 $\pm$ 0.0144	0.624 $\pm$ 0.0147	0.644 $\pm$ 0.0138	0.645 $\pm$ 0.0134
PRISM	0.784 $\pm$ 0.0138	0.711 $\pm$ 0.0196	0.635 $\pm$ 0.0273	0.633 $\pm$ 0.0281	0.680 $\pm$ 0.0110	<u>0.681</u> $\pm$ 0.0109
Mean pool (CHIEF)	0.750 $\pm$ 0.0178	0.674 $\pm$ 0.0157	0.642 $\pm$ 0.0128	0.638 $\pm$ 0.0146	0.641 $\pm$ 0.0182	0.640 $\pm$ 0.0174
CHIEF	0.789 $\pm$ 0.0277	0.714 $\pm$ 0.0252	0.646 $\pm$ 0.0120	0.645 $\pm$ 0.0119	0.669 $\pm$ 0.0174	0.668 $\pm$ 0.0169
Mean pool (CONCHv1.5)	0.771 $\pm$ 0.0187	0.710 $\pm$ 0.0142	0.625 $\pm$ 0.0222	0.624 $\pm$ 0.0222	0.635 $\pm$ 0.0167	0.635 $\pm$ 0.0164
TITAN _V	0.790 $\pm$ 0.0081	0.705 $\pm$ 0.0106	<u>0.672</u> $\pm$ 0.0098	<u>0.669</u> $\pm$ 0.0104	<u>0.681</u> $\pm$ 0.0209	<u>0.681</u> $\pm$ 0.0212
TITAN	0.775 $\pm$ 0.0205	0.713 $\pm$ 0.0192	0.674 $\pm$ 0.0114	0.674 $\pm$ 0.0110	0.685 $\pm$ 0.0237	0.685 $\pm$ 0.0232

Supplementary Table 38: Linear probing results for PBRM1 mutation ($C = 2$) prediction on MUT-HET-RCC. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.714 $\pm$ 0.0193	0.559 $\pm$ 0.0158	0.626 $\pm$ 0.0339	0.636 $\pm$ 0.0319	0.512 $\pm$ 0.0261	0.639 $\pm$ 0.0267
GigaPath	0.719 $\pm$ 0.0268	0.574 $\pm$ 0.0266	<u>0.651</u> $\pm$ 0.0340	0.655 $\pm$ 0.0314	0.526 $\pm$ 0.0109	0.652 $\pm$ 0.0130
Mean pool (Virchow)	0.715 $\pm$ 0.0199	0.559 $\pm$ 0.0297	0.628 $\pm$ 0.0282	0.638 $\pm$ 0.0252	0.517 $\pm$ 0.0058	0.644 $\pm$ 0.0055
PRISM	0.709 $\pm$ 0.0103	0.563 $\pm$ 0.0106	0.633 $\pm$ 0.0252	0.651 $\pm$ 0.0238	0.552 $\pm$ 0.0149	0.677 $\pm$ 0.0142
Mean pool (CHIEF)	0.711 $\pm$ 0.0120	0.560 $\pm$ 0.0120	0.645 $\pm$ 0.0232	0.656 $\pm$ 0.0277	0.511 $\pm$ 0.0070	0.637 $\pm$ 0.0079
CHIEF	<u>0.730</u> $\pm$ 0.0249	0.565 $\pm$ 0.0155	0.644 $\pm$ 0.0174	0.673 $\pm$ 0.0039	0.541 $\pm$ 0.0253	0.667 $\pm$ 0.0253
Mean pool (CONCHv1.5)	0.709 $\pm$ 0.0290	0.568 $\pm$ 0.0142	0.647 $\pm$ 0.0296	0.669 $\pm$ 0.0201	0.559 $\pm$ 0.0360	0.684 $\pm$ 0.0360
TITAN _V	0.734 $\pm$ 0.0155	0.592 $\pm$ 0.0218	<u>0.651</u> $\pm$ 0.0195	0.686 $\pm$ 0.0140	<u>0.561</u> $\pm$ 0.0145	<u>0.686</u> $\pm$ 0.0128
TITAN	0.727 $\pm$ 0.0154	<u>0.586</u> $\pm$ 0.0158	0.661 $\pm$ 0.0147	<u>0.685</u> $\pm$ 0.0069	0.572 $\pm$ 0.0190	0.695 $\pm$ 0.0173

Supplementary Table 39: Linear probing results for SETD2 mutation ($C = 2$) prediction on MUT-HET-RCC. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.893 $\pm$ 0.0285	0.711 $\pm$ 0.0441	0.732 $\pm$ 0.0451	0.767 $\pm$ 0.0376	0.595 $\pm$ 0.0255	0.771 $\pm$ 0.0193
GigaPath	0.878 $\pm$ 0.0251	0.684 $\pm$ 0.0331	0.724 $\pm$ 0.0494	0.764 $\pm$ 0.0377	0.560 $\pm$ 0.0219	0.744 $\pm$ 0.0177
Mean pool (Virchow)	0.879 $\pm$ 0.0150	0.691 $\pm$ 0.0433	0.666 $\pm$ 0.0477	0.701 $\pm$ 0.0442	0.534 $\pm$ 0.0184	0.723 $\pm$ 0.0163
PRISM	0.901 $\pm$ 0.0365	0.748 $\pm$ 0.0535	0.779 $\pm$ 0.0456	0.792 $\pm$ 0.0348	0.727 $\pm$ 0.0168	0.843 $\pm$ 0.0132
Mean pool (CHIEF)	0.852 $\pm$ 0.0331	0.660 $\pm$ 0.0462	0.686 $\pm$ 0.0461	0.719 $\pm$ 0.0417	0.558 $\pm$ 0.0206	0.743 $\pm$ 0.0165
CHIEF	0.880 $\pm$ 0.0200	0.727 $\pm$ 0.0361	0.749 $\pm$ 0.0202	0.766 $\pm$ 0.0206	0.654 $\pm$ 0.0313	0.801 $\pm$ 0.0207
Mean pool (CONCHv1.5)	0.887 $\pm$ 0.0249	0.732 $\pm$ 0.0367	0.751 $\pm$ 0.0195	0.768 $\pm$ 0.0149	0.678 $\pm$ 0.0320	0.806 $\pm$ 0.0157
TITAN _V	<u>0.917</u> $\pm$ 0.0248	0.769 $\pm$ 0.0394	<u>0.800</u> $\pm$ 0.0230	0.813 $\pm$ 0.0239	<u>0.764</u> $\pm$ 0.0359	0.848 $\pm$ 0.0190
TITAN	0.920 $\pm$ 0.0191	<u>0.764</u> $\pm$ 0.0280	0.805 $\pm$ 0.0207	<u>0.802</u> $\pm$ 0.0263	0.775 $\pm$ 0.0451	<u>0.844</u> $\pm$ 0.0313

Supplementary Table 40: Linear probing results for ER ($C = 2$) prediction on BCNC. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.841 $\pm$ 0.0263	0.716 $\pm$ 0.0364	0.704 $\pm$ 0.0533	0.742 $\pm$ 0.0431	0.595 $\pm$ 0.0212	0.731 $\pm$ 0.0174
GigaPath	0.827 $\pm$ 0.0298	0.705 $\pm$ 0.0325	0.698 $\pm$ 0.0540	0.736 $\pm$ 0.0453	0.568 $\pm$ 0.0139	0.708 $\pm$ 0.0121
Mean pool (Virchow)	0.820 $\pm$ 0.0196	0.682 $\pm$ 0.0232	0.638 $\pm$ 0.0486	0.674 $\pm$ 0.0474	0.546 $\pm$ 0.0115	0.690 $\pm$ 0.0110
PRISM	0.844 $\pm$ 0.0322	0.734 $\pm$ 0.0279	0.730 $\pm$ 0.0345	0.749 $\pm$ 0.0257	0.714 $\pm$ 0.0325	<u>0.807</u> $\pm$ 0.0221
Mean pool (CHIEF)	0.808 $\pm$ 0.0441	0.697 $\pm$ 0.0392	0.657 $\pm$ 0.0535	0.694 $\pm$ 0.0475	0.563 $\pm$ 0.0106	0.705 $\pm$ 0.0107
CHIEF	0.824 $\pm$ 0.0362	0.713 $\pm$ 0.0196	0.717 $\pm$ 0.0299	0.738 $\pm$ 0.0235	0.654 $\pm$ 0.0292	0.770 $\pm$ 0.0206
Mean pool (CONCHv1.5)	0.821 $\pm$ 0.0400	0.699 $\pm$ 0.0467	0.703 $\pm$ 0.0398	0.727 $\pm$ 0.0279	0.659 $\pm$ 0.0451	0.764 $\pm$ 0.0358
TITAN _V	<u>0.856</u> $\pm$ 0.0378	0.741 $\pm$ 0.0332	<u>0.765</u> $\pm$ 0.0474	0.783 $\pm$ 0.0355	0.752 $\pm$ 0.0346	0.822 $\pm$ 0.0267
TITAN	0.857 $\pm$ 0.0336	<u>0.739</u> $\pm$ 0.0423	0.770 $\pm$ 0.0362	<u>0.775</u> $\pm$ 0.0282	<u>0.746</u> $\pm$ 0.0435	<u>0.807</u> $\pm$ 0.0337

Supplementary Table 41: Linear probing results for PR ($C = 2$) prediction on BCNC. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.745±0.0390	0.593±0.0322	0.631±0.0402	0.662±0.0198	0.538±0.0212	0.672±0.0209
GigaPath	0.725±0.0375	0.569±0.0355	0.620±0.0393	0.656±0.0215	0.528±0.0086	0.662±0.0103
Mean pool (Virchow)	0.722±0.0233	0.557±0.0170	0.589±0.0282	0.624±0.0304	0.514±0.0213	0.646±0.0230
PRISM	0.755±0.0268	0.615±0.0373	0.694±0.0326	0.727 ±0.0331	0.567±0.0094	0.699±0.0070
Mean pool (CHIEF)	0.695±0.0427	0.559±0.0260	0.590±0.0247	0.621±0.0198	0.518±0.0131	0.652±0.0149
CHIEF	0.702±0.0496	0.573±0.0264	0.637±0.0347	0.676±0.0302	0.533±0.0267	0.667±0.0246
Mean pool (CONCHv1.5)	0.731±0.0225	0.584±0.0335	0.632±0.0332	0.666±0.0172	0.558±0.0099	0.691±0.0083
TITAN _V	0.762 ±0.0242	<u>0.630</u> ±0.0141	<u>0.699</u> ±0.0154	<u>0.723</u> ±0.0121	<u>0.594</u> ±0.0167	<u>0.720</u> ±0.0110
TITAN	<u>0.761</u> ±0.0244	0.639 ±0.0420	0.703 ±0.0277	0.718±0.0202	0.612 ±0.0199	0.731 ±0.0160

Supplementary Table 42: Linear probing results for HER2 ($C = 2$) prediction on BCNC. The best result is marked in bold and the second best is underlined.

Encoder	Cohort	Logistic regression		SimpleShot		20-nearest neighbors	
		AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	TCGA	0.960±0.0255	0.886±0.0426	0.795±0.0258	0.813±0.0252	0.737±0.0105	0.747±0.0151
GigaPath	TCGA	0.956±0.0318	0.887±0.0432	0.783±0.0391	0.795±0.0440	0.723±0.0132	0.726±0.0219
Mean pool (Virchow)	TCGA	0.925±0.0499	0.851±0.0522	0.722±0.0626	0.725±0.0730	0.671±0.0119	0.692±0.0071
PRISM	TCGA	0.936±0.0253	0.851±0.0435	0.774±0.0731	0.776±0.0749	0.851±0.0040	0.854±0.0057
Mean pool (CHIEF)	TCGA	0.922±0.0197	0.819±0.0361	0.665±0.0224	0.690±0.0491	0.720±0.0137	0.735±0.0157
CHIEF	TCGA	0.932±0.0245	0.848±0.0332	0.704±0.0254	0.725±0.0477	0.765±0.0152	0.769±0.0217
Mean pool (CONCHv1.5)	TCGA	0.942±0.0256	0.865±0.0356	0.785±0.0462	0.788±0.0531	0.757±0.0070	0.783±0.0046
TITAN _V	TCGA	<u>0.966</u> ±0.0192	<u>0.896</u> ±0.0394	<u>0.851</u> ±0.0528	<u>0.864</u> ±0.0563	<u>0.867</u> ±0.0046	<u>0.871</u> ±0.0065
TITAN	TCGA	0.972 ±0.0237	0.919 ±0.0321	0.873 ±0.0521	0.880 ±0.0583	0.896 ±0.0047	0.899 ±0.0021
Mean pool (GigaPath)	EBRAINS	0.924±0.0074	0.838±0.0223	0.737±0.0447	0.753±0.0409	0.642±0.0288	0.574±0.0589
GigaPath	EBRAINS	0.916±0.0069	0.833±0.0144	0.744±0.0367	0.742±0.0364	0.659±0.0282	0.688±0.0269
Mean pool (Virchow)	EBRAINS	0.873±0.0196	0.788±0.0135	0.733±0.0111	0.729±0.0090	0.528±0.0079	0.298±0.0223
PRISM	EBRAINS	0.934±0.0085	<u>0.874</u> ±0.0100	0.814±0.0105	0.794±0.0143	0.821±0.0232	0.799±0.0339
Mean pool (CHIEF)	EBRAINS	0.908±0.0041	0.805±0.0310	0.729±0.0140	0.731±0.0090	0.680±0.0301	0.625±0.0487
CHIEF	EBRAINS	0.923±0.0068	0.836±0.0144	0.753±0.0103	0.748±0.0040	0.754±0.0259	0.724±0.0392
Mean pool (CONCHv1.5)	EBRAINS	0.892±0.0270	0.788±0.0306	0.761±0.0051	0.780±0.0039	0.760±0.0435	0.727±0.0727
TITAN _V	EBRAINS	<u>0.951</u> ±0.0044	0.848±0.0557	<u>0.874</u> ±0.0034	<u>0.875</u> ±0.0019	<u>0.877</u> ±0.0066	<u>0.875</u> ±0.0095
TITAN	EBRAINS	0.960 ±0.0026	0.908 ±0.0077	0.883 ±0.0023	0.881 ±0.0053	0.899 ±0.0044	0.893 ±0.0056

Supplementary Table 43: Linear probing results for Isocitrate dehydrogenase (IDH) mutation ($C = 2$) prediction on TCGA-GBMLGG and external dataset EBRAINS. The best result is marked in bold and the second best is underlined.

Encoder	Cohort	Logistic regression		SimpleShot		20-nearest neighbors	
		AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	TCGA	0.871±0.0499	0.734±0.0761	0.751±0.0543	0.758±0.0809	0.503±0.0069	0.602±0.0090
GigaPath	TCGA	0.877±0.0443	0.723±0.0615	0.744±0.0540	0.760±0.0855	0.525±0.0248	0.628±0.0307
Mean pool (Virchow)	TCGA	0.868±0.0543	0.707±0.0467	0.641±0.0658	0.648±0.1091	0.500±0.0000	0.597±0.0000
PRISM	TCGA	0.889 ±0.0425	<u>0.773</u> ±0.0385	0.800±0.0416	0.808±0.0383	0.650±0.0361	<u>0.745</u> ±0.0258
Mean pool (CHIEF)	TCGA	0.859±0.0467	0.703±0.0668	0.686±0.0301	0.708±0.0521	0.599±0.0169	0.702±0.0157
CHIEF	TCGA	<u>0.882</u> ±0.0403	0.759±0.0731	0.725±0.0366	0.738±0.0571	<u>0.692</u> ±0.0158	0.778 ±0.0100
Mean pool (CONCHv1.5)	TCGA	0.870±0.0494	0.756±0.0417	0.765±0.0616	0.782±0.0674	0.632±0.0390	0.717±0.0099
TITAN _V	TCGA	<u>0.882</u> ±0.0678	0.782 ±0.0486	0.815 ±0.0763	0.828 ±0.0761	0.657±0.0830	0.727±0.0390
TITAN	TCGA	0.878±0.0675	0.772±0.0656	<u>0.814</u> ±0.0605	<u>0.813</u> ±0.0588	0.759 ±0.0206	0.718±0.0446
Mean pool (GigaPath)	CPTAC	0.881 ±0.0266	0.618±0.0450	0.792 ±0.0140	0.813 ±0.0379	0.507±0.0084	0.606±0.0110
GigaPath	CPTAC	<u>0.873</u> ±0.0222	0.713±0.0352	<u>0.783</u> ±0.0230	<u>0.775</u> ±0.0515	0.555±0.0233	0.663±0.0266
Mean pool (Virchow)	CPTAC	0.860±0.0170	<u>0.750</u> ±0.0423	0.617±0.0521	0.660±0.0329	0.508±0.0152	0.607±0.0204
PRISM	CPTAC	0.852±0.0187	0.708±0.0554	0.743±0.0149	0.708±0.0397	0.568±0.0128	0.679±0.0128
Mean pool (CHIEF)	CPTAC	0.808±0.0128	0.664±0.0457	0.645±0.0184	0.528±0.0365	0.555±0.0207	0.665±0.0224
CHIEF	CPTAC	0.840±0.0125	0.686±0.0597	0.746±0.0157	0.738±0.0205	0.529±0.0112	0.636±0.0130
Mean pool (CONCHv1.5)	CPTAC	0.812±0.0554	0.765 ±0.0424	0.603±0.0061	0.386±0.0132	0.510±0.0084	0.611±0.0110
TITAN _V	CPTAC	0.832±0.0249	0.685±0.0548	0.670±0.0182	0.541±0.0310	<u>0.591</u> ±0.0266	<u>0.699</u> ±0.0252
TITAN	CPTAC	0.838±0.0284	0.735±0.0315	0.690±0.0109	0.571±0.0241	0.776 ±0.0167	0.757 ±0.0082

Supplementary Table 44: Linear probing results for ER ($C = 2$) prediction on TCGA-BRCA and external dataset CPTAC-BRCA. The best result is marked in bold and the second best is underlined.

Encoder	Cohort	Logistic regression		SimpleShot		20-nearest neighbors	
		AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	TCGA	0.791±0.0396	0.688±0.0509	0.685±0.0420	0.686±0.0530	0.536±0.0268	0.553±0.0406
GigaPath	TCGA	0.793±0.0495	0.705±0.0499	0.686±0.0356	0.693±0.0460	0.563±0.0314	0.594±0.0454
Mean pool (Virchow)	TCGA	0.779±0.0394	0.692±0.0364	0.598±0.0665	0.587±0.1042	0.510±0.0137	0.515±0.0235
PRISM	TCGA	0.808 ±0.0403	0.725±0.0341	<u>0.739</u> ±0.0487	<u>0.749</u> ±0.0465	0.643±0.0216	0.655±0.0220
Mean pool (CHIEF)	TCGA	0.762±0.0513	0.668±0.0329	0.644±0.0401	0.653±0.0478	<u>0.667</u> ±0.0456	<u>0.707</u> ±0.0396
CHIEF	TCGA	<u>0.807</u> ±0.0413	0.728 ±0.0288	0.673±0.0277	0.685±0.0315	0.702 ±0.0401	0.741 ±0.0293
Mean pool (CONCHv1.5)	TCGA	0.778±0.0528	0.692±0.0457	0.687±0.0546	0.699±0.0853	0.615±0.0280	0.657±0.0237
TITAN _V	TCGA	0.802±0.0436	<u>0.727</u> ±0.0368	0.735±0.0631	0.752 ±0.0824	0.630±0.0334	0.646±0.0251
TITAN	TCGA	0.785±0.0609	0.703±0.0335	0.745 ±0.0498	0.747±0.0643	0.659±0.0186	0.608±0.0220
Mean pool (GigaPath)	CPTAC	0.784±0.0119	0.561±0.0453	0.738 ±0.0296	0.771 ±0.0163	0.541±0.0269	0.562±0.0386
GigaPath	CPTAC	0.777±0.0217	0.667±0.0378	<u>0.733</u> ±0.0284	<u>0.733</u> ±0.0526	0.568±0.0361	0.601±0.0468
Mean pool (Virchow)	CPTAC	0.773±0.0098	<u>0.702</u> ±0.0363	0.584±0.0423	0.573±0.0685	0.527±0.0340	0.541±0.0513
PRISM	CPTAC	<u>0.799</u> ±0.0162	0.713 ±0.0164	0.627±0.0208	0.528±0.0374	0.635±0.0464	<u>0.683</u> ±0.0453
Mean pool (CHIEF)	CPTAC	<u>0.799</u> ±0.0161	0.651±0.0397	0.592±0.0288	0.443±0.0585	0.542±0.0145	0.568±0.0240
CHIEF	CPTAC	0.804 ±0.0145	0.686±0.0400	0.679±0.0087	0.653±0.0143	0.549±0.0270	0.579±0.0329
Mean pool (CONCHv1.5)	CPTAC	0.746±0.0371	0.695±0.0632	0.544±0.0079	0.329±0.0177	0.534±0.0173	0.560±0.0195
TITAN _V	CPTAC	0.754±0.0222	0.692±0.0442	0.541±0.0132	0.387±0.0302	<u>0.666</u> ±0.0382	0.712 ±0.0343
TITAN	CPTAC	0.755±0.0230	0.677±0.0235	0.597±0.0174	0.476±0.0302	0.679 ±0.0309	0.655±0.0341

Supplementary Table 45: Linear probing results for PR ($C = 2$) prediction on TCGA-BRCA and external dataset CPTAC-BRCA. The best result is marked in bold and the second best is underlined.

Encoder	Cohort	Logistic regression		SimpleShot		20-nearest neighbors	
		AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	TCGA	0.643±0.0608	0.509±0.0176	0.581±0.0620	0.652±0.0428	0.500±0.0000	0.815±0.0000
GigaPath	TCGA	0.635±0.0339	0.497±0.0039	0.557±0.0346	0.629±0.0509	0.492±0.0057	0.808±0.0050
Mean pool (Virchow)	TCGA	0.522±0.0475	0.500±0.0000	0.484±0.0348	0.594±0.0931	0.500±0.0000	0.815±0.0000
PRISM	TCGA	0.687 ±0.0309	0.547 ±0.0362	0.604 ±0.0230	0.652±0.0418	0.556 ±0.0373	0.830 ±0.0119
Mean pool (CHIEF)	TCGA	0.649±0.0382	0.510±0.0280	0.565±0.0424	0.633±0.0716	0.500±0.0000	0.815±0.0000
CHIEF	TCGA	0.659±0.0305	0.514±0.0371	0.548±0.0346	0.636±0.0965	0.500±0.0000	0.815±0.0000
Mean pool (CONCHv1.5)	TCGA	0.628±0.0160	0.502±0.0074	0.582±0.0764	0.605±0.0432	0.498±0.0027	0.813±0.0024
TITAN _V	TCGA	0.657±0.0363	0.513±0.0389	<u>0.599</u> ±0.0272	0.660 ±0.0557	0.502±0.0266	0.810±0.0105
TITAN	TCGA	<u>0.661</u> ±0.0324	<u>0.529</u> ±0.0318	0.598±0.0570	<u>0.657</u> ±0.0635	<u>0.504</u> ±0.0145	<u>0.816</u> ±0.0078
Mean pool (GigaPath)	CPTAC	0.625±0.0185	0.534±0.0438	0.535±0.0247	0.180±0.1111	0.491±0.0134	0.793±0.0214
GigaPath	CPTAC	0.623±0.0629	<u>0.554</u> ±0.0640	0.516±0.0349	0.210±0.1196	0.500±0.0000	0.815±0.0000
Mean pool (Virchow)	CPTAC	0.512±0.0292	0.495±0.0094	0.501±0.0275	0.249±0.1759	0.498±0.0176	0.806±0.0105
PRISM	CPTAC	<u>0.717</u> ±0.0264	0.555 ±0.0821	0.649 ±0.0243	<u>0.449</u> ±0.0737	0.521 ±0.0112	0.822 ±0.0056
Mean pool (CHIEF)	CPTAC	0.505±0.0450	0.500±0.0030	0.445±0.0312	0.406±0.0976	0.500±0.0000	0.815±0.0000
CHIEF	CPTAC	0.606±0.0319	0.523±0.0548	0.496±0.0317	0.544 ±0.1194	0.500±0.0000	0.815±0.0000
Mean pool (CONCHv1.5)	CPTAC	0.582±0.0718	0.508±0.0095	0.480±0.0271	0.298±0.1414	<u>0.511</u> ±0.0357	0.816±0.0216
TITAN _V	CPTAC	0.755 ±0.0348	0.534±0.0775	0.576±0.0549	0.299±0.1709	<u>0.511</u> ±0.0226	<u>0.820</u> ±0.0142
TITAN	CPTAC	0.669±0.0463	0.544±0.1170	<u>0.617</u> ±0.0282	0.397±0.0564	0.499±0.0022	0.814±0.0019

Supplementary Table 46: Linear probing results for HER2 ($C = 2$) prediction on TCGA-BRCA and external dataset CPTAC-BRCA. The best result is marked in bold and the second best is underlined.

Encoder	Cohort	Logistic regression		SimpleShot		5-nearest neighbors	
		AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	TCGA	0.597±0.0319	0.507±0.0110	0.546±0.0183	0.577±0.0178	0.477±0.0149	0.525±0.0154
GigaPath	TCGA	0.597±0.0392	0.504±0.0129	0.558±0.0294	0.583±0.0267	0.497±0.0092	0.547±0.0178
Mean pool (Virchow)	TCGA	0.597±0.0290	0.508±0.0112	0.557±0.0390	0.590±0.0224	0.493±0.0429	0.546±0.0465
PRISM	TCGA	0.656 ±0.0292	0.543 ±0.0299	0.603±0.0186	0.614±0.0252	0.525±0.0132	0.576±0.0137
Mean pool (CHIEF)	TCGA	0.587±0.0400	0.502±0.0081	0.576±0.0223	0.589±0.0318	0.509±0.0234	0.562±0.0224
CHIEF	TCGA	0.632±0.0289	<u>0.522</u> ±0.0187	0.606±0.0166	<u>0.615</u> ±0.0156	0.492±0.0316	0.546±0.0340
Mean pool (CONCHv1.5)	TCGA	0.615±0.0569	0.503±0.0124	0.593±0.0355	0.587±0.0382	0.515±0.0285	0.556±0.0145
TITAN _V	TCGA	0.636±0.0582	0.505±0.0134	<u>0.609</u> ±0.0472	0.605±0.0250	<u>0.537</u> ±0.0159	0.573±0.0278
TITAN	TCGA	<u>0.645</u> ±0.0545	0.513±0.0140	0.619 ±0.0395	0.620 ±0.0193	0.560 ±0.0207	0.605 ±0.0199
Mean pool (GigaPath)	CPTAC	0.639±0.0222	0.500±0.0000	<u>0.564</u> ±0.0296	0.613±0.0320	0.497±0.0116	0.551±0.0114
GigaPath	CPTAC	0.651±0.0145	0.499±0.0030	0.573 ±0.0297	0.620 ±0.0324	<u>0.556</u> ±0.0096	0.603 ±0.0111
Mean pool (Virchow)	CPTAC	0.652±0.0162	0.509 ±0.0227	0.554±0.0336	0.602±0.0384	0.486±0.0061	0.512±0.0056
PRISM	CPTAC	0.619±0.0271	0.503±0.0056	0.506±0.0088	0.529±0.0133	0.532±0.0078	0.579±0.0089
Mean pool (CHIEF)	CPTAC	0.620±0.0162	0.503±0.0051	0.517±0.0186	0.559±0.0268	0.456±0.0220	0.507±0.0221
CHIEF	CPTAC	0.639±0.0206	0.503±0.0050	0.541±0.0125	0.590±0.0154	0.562 ±0.0325	<u>0.602</u> ±0.0280
Mean pool (CONCHv1.5)	CPTAC	0.637±0.0197	0.499±0.0030	0.531±0.0110	0.570±0.0169	0.508±0.0168	0.519±0.0217
TITAN _V	CPTAC	0.699 ±0.0136	<u>0.507</u> ±0.0133	0.547±0.0218	0.592±0.0290	0.477±0.0363	0.449±0.0309
TITAN	CPTAC	<u>0.693</u> ±0.0150	0.506±0.0111	<u>0.564</u> ±0.0223	<u>0.619</u> ±0.0229	0.521±0.0215	0.575±0.0223

Supplementary Table 47: Linear probing results for PIK3CA ($C = 2$) prediction on TCGA-BRCA and external dataset CPTAC-BRCA. The best result is marked in bold and the second best is underlined.

Encoder	Cohort	Logistic regression		SimpleShot		5-nearest neighbors	
		AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	TCGA	0.638±0.0945	0.509 ±0.0175	0.565±0.0733	0.708±0.0464	0.530±0.0135	0.551±0.0213
GigaPath	TCGA	0.656±0.1019	0.499±0.0025	0.557±0.0908	0.698±0.0534	0.520±0.0183	0.539±0.0305
Mean pool (Virchow)	TCGA	0.628±0.0470	0.498±0.0049	0.544±0.0747	0.658±0.0779	0.524±0.0188	0.539±0.0286
PRISM	TCGA	<u>0.716</u> ±0.0764	0.500±0.0000	0.608±0.0738	0.703±0.0243	0.593 ±0.0124	0.636 ±0.0147
Mean pool (CHIEF)	TCGA	0.641±0.0577	0.496±0.0074	0.584±0.0741	0.696±0.0447	0.516±0.0207	0.534±0.0325
CHIEF	TCGA	0.675±0.0286	0.496±0.0049	0.630±0.0727	0.731 ±0.0374	0.544±0.0365	0.576±0.0442
Mean pool (CONCHv1.5)	TCGA	0.714±0.0404	0.499±0.0025	0.644±0.0996	0.706±0.0271	0.552±0.0261	0.580±0.0356
TITAN _V	TCGA	0.721 ±0.0510	0.500±0.0000	0.672 ±0.0215	<u>0.725</u> ±0.0231	0.572±0.0176	0.607±0.0236
TITAN	TCGA	0.700±0.0670	<u>0.508</u> ±0.0167	<u>0.661</u> ±0.0772	0.717±0.0262	<u>0.589</u> ±0.0212	<u>0.628</u> ±0.0283
Mean pool (GigaPath)	CPTAC	0.780±0.0365	0.526 ±0.0281	<u>0.726</u> ±0.0329	0.759 ±0.0322	0.614 ±0.0195	0.661 ±0.0210
GigaPath	CPTAC	0.787±0.0368	<u>0.521</u> ±0.0264	0.718±0.0274	<u>0.753</u> ±0.0233	0.553±0.0180	0.582±0.0250
Mean pool (Virchow)	CPTAC	0.697±0.0509	0.506±0.0164	0.593±0.0545	0.541±0.1452	0.517±0.0404	0.532±0.0615
PRISM	CPTAC	0.796±0.0101	0.500±0.0000	0.665±0.0116	0.680±0.0143	<u>0.608</u> ±0.0593	<u>0.636</u> ±0.0601
Mean pool (CHIEF)	CPTAC	0.730±0.0209	0.513±0.0256	0.679±0.0035	0.705±0.0076	0.533±0.0281	0.566±0.0355
CHIEF	CPTAC	0.731±0.0041	0.515±0.0150	0.653±0.0215	0.668±0.0180	0.547±0.0173	0.583±0.0176
Mean pool (CONCHv1.5)	CPTAC	0.764±0.0249	0.513±0.0140	0.697±0.0081	0.736±0.0087	0.526±0.0081	0.539±0.0124
TITAN _V	CPTAC	<u>0.806</u> ±0.0234	0.503±0.0051	0.711±0.0092	0.742±0.0092	0.587±0.0274	0.625±0.0339
TITAN	CPTAC	0.815 ±0.0252	0.505±0.0103	0.727 ±0.0168	0.748±0.0129	0.516±0.0207	0.525±0.0304

Supplementary Table 48: Linear probing results for epidermal growth factor receptor (EGFR) ($C = 2$) prediction on TCGA-NSCLC and external dataset CPTAC-LUAD. The best result is marked in bold and the second best is underlined.

Encoder	Cohort	Logistic regression		SimpleShot		20-nearest neighbors	
		AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	TCGA	0.763±0.0522	0.693±0.0390	0.652±0.0200	0.649±0.0203	0.653±0.0227	0.657±0.0249
GigaPath	TCGA	0.738±0.0372	0.670±0.0371	0.639±0.0240	0.634±0.0271	0.610±0.0305	0.613±0.0366
Mean pool (Virchow)	TCGA	0.702±0.0687	0.642±0.0535	0.564±0.0176	0.553±0.0207	0.603±0.0224	0.593±0.0406
PRISM	TCGA	0.765 ±0.0875	0.706 ±0.0708	0.677±0.0706	0.678±0.0704	0.658±0.0239	0.666±0.0229
Mean pool (CHIEF)	TCGA	0.722±0.0584	0.660±0.0692	0.641±0.0439	0.638±0.0486	0.616±0.0363	0.628±0.0347
CHIEF	TCGA	0.757±0.0481	0.690±0.0407	0.666±0.0631	0.665±0.0683	0.601±0.0195	0.616±0.0182
Mean pool (CONCHv1.5)	TCGA	0.734±0.0784	0.663±0.0508	<u>0.682</u> ±0.0549	<u>0.680</u> ±0.0553	0.625±0.0178	0.640±0.0188
TITAN _V	TCGA	0.765 ±0.0589	<u>0.702</u> ±0.0487	0.683 ±0.0515	0.682 ±0.0501	0.710 ±0.0239	0.719 ±0.0233
TITAN	TCGA	0.758±0.0628	0.699±0.0535	0.671±0.0491	0.671±0.0493	<u>0.662</u> ±0.0094	0.664±0.0093
Mean pool (GigaPath)	CPTAC	0.751±0.0174	0.670±0.0301	<u>0.686</u> ±0.0109	<u>0.690</u> ±0.0070	0.607±0.0152	0.606±0.0170
GigaPath	CPTAC	0.752±0.0093	0.677±0.0248	0.684±0.0159	<u>0.690</u> ±0.0217	0.634±0.0176	0.655±0.0181
Mean pool (Virchow)	CPTAC	0.728±0.0176	0.629±0.0429	0.556±0.0617	0.407±0.1610	0.572±0.0422	0.530±0.0883
PRISM	CPTAC	<u>0.756</u> ±0.0056	<u>0.693</u> ±0.0222	0.668±0.0091	0.671±0.0105	0.692 ±0.0156	0.712 ±0.0150
Mean pool (CHIEF)	CPTAC	0.675±0.0163	0.625±0.0237	0.618±0.0170	0.620±0.0167	0.558±0.0106	0.578±0.0104
CHIEF	CPTAC	0.714±0.0307	0.647±0.0329	0.615±0.0195	0.610±0.0207	0.565±0.0134	0.578±0.0163
Mean pool (CONCHv1.5)	CPTAC	0.738±0.0204	0.669±0.0285	0.714 ±0.0122	0.729 ±0.0118	0.606±0.0105	0.622±0.0134
TITAN _V	CPTAC	0.787 ±0.0126	0.713 ±0.0148	0.679±0.0017	0.686±0.0004	<u>0.670</u> ±0.0208	<u>0.689</u> ±0.0204
TITAN	CPTAC	0.728±0.0088	0.689±0.0137	0.669±0.0048	0.673±0.0045	0.667±0.0289	0.687±0.0268

Supplementary Table 49: Linear probing results for *TP53* mutation ($C = 2$) prediction on TCGA-NSCLC and external dataset CPTAC-LUAD. The best result is marked in bold and the second best is underlined.

Encoder	Cohort	Logistic regression		SimpleShot		5-nearest neighbors	
		AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	TCGA	0.906 ±0.0328	0.712 ±0.0843	<u>0.780</u> ±0.0388	<u>0.827</u> ±0.0681	0.542±0.0236	0.708±0.0214
GigaPath	TCGA	0.890±0.0428	0.687±0.0861	0.750±0.0370	0.800±0.0603	0.585±0.0344	0.735±0.0251
Mean pool (Virchow)	TCGA	0.795±0.0480	0.557±0.0476	0.602±0.0944	0.617±0.1341	0.550±0.0145	0.703±0.0183
PRISM	TCGA	<u>0.893</u> ±0.0440	0.695±0.0459	0.694±0.0400	0.703±0.0895	0.601 ±0.0398	0.758 ±0.0358
Mean pool (CHIEF)	TCGA	0.829±0.0586	0.598±0.0562	0.614±0.0248	0.670±0.1197	<u>0.597</u> ±0.0294	0.706±0.0372
CHIEF	TCGA	0.873±0.0403	0.655±0.0850	0.740±0.0765	0.748±0.1431	0.581±0.0276	0.686±0.0202
Mean pool (CONCHv1.5)	TCGA	0.797±0.0296	0.566±0.0624	0.701±0.0260	0.751±0.0252	0.535±0.0186	0.703±0.0177
TITAN _V	TCGA	0.859±0.0507	0.712 ±0.0439	0.728±0.0520	0.780±0.0612	0.574±0.0282	<u>0.737</u> ±0.0255
TITAN	TCGA	0.872±0.0551	<u>0.700</u> ±0.0730	0.800 ±0.0581	0.831 ±0.0480	0.549±0.0114	0.713±0.0093
Mean pool (GigaPath)	CPTAC	0.890 ±0.0274	0.557±0.0360	0.818 ±0.0277	0.828 ±0.0320	<u>0.561</u> ±0.0197	<u>0.725</u> ±0.0177
GigaPath	CPTAC	<u>0.870</u> ±0.0474	0.553±0.0344	0.732±0.0430	0.693±0.0885	0.544±0.0380	0.703±0.0308
Mean pool (Virchow)	CPTAC	0.771±0.0677	0.681 ±0.0648	0.530±0.0033	0.189±0.0122	0.508±0.0224	0.585±0.0525
PRISM	CPTAC	0.830±0.0122	0.615±0.0314	0.592±0.0220	0.450±0.0860	0.535±0.0138	0.703±0.0131
Mean pool (CHIEF)	CPTAC	0.802±0.0423	0.646±0.0516	0.556±0.0336	0.290±0.0996	0.542±0.0161	0.703±0.0152
CHIEF	CPTAC	0.857±0.0234	0.609±0.0631	0.591±0.0520	0.389±0.1169	0.595 ±0.0261	0.749 ±0.0198
Mean pool (CONCHv1.5)	CPTAC	0.793±0.0275	<u>0.676</u> ±0.0621	0.636±0.0227	0.540±0.0836	0.550±0.0165	0.704±0.0288
TITAN _V	CPTAC	0.830±0.0337	0.614±0.0472	0.676±0.0369	0.678±0.0871	0.543±0.0159	0.710±0.0143
TITAN	CPTAC	0.828±0.0287	0.653±0.0302	<u>0.771</u> ±0.0105	<u>0.745</u> ±0.0238	0.545±0.0254	0.707±0.0237

Supplementary Table 50: Linear probing results for microsatellite instability (MSI) high ($C = 2$) prediction on TCGA-CRC and external dataset CPTAC-COAD. The best result is marked in bold and the second best is underlined.

Encoder	Cohort	Logistic regression		SimpleShot		5-nearest neighbors	
		AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	TCGA	0.761±0.0916	0.515±0.0188	0.657±0.0818	0.566±0.2283	0.473±0.0183	0.746±0.0156
GigaPath	TCGA	0.724±0.1200	0.506±0.0164	0.596±0.0812	0.530±0.2415	0.513±0.0069	0.773±0.0074
Mean pool (Virchow)	TCGA	0.630±0.1246	0.500±0.0000	0.529±0.0550	0.422±0.2608	0.559±0.0328	0.797±0.0262
PRISM	TCGA	0.764±0.0719	<u>0.532</u> ±0.0434	0.631±0.0604	0.634±0.1285	0.566±0.0284	0.803±0.0210
Mean pool (CHIEF)	TCGA	0.698±0.0901	0.521±0.0354	0.542±0.0633	0.387±0.3078	0.614 ±0.0727	0.780±0.0438
CHIEF	TCGA	0.752±0.0874	0.523±0.0498	0.609±0.0445	0.557±0.1888	0.560±0.0342	0.745±0.0285
Mean pool (CONCHv1.5)	TCGA	0.724±0.0771	0.513±0.0180	0.649±0.0843	0.611±0.1636	0.565±0.0088	0.816±0.0035
TITAN _V	TCGA	<u>0.800</u> ±0.0731	0.516±0.0439	<u>0.658</u> ±0.0323	<u>0.694</u> ±0.0701	<u>0.595</u> ±0.0377	0.826 ±0.0216
TITAN	TCGA	0.817 ±0.0717	0.542 ±0.0343	0.770 ±0.0413	0.771 ±0.0502	0.581±0.0187	<u>0.819</u> ±0.0106
Mean pool (GigaPath)	CPTAC	0.697 ±0.0451	0.547±0.0535	0.538±0.0494	0.349±0.1680	0.521±0.0156	0.782±0.0068
GigaPath	CPTAC	0.675±0.0593	0.552±0.0667	0.482±0.0216	0.255±0.1239	0.493±0.0127	0.754±0.0214
Mean pool (Virchow)	CPTAC	0.604±0.0351	0.510±0.0204	0.543±0.0144	0.255±0.1432	0.512±0.0496	0.752±0.0489
PRISM	CPTAC	0.660±0.0243	<u>0.571</u> ±0.0275	<u>0.597</u> ±0.0554	0.461±0.1346	0.490±0.0183	0.761±0.0135
Mean pool (CHIEF)	CPTAC	0.620±0.0485	0.563±0.0584	0.501±0.0108	0.065±0.0139	<u>0.583</u> ±0.0608	0.797±0.0123
CHIEF	CPTAC	<u>0.687</u> ±0.0384	0.549±0.0502	0.507±0.0043	0.065±0.0144	0.598 ±0.0414	0.820 ±0.0235
Mean pool (CONCHv1.5)	CPTAC	0.647±0.0442	0.602 ±0.0598	0.512±0.0133	0.372±0.1000	0.504±0.0218	0.775±0.0167
TITAN _V	CPTAC	0.636±0.0361	0.566±0.0390	0.569±0.0372	0.586 ±0.1379	0.497±0.0028	0.771±0.0024
TITAN	CPTAC	0.624±0.0402	0.555±0.0254	0.622 ±0.0232	<u>0.556</u> ±0.0429	0.570±0.0296	<u>0.805</u> ±0.0206

Supplementary Table 51: Linear probing results for *BRAF* mutation ($C = 2$) prediction on TCGA-CRC and external dataset CPTAC-COAD. The best result is marked in bold and the second best is underlined.

Encoder	Cohort	Logistic regression		SimpleShot		20-nearest neighbors	
		AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	TCGA	<u>0.605</u> ±0.0604	<u>0.567</u> ±0.0377	0.510±0.0481	0.383±0.1048	0.497±0.0065	0.480±0.0187
GigaPath	TCGA	0.569±0.0359	0.552±0.0425	0.521±0.0457	0.401±0.1042	0.518±0.0450	0.504±0.0446
Mean pool (Virchow)	TCGA	0.509±0.1003	0.508±0.0166	0.506±0.0403	0.392±0.1362	0.484±0.0120	0.472±0.0265
PRISM	TCGA	0.555±0.0445	0.535±0.0320	0.529±0.0426	0.461±0.0905	0.509±0.0294	<u>0.533</u> ±0.0309
Mean pool (CHIEF)	TCGA	0.575±0.0731	0.510±0.0149	0.528±0.0490	0.411±0.1003	0.495±0.0205	0.501±0.0324
CHIEF	TCGA	0.603±0.0701	0.534±0.0468	0.529±0.0521	0.432±0.0868	0.536 ±0.0368	0.553 ±0.0507
Mean pool (CONCHv1.5)	TCGA	0.573±0.0267	0.561±0.0222	<u>0.531</u> ±0.0293	<u>0.478</u> ±0.1036	0.512±0.0299	0.501±0.0490
TITAN _V	TCGA	0.601±0.0315	0.537±0.0220	0.535 ±0.0473	0.501 ±0.0848	0.520±0.0391	0.503±0.0643
TITAN	TCGA	0.630 ±0.0710	0.569 ±0.0560	0.530±0.0440	0.464±0.0984	<u>0.522</u> ±0.0357	0.553 ±0.0366
Mean pool (GigaPath)	CPTAC	0.561±0.0375	0.507±0.0233	0.539±0.0256	0.464±0.0595	0.469±0.0543	0.460±0.0337
GigaPath	CPTAC	0.590±0.0295	0.520±0.0259	0.531±0.0219	0.447±0.1018	0.507±0.0133	0.494±0.0259
Mean pool (Virchow)	CPTAC	0.517±0.0795	0.498±0.0034	0.490±0.0073	0.485±0.0244	0.481±0.0137	0.468±0.0127
PRISM	CPTAC	0.616±0.0508	0.532 ±0.0338	0.528±0.0282	0.544±0.0225	0.503±0.0202	0.511±0.0210
Mean pool (CHIEF)	CPTAC	0.646±0.0376	0.501±0.0021	0.593±0.0154	0.565±0.0603	0.497±0.0160	0.511±0.0184
CHIEF	CPTAC	<u>0.659</u> ±0.0182	0.502±0.0034	0.593±0.0359	0.561±0.0662	0.508±0.0150	0.503±0.0323
Mean pool (CONCHv1.5)	CPTAC	0.641±0.0681	0.525±0.0208	0.664 ±0.0554	<u>0.618</u> ±0.0957	0.532 ±0.0052	0.535±0.0171
TITAN _V	CPTAC	0.675 ±0.0350	0.532 ±0.0176	<u>0.626</u> ±0.0147	0.654 ±0.0107	<u>0.526</u> ±0.0206	<u>0.542</u> ±0.0283
TITAN	CPTAC	0.625±0.0192	<u>0.526</u> ±0.0252	0.558±0.0126	0.460±0.0599	0.513±0.0377	0.547 ±0.0372

Supplementary Table 52: Linear probing results for *KRAS* mutation ($C = 2$) prediction on TCGA-CRC and external dataset CPTAC-COAD. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Cohen's κ	Bal. acc.	Cohen's κ	Bal. acc.	Cohen's κ	Bal. acc.
Mean pool (GigaPath)	0.555 $\pm$ 0.0558	0.364 $\pm$ 0.0331	0.373 $\pm$ 0.0655	0.330 $\pm$ 0.0338	0.283 $\pm$ 0.0683	0.269 $\pm$ 0.0303
GigaPath	0.462 $\pm$ 0.0583	0.311 $\pm$ 0.0310	0.354 $\pm$ 0.0666	0.314 $\pm$ 0.0329	0.270 $\pm$ 0.0686	0.290 $\pm$ 0.0309
Mean pool (Virchow)	0.432 $\pm$ 0.0637	0.294 $\pm$ 0.0297	0.124 $\pm$ 0.0704	0.194 $\pm$ 0.0267	0.081 $\pm$ 0.0704	0.233 $\pm$ 0.0306
PRISM	<u>0.708</u> $\pm$ 0.0410	0.389 $\pm$ 0.0329	0.671 $\pm$ 0.0396	0.385 $\pm$ 0.0338	0.653 $\pm$ 0.0440	0.377 $\pm$ 0.0303
Mean pool (CHIEF)	0.533 $\pm$ 0.0523	0.316 $\pm$ 0.0319	0.339 $\pm$ 0.0636	0.297 $\pm$ 0.0289	0.321 $\pm$ 0.0646	0.285 $\pm$ 0.0299
CHIEF	0.662 $\pm$ 0.0449	0.379 $\pm$ 0.0331	0.462 $\pm$ 0.0644	0.343 $\pm$ 0.0314	0.492 $\pm$ 0.0596	0.352 $\pm$ 0.0306
Mean pool (CONCHv1.5)	0.442 $\pm$ 0.0594	0.344 $\pm$ 0.0320	0.383 $\pm$ 0.0652	0.285 $\pm$ 0.0317	0.388 $\pm$ 0.0641	0.256 $\pm$ 0.0291
TITAN _V	0.723 $\pm$ 0.0390	0.425 $\pm$ 0.0345	0.585 $\pm$ 0.0540	<u>0.365</u> $\pm$ 0.0325	<u>0.618</u> $\pm$ 0.0492	0.342 $\pm$ 0.0306
TITAN	0.702 $\pm$ 0.0423	<u>0.394</u> $\pm$ 0.0328	<u>0.631</u> $\pm$ 0.0430	0.329 $\pm$ 0.0330	0.613 $\pm$ 0.0482	0.377 $\pm$ 0.0347

Supplementary Table 53: Linear probing results for ER expression level ($C = 6$) prediction on MGH-BRCA. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Cohen's κ	Bal. acc.	Cohen's κ	Bal. acc.	Cohen's κ	Bal. acc.
Mean pool (GigaPath)	0.538 $\pm$ 0.0555	0.307 $\pm$ 0.0307	0.458 $\pm$ 0.0540	0.259 $\pm$ 0.0291	0.414 $\pm$ 0.0637	0.244 $\pm$ 0.0310
GigaPath	0.560 $\pm$ 0.0514	0.306 $\pm$ 0.0298	0.451 $\pm$ 0.0576	0.247 $\pm$ 0.0293	0.310 $\pm$ 0.0693	0.215 $\pm$ 0.0281
Mean pool (Virchow)	0.443 $\pm$ 0.0622	0.247 $\pm$ 0.0277	0.137 $\pm$ 0.0694	0.221 $\pm$ 0.0279	0.172 $\pm$ 0.0683	0.165 $\pm$ 0.0242
PRISM	0.594 $\pm$ 0.0502	0.345 $\pm$ 0.0327	0.536 $\pm$ 0.0527	<u>0.359</u> $\pm$ 0.0320	0.556 $\pm$ 0.0505	<u>0.350</u> $\pm$ 0.0311
Mean pool (CHIEF)	0.536 $\pm$ 0.0575	0.350 $\pm$ 0.0315	0.393 $\pm$ 0.0575	0.263 $\pm$ 0.0277	0.408 $\pm$ 0.0598	0.264 $\pm$ 0.0309
CHIEF	0.674 $\pm$ 0.0478	0.417 $\pm$ 0.0341	0.543 $\pm$ 0.0534	0.331 $\pm$ 0.0300	0.565 $\pm$ 0.0551	0.349 $\pm$ 0.0305
Mean pool (CONCHv1.5)	0.582 $\pm$ 0.0512	0.330 $\pm$ 0.0320	0.414 $\pm$ 0.0552	0.234 $\pm$ 0.0295	0.462 $\pm$ 0.0548	0.256 $\pm$ 0.0287
TITAN _V	0.767 $\pm$ 0.0375	0.476 $\pm$ 0.0329	0.694 $\pm$ 0.0408	0.381 $\pm$ 0.0318	0.632 $\pm$ 0.0471	0.357 $\pm$ 0.0314
TITAN	<u>0.731</u> $\pm$ 0.0361	<u>0.418</u> $\pm$ 0.0318	<u>0.544</u> $\pm$ 0.0512	0.336 $\pm$ 0.0313	<u>0.578</u> $\pm$ 0.0465	0.311 $\pm$ 0.0305

Supplementary Table 54: Linear probing results for PR expression level ($C = 6$) prediction on MGH-BRCA. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Cohen's κ	Bal. acc.	Cohen's κ	Bal. acc.	Cohen's κ	Bal. acc.
Mean pool (GigaPath)	<u>0.656</u> $\pm$ 0.0811	0.565 $\pm$ 0.0458	0.338 $\pm$ 0.1831	0.421 $\pm$ 0.0491	0.305 $\pm$ 0.0784	0.430 $\pm$ 0.0367
GigaPath	0.620 $\pm$ 0.0685	0.554 $\pm$ 0.0419	0.444 $\pm$ 0.1551	0.440 $\pm$ 0.0433	0.380 $\pm$ 0.1876	0.471 $\pm$ 0.1059
Mean pool (Virchow)	0.599 $\pm$ 0.0861	0.581 $\pm$ 0.0383	0.477 $\pm$ 0.0712	0.493 $\pm$ 0.0538	0.401 $\pm$ 0.0926	0.476 $\pm$ 0.0518
PRISM	0.614 $\pm$ 0.1431	0.578 $\pm$ 0.0747	0.569 $\pm$ 0.1208	0.583 $\pm$ 0.0652	0.543 $\pm$ 0.1391	0.579 $\pm$ 0.0670
Mean pool (CHIEF)	0.596 $\pm$ 0.1373	0.583 $\pm$ 0.0765	0.411 $\pm$ 0.1530	0.481 $\pm$ 0.0785	0.354 $\pm$ 0.1347	0.461 $\pm$ 0.0673
CHIEF	0.549 $\pm$ 0.1125	0.579 $\pm$ 0.0423	0.326 $\pm$ 0.1146	0.466 $\pm$ 0.0782	0.310 $\pm$ 0.1045	0.474 $\pm$ 0.0528
Mean pool (CONCHv1.5)	0.621 $\pm$ 0.0748	0.578 $\pm$ 0.0450	0.485 $\pm$ 0.1483	0.480 $\pm$ 0.0742	0.364 $\pm$ 0.0905	0.458 $\pm$ 0.0554
TITAN _V	0.716 $\pm$ 0.0453	0.620 $\pm$ 0.0521	0.469 $\pm$ 0.1651	0.478 $\pm$ 0.0561	<u>0.470</u> $\pm$ 0.0521	<u>0.515</u> $\pm$ 0.0367
TITAN	0.637 $\pm$ 0.1402	<u>0.593</u> $\pm$ 0.0231	<u>0.513</u> $\pm$ 0.1397	<u>0.572</u> $\pm$ 0.0447	0.430 $\pm$ 0.0859	0.502 $\pm$ 0.0294

Supplementary Table 55: Linear probing results for PD-L1 expression level ($C = 3$) prediction on PD-L1. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.732 $\pm$ 0.0548	0.595 $\pm$ 0.0309	0.657 $\pm$ 0.0402	0.669 $\pm$ 0.0295	0.567 $\pm$ 0.0281	0.663 $\pm$ 0.0270
GigaPath	0.717 $\pm$ 0.0510	0.580 $\pm$ 0.0224	0.642 $\pm$ 0.0337	0.659 $\pm$ 0.0247	0.555 $\pm$ 0.0176	0.652 $\pm$ 0.0186
Mean pool (Virchow)	0.730 $\pm$ 0.0509	0.588 $\pm$ 0.0203	0.573 $\pm$ 0.0447	0.605 $\pm$ 0.0347	0.558 $\pm$ 0.0194	0.653 $\pm$ 0.0180
PRISM	<u>0.787</u> $\pm$ 0.0517	0.632 $\pm$ 0.0486	0.736 $\pm$ 0.0264	0.744 $\pm$ 0.0184	0.688 $\pm$ 0.0341	0.758 $\pm$ 0.0283
Mean pool (CHIEF)	0.685 $\pm$ 0.0463	0.562 $\pm$ 0.0351	0.585 $\pm$ 0.0288	0.608 $\pm$ 0.0270	0.557 $\pm$ 0.0084	0.653 $\pm$ 0.0056
CHIEF	0.732 $\pm$ 0.0576	0.612 $\pm$ 0.0220	0.635 $\pm$ 0.0197	0.654 $\pm$ 0.0215	0.595 $\pm$ 0.0342	0.685 $\pm$ 0.0317
Mean pool (CONCHv1.5)	0.735 $\pm$ 0.0573	0.577 $\pm$ 0.0200	0.647 $\pm$ 0.0255	0.664 $\pm$ 0.0195	0.612 $\pm$ 0.0166	0.703 $\pm$ 0.0156
TITAN _V	0.779 $\pm$ 0.0442	0.651 $\pm$ 0.0269	0.712 $\pm$ 0.0164	0.735 $\pm$ 0.0117	0.650 $\pm$ 0.0294	0.732 $\pm$ 0.0264
TITAN	0.789 $\pm$ 0.0445	<u>0.648</u> $\pm$ 0.0397	<u>0.729</u> $\pm$ 0.0182	<u>0.738</u> $\pm$ 0.0158	<u>0.684</u> $\pm$ 0.0352	<u>0.752</u> $\pm$ 0.0323

Supplementary Table 56: Linear probing results for ER ($C = 2$) prediction on MGB-BRCA. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.733±0.0444	0.668±0.0205	0.637±0.0334	0.636±0.0325	0.615±0.0165	0.629±0.0160
GigaPath	0.720±0.0464	0.669±0.0263	0.634±0.0291	0.637±0.0259	0.616±0.0271	0.630±0.0272
Mean pool (Virchow)	0.697±0.0385	0.645±0.0283	0.573±0.0161	0.580±0.0161	0.563±0.0411	0.576±0.0402
PRISM	0.742±0.0398	0.680±0.0342	0.693 ±0.0380	0.694 ±0.0336	<u>0.675</u> ±0.0306	<u>0.686</u> ±0.0304
Mean pool (CHIEF)	0.715±0.0409	0.639±0.0325	0.585±0.0265	0.585±0.0274	0.580±0.0311	0.594±0.0311
CHIEF	0.722±0.0434	0.662±0.0283	0.610±0.0185	0.615±0.0184	0.617±0.0254	0.632±0.0261
Mean pool (CONCHv1.5)	0.717±0.0287	0.649±0.0250	0.646±0.0338	0.650±0.0317	0.631±0.0298	0.645±0.0290
TITAN _V	<u>0.752</u> ±0.0329	<u>0.685</u> ±0.0277	0.672±0.0316	0.680±0.0301	0.637±0.0368	0.651±0.0365
TITAN	0.758 ±0.0335	0.686 ±0.0275	<u>0.682</u> ±0.0193	<u>0.685</u> ±0.0160	0.681 ±0.0179	0.693 ±0.0175

Supplementary Table 57: Linear probing results for PR ($C = 2$) prediction on MGB-BRCA. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		5-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.630±0.0366	0.506±0.0052	0.550±0.0249	0.626±0.0107	0.516±0.0117	0.734±0.0081
GigaPath	0.613±0.0385	0.513±0.0143	0.557±0.0403	0.642±0.0179	0.523±0.0198	0.738±0.0125
Mean pool (Virchow)	0.575±0.0789	0.507±0.0080	0.512±0.0587	0.620±0.0272	0.526±0.0180	0.738±0.0093
PRISM	<u>0.748</u> ±0.0669	0.536 ±0.0334	<u>0.653</u> ±0.0471	0.682 ±0.0240	0.594 ±0.0217	0.781 ±0.0150
Mean pool (CHIEF)	0.568±0.0478	0.500±0.0000	0.527±0.0480	0.593±0.0164	0.516±0.0242	0.731±0.0147
CHIEF	0.696±0.0418	0.513±0.0194	0.613±0.0469	0.663±0.0198	0.529±0.0338	0.740±0.0191
Mean pool (CONCHv1.5)	0.654±0.0947	0.516±0.0204	0.533±0.0534	0.605±0.0301	0.530±0.0205	0.741±0.0134
TITAN _V	0.727±0.0681	<u>0.517</u> ±0.0102	0.627±0.0492	<u>0.673</u> ±0.0237	<u>0.554</u> ±0.0527	<u>0.758</u> ±0.0306
TITAN	0.749 ±0.0416	0.502±0.0076	0.662 ±0.0564	0.667±0.0400	<u>0.554</u> ±0.0351	0.753±0.0155

Supplementary Table 58: Linear probing results for HER2 ($C = 2$) prediction on MGB-BRCA. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		5-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.536±0.0813	0.500±0.0000	0.514±0.1075	0.563±0.0831	0.585±0.0477	0.656±0.0594
GigaPath	0.515±0.1371	0.500±0.0000	0.512±0.0640	0.568±0.0377	0.536±0.0679	0.619±0.0604
Mean pool (Virchow)	0.572±0.1610	0.500±0.0000	0.441±0.1094	0.468±0.1234	0.532±0.1186	0.612±0.1092
PRISM	0.701±0.1304	0.607 ±0.1044	0.710 ±0.0930	0.748 ±0.0725	<u>0.688</u> ±0.0560	<u>0.714</u> ±0.0322
Mean pool (CHIEF)	0.453±0.1495	0.491±0.0182	0.472±0.0990	0.480±0.1053	0.494±0.0940	0.588±0.0919
CHIEF	0.499±0.1212	0.473±0.0545	0.492±0.0943	0.560±0.0763	0.565±0.0706	0.644±0.0598
Mean pool (CONCHv1.5)	0.580±0.0921	0.500±0.0000	0.579±0.1528	0.608±0.1384	0.608±0.0821	0.679±0.0711
TITAN _V	0.638±0.1947	0.525±0.0500	<u>0.672</u> ±0.1171	<u>0.712</u> ±0.0937	0.672±0.1141	0.708±0.0966
TITAN	0.705 ±0.1338	<u>0.567</u> ±0.1233	0.663±0.1054	0.702±0.0910	0.755 ±0.0949	0.774 ±0.0870

Supplementary Table 59: Linear probing results for CDX-2 expression ($C = 2$) prediction on MGB-LUAD. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.656±0.1128	0.527±0.1181	0.607±0.1957	0.595±0.1991	0.643±0.1580	0.636±0.1555
GigaPath	0.624±0.1530	0.510±0.0873	0.590±0.0742	0.584±0.0754	0.527±0.1618	0.491±0.1760
Mean pool (Virchow)	0.738±0.1436	0.657±0.1138	0.623±0.1158	0.622±0.1173	0.627±0.1587	0.623±0.1569
PRISM	<u>0.908</u> ±0.0570	0.833 ±0.0913	0.917 ±0.0527	0.914 ±0.0543	<u>0.850</u> ±0.0816	<u>0.838</u> ±0.0935
Mean pool (CHIEF)	0.619±0.1362	0.530±0.1481	0.577±0.2099	0.560±0.2227	0.510±0.1555	0.491±0.1659
CHIEF	0.760±0.1603	0.747±0.1376	0.637±0.1267	0.630±0.1264	0.597±0.1540	0.591±0.1527
Mean pool (CONCHv1.5)	0.833±0.1394	0.710±0.1659	0.680±0.2031	0.674±0.2068	0.607±0.0910	0.593±0.0796
TITAN _V	0.864±0.0761	0.760±0.0904	0.847±0.0636	0.844±0.0625	0.830±0.0748	0.828±0.0737
TITAN	0.953 ±0.0295	<u>0.813</u> ±0.0968	<u>0.897</u> ±0.0323	<u>0.896</u> ±0.0317	0.897 ±0.0323	0.896 ±0.0317

Supplementary Table 60: Linear probing results for Cytokeratin 5 & 6 expression ($C = 2$) prediction on MGB-LUAD. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.662±0.1120	0.600±0.0825	0.604±0.0567	0.602±0.0540	0.496±0.0417	0.495±0.0456
GigaPath	0.645±0.1395	0.625±0.1053	0.562±0.0926	0.557±0.0965	0.515±0.0967	0.513±0.0970
Mean pool (Virchow)	0.611±0.0824	0.562±0.0447	0.550±0.0683	0.548±0.0682	0.529±0.0855	0.530±0.0851
PRISM	0.770±0.0670	0.657±0.0578	0.635±0.0644	0.628±0.0657	<u>0.638</u> ±0.1001	0.627±0.0958
Mean pool (CHIEF)	0.582±0.1049	0.551±0.0498	0.524±0.0484	0.522±0.0468	0.500±0.0570	0.497±0.0579
CHIEF	0.658±0.0749	0.603±0.0671	0.569±0.1033	0.564±0.1053	0.585±0.0721	0.578±0.0761
Mean pool (CONCHv1.5)	0.682±0.0249	0.543±0.0384	0.590±0.0642	0.582±0.0626	0.538±0.1001	0.535±0.1000
TITAN _V	<u>0.772</u> ±0.0673	<u>0.687</u> ±0.1010	<u>0.684</u> ±0.1227	<u>0.680</u> ±0.1201	0.633±0.0736	<u>0.631</u> ±0.0730
TITAN	0.854 ±0.0373	0.761 ±0.0716	0.692 ±0.1049	0.690 ±0.1040	0.700 ±0.0706	0.697 ±0.0688

Supplementary Table 61: Linear probing results for Napsin A expression ($C = 2$) prediction on MGB-LUAD. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.646±0.0920	0.591±0.0629	0.472±0.0325	0.477±0.0315	0.503±0.0643	0.519±0.0681
GigaPath	0.579±0.1112	0.549±0.0512	0.459±0.0894	0.470±0.0885	0.473±0.0245	0.471±0.0279
Mean pool (Virchow)	0.673±0.1061	0.597±0.0408	0.444±0.0216	0.449±0.0127	0.507±0.0316	0.515±0.0238
PRISM	0.877±0.0576	<u>0.793</u> ±0.0861	0.784±0.0791	0.796±0.0677	<u>0.805</u> ±0.0852	<u>0.826</u> ±0.0758
Mean pool (CHIEF)	0.503±0.0518	0.522±0.0271	0.393±0.0437	0.397±0.0355	0.470±0.0679	0.479±0.0580
CHIEF	0.759±0.0841	0.680±0.0627	0.609±0.0796	0.613±0.0661	0.567±0.0399	0.582±0.0439
Mean pool (CONCHv1.5)	0.840±0.0571	0.754±0.0591	0.567±0.0584	0.578±0.0502	0.566±0.0357	0.585±0.0379
TITAN _V	<u>0.889</u> ±0.0387	0.771±0.0602	<u>0.831</u> ±0.0498	<u>0.832</u> ±0.0461	0.738±0.1012	0.765±0.0949
TITAN	0.913 ±0.0422	0.803 ±0.0558	0.872 ±0.0427	0.876 ±0.0367	0.870 ±0.0512	0.884 ±0.0449

Supplementary Table 62: Linear probing results for P40 expression ($C = 2$) prediction on MGB-LUAD. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	AUROC	Bal. acc.	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
Mean pool (GigaPath)	0.606±0.1164	0.543±0.0379	0.562±0.1023	0.558±0.0991	0.582±0.0772	0.581±0.0800
GigaPath	0.600±0.1071	0.557±0.0759	0.552±0.1093	0.552±0.1129	0.518±0.0994	0.518±0.1027
Mean pool (Virchow)	0.611±0.1399	0.536±0.1112	0.605±0.1078	0.602±0.1099	0.586±0.0891	0.586±0.0885
PRISM	0.822±0.0681	0.735±0.0846	0.744±0.0822	0.735±0.0915	<u>0.754</u> ±0.0974	<u>0.740</u> ±0.1031
Mean pool (CHIEF)	0.517±0.0872	0.512±0.0244	0.498±0.0532	0.489±0.0409	0.522±0.0637	0.519±0.0629
CHIEF	0.713±0.1397	0.583±0.0918	0.672±0.1047	0.672±0.1053	0.618±0.0973	0.619±0.0962
Mean pool (CONCHv1.5)	0.684±0.1107	0.600±0.0889	0.682±0.1037	0.678±0.1090	0.630±0.0703	0.626±0.0707
TITAN _V	0.866 ±0.0649	0.782 ±0.0743	<u>0.767</u> ±0.0671	<u>0.763</u> ±0.0720	0.713±0.0961	0.713±0.0959
TITAN	<u>0.860</u> ±0.0622	<u>0.770</u> ±0.1035	0.784 ±0.0786	0.777 ±0.0826	0.771 ±0.0733	0.763 ±0.0776

Supplementary Table 63: Linear probing results for P63 expression ($C = 2$) prediction on MGB-LUAD. The best result is marked in bold and the second best is underlined.

	CHIEF	GigaPath	PRISM	Mean	TITAN _V	TITAN
BLCA	0.599 ± 0.019	0.589 ± 0.054	<u>0.656</u> ± 0.023	0.630 ± 0.058	0.657 ± 0.055	<u>0.656</u> ± 0.040
BRCA	<u>0.737</u> ± 0.039	0.687 ± 0.083	0.685 ± 0.076	0.711 ± 0.048	0.713 ± 0.044	0.757 ± 0.015
CRC	0.680 ± 0.079	0.628 ± 0.085	0.622 ± 0.125	0.720 ± 0.089	<u>0.710</u> ± 0.110	0.705 ± 0.097
KIRC	0.736 ± 0.061	0.751 ± 0.072	<u>0.769</u> ± 0.061	0.774 ± 0.070	0.774 ± 0.060	0.768 ± 0.064
NSCLC	<u>0.633</u> ± 0.037	0.670 ± 0.031	0.600 ± 0.074	0.596 ± 0.049	0.624 ± 0.082	0.623 ± 0.041
UCEC	0.758 ± 0.109	0.779 ± 0.105	0.747 ± 0.026	0.761 ± 0.133	0.789 ± 0.091	<u>0.787</u> ± 0.067
Avg. (↑)	0.691	0.684	0.680	0.699	<u>0.711</u>	0.716

Supplementary Table 64: Survival prediction Results for TITAN and other slide encoders for measuring disease-specific survival (DSS) with c-index on six TCGA cancer cohorts. Except for CHIEF, all slide encoders have not used TCGA as the pretraining dataset. The best and second-best performances are denoted by **bold** and underlined, respectively.

Encoder	ECE ($\downarrow$)	Entropy ($\downarrow$)
GigaPath	0.010	1.19
PRISM	0.011	0.99
CHIEF	0.015	1.21
Mean pool (CONCHv1.5)	0.014	1.07
TITAN _V	0.008	<u>0.90</u>
TITAN	0.008	0.82

Supplementary Table 65: Calibration and confidence assessment results The expected calibration error (ECE) measures the calibration of the models and the entropy-based confidence score measures the uncertainty of predicted probabilities. For each model, the metrics are averaged across TCGA-UT-8K, TCGA-OT, OT108, and EBRAINS. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (abs)	0.816±0.0059	<u>0.870</u> ±0.0037	0.813±0.0053	0.858±0.0038	0.811±0.0050	0.839±0.0038
TITAN _V (none)	<u>0.819</u> ±0.0054	0.867±0.0038	<u>0.815</u> ±0.0054	<u>0.859</u> ±0.0039	0.814 ±0.0048	0.851 ±0.0037
TITAN _V (rope)	0.818±0.0059	0.873 ±0.0037	0.812±0.0053	<u>0.859</u> ±0.0040	0.804±0.0056	0.836±0.0040
TITAN _V	0.820 ±0.0055	<u>0.870</u> ±0.0037	0.818 ±0.0053	0.864 ±0.0039	<u>0.812</u> ±0.0050	<u>0.842</u> ±0.0038

Supplementary Table 66: Ablation study of positional encodings. Linear probing results for tumor subtype ($C = 32$) prediction on TCGA-UT-8K. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (abs)	0.673±0.0157	<u>0.753</u> ±0.0126	0.631±0.0184	0.721±0.0130	<u>0.706</u> ±0.0190	0.777 ±0.0116
TITAN _V (none)	0.664±0.0188	0.749±0.0127	<u>0.633</u> ±0.0175	<u>0.726</u> ±0.0129	0.708 ±0.0187	0.777 ±0.0112
TITAN _V (rope)	0.672±0.0170	0.735±0.0127	0.627±0.0164	0.719±0.0129	0.679±0.0207	0.765±0.0115
TITAN _V	0.690 ±0.0196	0.758 ±0.0123	0.639 ±0.0149	0.744 ±0.0124	<u>0.706</u> ±0.0183	<u>0.775</u> ±0.0116

Supplementary Table 67: Ablation study of positional encodings. Linear probing results for OncoTree code ($C = 46$) prediction on TCGA-OT. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (abs)	0.532±0.0106	0.508±0.0133	0.446±0.0102	0.411±0.0130	<u>0.506</u> ±0.0102	<u>0.497</u> ±0.0128
TITAN _V (none)	0.536±0.0103	<u>0.512</u> ±0.0130	<u>0.450</u> ±0.0104	<u>0.414</u> ±0.0130	0.488±0.0108	0.483±0.0130
TITAN _V (rope)	0.526±0.0103	0.505±0.0132	0.446±0.0102	<u>0.414</u> ±0.0129	0.495±0.0109	<u>0.497</u> ±0.0129
TITAN _V	0.558 ±0.0104	0.536 ±0.0127	0.464 ±0.0105	0.430 ±0.0128	0.524 ±0.0106	0.517 ±0.0129

Supplementary Table 68: Ablation study of positional encodings. Linear probing results for OncoTree code ($C = 108$) prediction on OT108. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (abs)	<u>0.728</u> ±0.0203	<u>0.781</u> ±0.0178	0.658 ±0.0190	0.713 ±0.0209	<u>0.722</u> ±0.0212	0.735 ±0.0185
TITAN _V (none)	0.693±0.0197	0.743±0.0195	0.648±0.0195	0.702±0.0209	0.714±0.0204	<u>0.728</u> ±0.0189
TITAN _V (rope)	0.702±0.0198	0.763±0.0187	0.591±0.0212	0.666±0.0212	0.675±0.0205	0.669±0.0198
TITAN _V	0.732 ±0.0208	0.785 ±0.0175	<u>0.656</u> ±0.0187	<u>0.709</u> ±0.0199	0.742 ±0.0192	0.727±0.0182

Supplementary Table 69: Ablation study of positional encodings. Linear probing results for tumor type ($C = 30$) prediction on EBRAINS. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (tbase)	0.818±0.0060	<u>0.873</u> ±0.0037	0.809±0.0058	0.857±0.0040	0.813 ±0.0052	0.843 ±0.0039
TITAN _V	<u>0.820</u> ±0.0055	0.870±0.0037	<u>0.818</u> ±0.0053	<u>0.864</u> ±0.0039	<u>0.812</u> ±0.0050	<u>0.842</u> ±0.0038
TITAN _V (base)	0.827 ±0.0052	0.876 ±0.0037	0.821 ±0.0052	0.868 ±0.0037	0.803±0.0053	0.841±0.0039

Supplementary Table 70: Ablation study of model sizes. Linear probing results for tumor subtype ($C = 32$) prediction on TCGA-UT-8K. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (tbase)	0.675±0.0190	0.747±0.0117	0.643 ±0.0155	0.732±0.0127	0.706±0.0189	0.771±0.0114
TITAN _V	0.690 ±0.0196	0.758 ±0.0123	0.639±0.0149	0.744 ±0.0124	0.706±0.0183	0.775±0.0116
TITAN _V (base)	0.670±0.0178	<u>0.750</u> ±0.0119	0.621±0.0165	0.723±0.0126	0.709 ±0.0186	0.779 ±0.0117

Supplementary Table 71: Ablation study of model sizes. Linear probing results for OncoTree code ($C = 46$) prediction on TCGA-OT. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (tbase)	0.551±0.0107	0.529±0.0130	0.467 ±0.0102	0.428±0.0131	0.528 ±0.0108	0.523 ±0.0127
TITAN _V	0.558 ±0.0104	0.536 ±0.0127	0.464±0.0105	0.430 ±0.0128	0.524±0.0106	0.517±0.0129
TITAN _V (base)	0.539±0.0104	0.521±0.0126	0.449±0.0100	0.416±0.0128	0.484±0.0105	0.474±0.0131

Supplementary Table 72: Ablation study of model sizes. Linear probing results for OncoTree code ($C = 108$) prediction on OT108. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (tbase)	0.709±0.0211	0.761±0.0187	0.636±0.0202	0.696±0.0201	0.693±0.0219	0.701±0.0192
TITAN _V	0.732 ±0.0208	0.785 ±0.0175	0.656 ±0.0187	0.709 ±0.0199	0.742 ±0.0192	0.727 ±0.0182
TITAN _V (base)	0.732 ±0.0199	<u>0.781</u> ±0.0177	0.621±0.0203	0.682±0.0209	0.698±0.0201	0.691±0.0192

Supplementary Table 73: Ablation study of model sizes. Linear probing results for tumor type ($C = 30$) prediction on EBRAINS. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (4,096×4,096)	0.808±0.0057	0.856±0.0039	0.786±0.0060	0.826±0.0043	0.785±0.0056	0.817±0.0042
TITAN _V (8,192×8,192)	0.820±0.0055	0.870±0.0037	0.818 ±0.0053	0.864 ±0.0039	0.812±0.0050	0.842±0.0038
TITAN _V (16,384×16,384)	0.825 ±0.0056	0.876 ±0.0038	0.818 ±0.0057	0.860±0.0038	0.825 ±0.0051	0.860 ±0.0037

Supplementary Table 74: Ablation study of region size in vision-only pretraining (Stage 1). Linear probing results for tumor subtype ($C = 32$) prediction on TCGA-UT-8K. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (4,096×4,096)	0.674±0.0190	0.739±0.0126	0.589±0.0164	0.702±0.0131	0.622±0.0179	0.726±0.0123
TITAN _V (8,192×8,192)	0.690 ±0.0196	0.758±0.0123	0.639±0.0149	0.744 ±0.0124	0.706±0.0183	0.775±0.0116
TITAN _V (16,384×16,384)	0.686±0.0180	0.765 ±0.0126	0.647 ±0.0160	0.742±0.0125	0.718 ±0.0169	0.776 ±0.0120

Supplementary Table 75: Ablation study of region size in vision-only pretraining (Stage 1). Linear probing results for OncoTree code ($C = 46$) prediction on TCGA-OT. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (4,096×4,096)	0.532±0.0105	0.513±0.0131	0.435±0.0112	0.423±0.0131	0.466±0.0109	0.459±0.0128
TITAN _V (8,192×8,192)	0.558 ±0.0104	0.536 ±0.0127	0.488 ±0.0107	0.475 ±0.0129	0.524 ±0.0106	0.517 ±0.0129
TITAN _V (16,384×16,384)	0.536±0.0104	0.516±0.0130	0.486±0.0107	0.472±0.0129	0.502±0.0108	0.493±0.0128

Supplementary Table 76: Ablation study of region size in vision-only pretraining (Stage 1). Linear probing results for OncoTree code ($C = 108$) prediction on OT108. The best result is marked in bold and the second best is underlined.

Encoder	Logistic regression		SimpleShot		20-nearest neighbors	
	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V (4,096×4,096)	0.688±0.0207	0.746±0.0189	0.585±0.0219	0.649±0.0212	0.620±0.0220	0.616±0.0205
TITAN _V (8,192×8,192)	0.732 ±0.0208	0.785 ±0.0175	0.656±0.0187	0.709±0.0199	0.742 ±0.0192	<u>0.727</u> ±0.0182
TITAN _V (16,384×16,384)	<u>0.703</u> ±0.0213	<u>0.759</u> ±0.0181	0.662 ±0.0206	0.718 ±0.0197	<u>0.714</u> ±0.0195	0.730 ±0.0181

Supplementary Table 77: Ablation study of region size in vision-only pretraining (Stage 1). Linear probing results for tumor type ($C = 30$) prediction on EBRAINS. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
ABMIL (CONCHv1.5) (finetuned)	0.807±0.0058	0.854±0.0039	<u>0.991</u> ±0.0004
GigaPath	0.700±0.0069	0.782±0.0046	0.979±0.0010
GigaPath (finetuned)	0.772±0.0061	0.841±0.0039	0.983±0.0008
PRISM	0.774±0.0062	0.824±0.0042	0.989±0.0005
PRISM (finetuned)	0.746±0.0065	0.811±0.0045	0.987±0.0007
CHIEF	0.625±0.0079	0.723±0.0051	0.973±0.0011
CHIEF (finetuned)	0.609±0.0078	0.708±0.0051	0.960±0.0017
TITAN _V	0.820±0.0055	0.870±0.0037	0.994 ±0.0003
TITAN _V (finetuned)	<u>0.836</u> ±0.0054	0.874±0.0037	0.984±0.0010
TITAN	0.832±0.0056	<u>0.881</u> ±0.0036	0.994 ±0.0003
TITAN (finetuned)	0.841 ±0.0055	0.882 ±0.0036	0.989±0.0008

Supplementary Table 78: Finetuning results for tumor subtype ($C = 32$) prediction on TCGA-UT-8K for all baselines. Finetuned results are trained on the specific task, while non-finetuned results are logistic regression fits of the frozen slide embeddings. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
ABMIL (CONCHv1.5) (finetuned)	0.677±0.0204	0.735±0.0126	0.982±0.0026
GigaPath	0.543±0.0178	0.659±0.0134	0.976 ±0.0021
GigaPath (finetuned)	0.664±0.0175	0.736±0.0126	0.979±0.0022
PRISM	0.643±0.0181	0.732±0.0129	0.986±0.0014
PRISM (finetuned)	0.548±0.0172	0.644±0.0134	0.980±0.0015
CHIEF	0.528±0.0205	0.640±0.0142	0.968±0.0028
CHIEF (finetuned)	0.518±0.0200	0.630±0.0143	0.944±0.0043
TITAN _V	0.690±0.0196	0.758±0.0123	<u>0.989</u> ±0.0014
TITAN _V (finetuned)	0.695±0.0170	<u>0.767</u> ±0.0117	0.974±0.0028
TITAN	<u>0.704</u> ±0.0192	0.764±0.0116	0.990 ±0.0012
TITAN (finetuned)	0.716 ±0.0182	0.774 ±0.0113	0.985±0.0016

Supplementary Table 79: Finetuning results for OncoTree code ($C = 46$) prediction on TCGA-OT for all baselines. Finetuned results are trained on the specific task, while non-finetuned results are logistic regression fits of the frozen slide embeddings. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
ABMIL (CONCHv1.5) (finetuned)	0.538±0.0109	0.521±0.0134	0.977±0.0016
GigaPath	0.437±0.0110	0.423±0.0124	0.949±0.0030
GigaPath (finetuned)	0.525±0.0109	0.508±0.0134	0.972±0.0019
PRISM	0.508±0.0110	0.481±0.0133	0.976±0.0018
PRISM (finetuned)	0.492±0.0110	0.478±0.0128	0.967±0.0022
CHIEF	0.413±0.0109	0.394±0.0130	0.944±0.0029
CHIEF (finetuned)	0.330±0.0108	0.319±0.0121	0.916±0.0038
TITAN _V	0.558±0.0104	0.536±0.0127	<u>0.979</u> ±0.0017
TITAN _V (finetuned)	<u>0.575</u> ±0.0103	0.554±0.0129	0.966±0.0023
TITAN	0.587 ±0.0103	0.563 ±0.0130	0.983 ±0.0014
TITAN (finetuned)	0.565±0.0105	0.541±0.0130	<u>0.979</u> ±0.0017

Supplementary Table 80: Finetuning results for OncoTree code ($C = 108$) prediction on OT108 for all baselines. Finetuned results are trained on the specific task, while non-finetuned results are logistic regression fits of the frozen slide embeddings. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
ABMIL (CONCHv1.5) (finetuned)	0.728±0.0203	0.778±0.0184	0.982±0.0024
GigaPath	0.680±0.0217	0.746±0.0197	0.978±0.0027
GigaPath (finetuned)	0.725±0.0209	0.780±0.0185	0.983±0.0028
PRISM	0.674±0.0200	0.732±0.0191	0.978±0.0026
PRISM (finetuned)	0.652±0.0224	0.707±0.0196	0.967±0.0039
CHIEF	0.598±0.0237	0.670±0.0206	0.969±0.0032
CHIEF (finetuned)	0.544±0.0247	0.622±0.0208	0.941±0.0076
TITAN _V	0.732±0.0208	0.785±0.0175	0.985±0.0021
TITAN _V (finetuned)	<u>0.746±0.0200</u>	0.794±0.0171	0.985±0.0022
TITAN	0.735±0.0204	0.786±0.0182	0.983±0.0023
TITAN (finetuned)	0.748±0.0192	<u>0.787±0.0176</u>	<u>0.984±0.0030</u>

Supplementary Table 81: Finetuning results for tumor type ($C = 30$) prediction on EBRAINS for all baselines. Finetuned results are trained on the specific task, while non-finnetuned results are logistic regression fits of the frozen slide embeddings. The best result is marked in bold and the second best is underlined.

Encoder	$k=1$	$k=2$	$k=4$	$k=8$	$k=16$	$k=32$
Mean pool (CONCHv1.5)	0.495±0.0367	0.597±0.0289	0.667±0.0201	0.711±0.0156	0.738±0.0132	0.755±0.0105
ABMIL (CONCHv1.5)	0.539±0.0459	0.662±0.0275	0.724±0.0133	0.759±0.0124	0.787±0.0111	0.805±0.0109
GigaPath	0.282±0.0286	0.381±0.0282	0.476±0.0193	0.557±0.0204	0.620±0.0138	0.659±0.0112
PRISM	0.469±0.0380	0.560±0.0284	0.627±0.0253	0.674±0.0181	0.704±0.0151	0.725±0.0121
CHIEF	0.255±0.0292	0.339±0.0304	0.424±0.0198	0.503±0.0153	0.564±0.0135	0.609±0.0113
TITAN _V	<u>0.634±0.0389</u>	<u>0.723±0.0236</u>	<u>0.767±0.0149</u>	<u>0.795±0.0118</u>	<u>0.810±0.0084</u>	<u>0.819±0.0094</u>
TITAN	0.683±0.0357	0.761±0.0223	0.796±0.0134	0.814±0.0131	0.824±0.0106	0.830±0.0096

Supplementary Table 82: Few shot experiments with $k \in \{1, 2, 4, 8, 16, 32\}$ shots per class for tumor subtype ($C = 32$) prediction on TCGA-UT-8K. Results are given in balanced accuracy of linear probing evaluation or ABMIL training, respectively. If a class contains less than k samples, all samples are used. The best result is marked in bold and the second best is underlined.

Encoder	$k=1$	$k=2$	$k=4$	$k=8$	$k=16$	$k=32$
Mean pool (CONCHv1.5)	0.396±0.0293	0.466±0.0302	0.521±0.0233	0.555±0.0217	0.583±0.0193	0.600±0.0173
ABMIL (CONCHv1.5)	0.407±0.0333	0.505±0.0257	0.563±0.0158	0.607±0.0170	0.634±0.0192	0.659±0.0138
GigaPath	0.210±0.0268	0.289±0.0294	0.373±0.0192	0.438±0.0193	0.502±0.0189	0.537±0.0171
PRISM	0.441±0.0282	0.519±0.0196	0.584±0.0159	0.621±0.0148	0.645±0.0110	0.662±0.0098
CHIEF	0.219±0.0248	0.287±0.0301	0.362±0.0256	0.423±0.0207	0.476±0.0177	0.510±0.0152
TITAN _V	<u>0.508±0.0292</u>	<u>0.580±0.0257</u>	<u>0.622±0.0198</u>	<u>0.647±0.0210</u>	<u>0.670±0.0164</u>	<u>0.681±0.0191</u>
TITAN	0.566±0.0333	0.629±0.0239	0.667±0.0196	0.687±0.0207	0.701±0.0191	0.702±0.0164

Supplementary Table 83: Few shot experiments with $k \in \{1, 2, 4, 8, 16, 32\}$ shots per class for OncoTree code ($C = 46$) prediction on TCGA-OT. Results are given in balanced accuracy of linear probing evaluation or ABMIL training, respectively. If a class contains less than k samples, all samples are used. The best result is marked in bold and the second best is underlined.

Encoder	$k=1$	$k=2$	$k=4$	$k=8$	$k=16$	$k=32$
Mean pool (CONCHv1.5)	0.201±0.0144	0.276±0.0123	0.338±0.0110	0.392±0.0094	0.430±0.0087	0.462±0.0065
ABMIL (CONCHv1.5)	0.236±0.0186	0.352±0.0161	0.437±0.0104	0.496±0.0086	0.535±0.0098	0.553±0.0065
GigaPath	0.136±0.0110	0.202±0.0121	0.276±0.0102	0.353±0.0106	0.416±0.0089	0.452±0.0054
PRISM	0.271±0.0161	0.346±0.0137	0.409±0.0096	0.457±0.0099	0.489±0.0086	0.501±0.0058
CHIEF	0.126±0.0111	0.179±0.0108	0.242±0.0089	0.311±0.0109	0.368±0.0072	0.405±0.0055
TITAN _V	<u>0.307±0.0160</u>	<u>0.394±0.0132</u>	<u>0.462±0.0097</u>	<u>0.512±0.0075</u>	<u>0.543±0.0079</u>	<u>0.554±0.0063</u>
TITAN	0.364±0.0164	0.449±0.0135	0.508±0.0098	0.550±0.0099	0.572±0.0081	0.578±0.0061

Supplementary Table 84: Few shot experiments with $k \in \{1, 2, 4, 8, 16, 32\}$ shots per class for OncoTree code ($C = 108$) prediction on OT108. Results are given in balanced accuracy of linear probing evaluation or ABMIL training, respectively. If a class contains less than k samples, all samples are used. The best result is marked in bold and the second best is underlined.

Encoder	$k=1$	$k=2$	$k=4$	$k=8$	$k=16$	$k=32$
Mean pool (CONCHv1.5)	0.354±0.0267	0.445±0.0310	0.526±0.0212	0.589±0.0147	0.638±0.0176	0.668±0.0127
ABMIL (CONCHv1.5)	0.388±0.0417	0.544±0.0372	<u>0.629±0.0230</u>	0.671±0.0195	0.702±0.0138	0.729±0.0118
GigaPath	0.292±0.0284	0.398±0.0250	0.507±0.0206	0.589±0.0190	0.658±0.0175	0.709±0.0122
PRISM	0.399±0.0328	0.484±0.0192	0.548±0.0225	0.595±0.0193	0.628±0.0173	0.659±0.0156
CHIEF	0.226±0.0280	0.319±0.0278	0.418±0.0237	0.509±0.0171	0.578±0.0158	0.637±0.0122
TITAN _V	<u>0.489±0.0261</u>	<u>0.568±0.0208</u>	0.627±0.0195	<u>0.672±0.0184</u>	<u>0.708±0.0154</u>	<u>0.730±0.0114</u>
TITAN	0.535±0.0303	0.609±0.0255	0.660±0.0206	0.695±0.0149	0.724±0.0146	0.733±0.0127

Supplementary Table 85: Few shot experiments with $k \in \{1, 2, 4, 8, 16, 32\}$ shots per class for tumor type ($C = 30$) prediction on EBRAINS. Results are given in balanced accuracy of linear probing evaluation or ABMIL training, respectively. If a class contains less than k samples, all samples are used. The best result is marked in bold and the second best is underlined.

Encoder	$k=1$	$k=2$	$k=4$	$k=8$	$k=16$	$k=32$
Mean pool (CONCHv1.5)	0.505±0.0387	0.597±0.0284	0.666±0.0173	0.711±0.0186	0.735±0.0116	0.748±0.0126
GigaPath	0.292±0.0297	0.366±0.0289	0.441±0.0205	0.505±0.0187	0.543±0.0145	0.562±0.0152
PRISM	0.478±0.0403	0.569±0.0276	0.641±0.0191	0.677±0.0137	0.694±0.0101	0.702±0.0091
CHIEF	0.262±0.0295	0.323±0.0286	0.391±0.0220	0.440±0.0162	0.468±0.0148	0.482±0.0121
TITAN _V	0.639±0.0385	0.727±0.0243	0.776±0.0155	0.798±0.0122	0.809±0.0094	0.816±0.0100
TITAN	0.684±0.0366	0.767±0.0232	0.808±0.0133	0.824±0.0113	0.832±0.0109	0.838±0.0097

Supplementary Table 86: Few shot experiments with $k \in \{1, 2, 4, 8, 16, 32\}$ shots per class for tumor subtype ($C = 32$) prediction on TCGA-UT-8K. Results are given in balanced accuracy of SimpleShot evaluation. If a class contains less than k samples, all samples are used. The best result is marked in bold and the second best is underlined.

Encoder	$k=1$	$k=2$	$k=4$	$k=8$	$k=16$	$k=32$
Mean pool (CONCHv1.5)	0.397±0.0312	0.466±0.0303	0.525±0.0223	0.565±0.0189	0.590±0.0152	0.603±0.0105
GigaPath	0.217±0.0285	0.276±0.0296	0.343±0.0206	0.391±0.0168	0.432±0.0203	0.455±0.0154
PRISM	0.455±0.0288	0.528±0.0224	0.589±0.0148	0.621±0.0112	0.637±0.0084	0.649±0.0077
CHIEF	0.223±0.0246	0.275±0.0290	0.329±0.0245	0.369±0.0168	0.401±0.0197	0.414±0.0118
TITAN _V	<u>0.517±0.0296</u>	<u>0.587±0.0233</u>	0.633±0.0185	0.664±0.0164	0.685±0.0135	0.696±0.0106
TITAN	0.568±0.0316	0.639±0.0215	0.685±0.0201	0.713±0.0132	0.730±0.0125	0.745±0.0074

Supplementary Table 87: Few shot experiments with $k \in \{1, 2, 4, 8, 16, 32\}$ shots per class for OncoTree code ($C = 46$) prediction on TCGA-OT. Results are given in balanced accuracy of SimpleShot evaluation. If a class contains less than k samples, all samples are used. The best result is marked in bold and the second best is underlined.

Encoder	$k=1$	$k=2$	$k=4$	$k=8$	$k=16$	$k=32$
Mean pool (CONCHv1.5)	0.203±0.0158	0.261±0.0139	0.315±0.0124	0.361±0.0091	0.392±0.0080	0.406±0.0043
GigaPath	0.139±0.0123	0.189±0.0108	0.240±0.0107	0.293±0.0100	0.330±0.0081	0.348±0.0054
PRISM	0.278±0.0165	0.347±0.0121	0.412±0.0110	0.455±0.0089	0.478±0.0062	0.486±0.0042
CHIEF	0.124±0.0102	0.162±0.0093	0.208±0.0097	0.249±0.0086	0.279±0.0062	0.293±0.0052
TITAN _V	<u>0.299±0.0148</u>	<u>0.380±0.0136</u>	<u>0.445±0.0104</u>	<u>0.491±0.0085</u>	<u>0.516±0.0065</u>	<u>0.525±0.0054</u>
TITAN	0.370±0.0165	0.452±0.0133	0.514±0.0112	0.552±0.0082	0.573±0.0058	0.581±0.0035

Supplementary Table 88: Few shot experiments with $k \in \{1, 2, 4, 8, 16, 32\}$ shots per class for OncoTree code ($C = 108$) prediction on OT108. Results are given in balanced accuracy of SimpleShot evaluation. If a class contains less than k samples, all samples are used. The best result is marked in bold and the second best is underlined.

Encoder	$k=1$	$k=2$	$k=4$	$k=8$	$k=16$	$k=32$
Mean pool (CONCHv1.5)	0.358±0.0248	0.417±0.0261	0.480±0.0233	0.519±0.0229	0.540±0.0151	0.548±0.0110
GigaPath	0.304±0.0276	0.388±0.0220	0.483±0.0203	0.544±0.0172	0.583±0.0165	0.610±0.0104
PRISM	0.425±0.0326	0.503±0.0229	0.549±0.0187	0.589±0.0187	0.609±0.0146	0.628±0.0099
CHIEF	0.221±0.0248	0.287±0.0268	0.355±0.0243	0.410±0.0221	0.445±0.0149	0.473±0.0131
TITAN _V	<u>0.502±0.0266</u>	<u>0.572±0.0242</u>	<u>0.633±0.0183</u>	<u>0.669±0.0163</u>	<u>0.703±0.0132</u>	<u>0.723±0.0080</u>
TITAN	0.549±0.0318	0.615±0.0193	0.669±0.0179	0.709±0.0139	0.731±0.0112	0.749±0.0082

Supplementary Table 89: Few shot experiments with $k \in \{1, 2, 4, 8, 16, 32\}$ shots per class for tumor type ($C = 30$) prediction on EBRAINS. Results are given in balanced accuracy of SimpleShot evaluation. If a class contains less than k samples, all samples are used. The best result is marked in bold and the second best is underlined.

CLASSNAME.
 an image of CLASSNAME.
 the image shows CLASSNAME.
 the image displays CLASSNAME.
 the image exhibits CLASSNAME.
 an example of CLASSNAME.
 CLASSNAME is shown.
 this is CLASSNAME.
 I observe CLASSNAME.
 the pathology image shows CLASSNAME.
 a pathology image shows CLASSNAME.
 the pathology slide shows CLASSNAME.
 shows CLASSNAME.
 contains CLASSNAME.
 presence of CLASSNAME.
 CLASSNAME is present.
 CLASSNAME is observed.
 the pathology image reveals CLASSNAME.
 a microscopic image of showing CLASSNAME.
 histology shows CLASSNAME.
 CLASSNAME can be seen.
 the tissue shows CLASSNAME.
 CLASSNAME is identified.

Supplementary Table 90: Prompt templates used for zero-shot slide classification. The name of the class replaces CLASSNAME. See **Supplementary Tables 104–109** for class prompts of each task.

Task	Class	Class names
TCGA NSCLC	LUAD	adenocarcinoma lung adenocarcinoma adenocarcinoma of the lung LUAD
	LUSC	squamous cell carcinoma lung squamous cell carcinoma squamous cell carcinoma of the lung LUSC
TCGA BRCA	IDC	invasive ductal carcinoma breast invasive ductal carcinoma invasive ductal carcinoma of the breast invasive carcinoma of the breast, ductal pattern breast IDC
	ILC	invasive lobular carcinoma breast invasive lobular carcinoma invasive lobular carcinoma of the breast invasive carcinoma of the breast, lobular pattern breast ILC

Supplementary Table 91: Class prompts for TCGA NSCLC and TCGA BRCA subtyping.

Task	Class	Class names
OT108	ANSC	anal squamous cell carcinoma squamous cell carcinoma of the anal canal anal SCC squamous carcinoma of the anal region anal squamous carcinoma
	CCOV	clear cell ovarian cancer clear cell carcinoma of the ovary clear cell adenocarcinoma of the ovary CCOV
	CHOL	cholangiocarcinoma bile duct carcinoma biliary tract cancer cholangiocellular carcinoma CHOL
	CSCC	cutaneous squamous cell carcinoma skin squamous cell carcinoma squamous cell carcinoma of the skin CSCC
	DLBCLNOS	diffuse large B-cell lymphoma DLBCL diffuse large B-cell lymphoma, not otherwise specified DLBCLNOS
	EOV	endometrioid ovarian cancer endometrioid carcinoma of the ovary endometrioid tumor EOV
	FL	follicular lymphoma follicular lymphoid neoplasm follicular non-Hodgkin lymphoma FL
	GBC	gallbladder cancer gallbladder adenocarcinoma gallbladder carcinoma GBC
	GEJ	adenocarcinoma of the gastroesophageal junction gastroesophageal junction adenocarcinoma GEJ adenocarcinoma gastroesophageal junction cancer adenocarcinoma at the gastroesophageal junction
	GINET	gastrointestinal neuroendocrine tumors GI neuroendocrine tumors gastrointestinal carcinoid tumors gastrointestinal neuroendocrine neoplasms GINET
	GIST	gastrointestinal stromal tumor gastric stromal tumor intestinal stromal tumor gastrointestinal mesenchymal tumor GIST
	HEMA	hemangioma vascular tumor hemangioma of soft tissue hemangioma of skin cavernous hemangioma capillary hemangioma HEMA

Task	Class	Class names
OT108	HGGNOS	high-grade glioma high-grade glioma, not otherwise specified high-grade glioma NOS HGGNOS
	LGGNOS	low-grade glioma low-grade glioma not otherwise specified low-grade glioma, NOS LGG NOS
	LGSOC	low-grade serous ovarian cancer low-grade serous carcinoma serous papillary ovarian carcinoma, low grade LGSOC
	MCC	Merkel cell carcinoma neuroendocrine carcinoma of the skin cutaneous neuroendocrine carcinoma MCC
	MDLC	mixed ductal and lobular carcinoma breast mixed ductal and lobular carcinoma mixed carcinoma of the breast MDLC
	MNG	meningioma meningeal tumor benign meningioma malignant meningioma MNG
	NBL	neuroblastoma neuroblastic tumor neuroblastic neoplasm NBL
	NSCLCPD	poorly differentiated non-small cell lung cancer poorly differentiated NSCLC non-small cell lung cancer (poorly differentiated) NSCLCPD
	PANET	pancreatic neuroendocrine tumor pancreatic endocrine tumor pancreatic neuroendocrine neoplasm neuroendocrine tumor of the pancreas PANET
	PTAD	pituitary adenoma adenoma of the pituitary gland pituitary gland adenoma PTAD
	SCLC	small cell lung cancer small cell carcinoma of the lung SCLC
	UTUC	urothelial carcinoma upper tract urothelial carcinoma urothelial carcinoma of the upper urinary tract UTUC
	BLAD	bladder adenocarcinoma adenocarcinoma of the bladder bladder cancer, adenocarcinomatous type BLAD

Task	Class	Class names
OT108	MBL	medulloblastoma primitive neuroectodermal tumor (PNET) medulloblastoma variant MBL
	SBC	duodenal adenocarcinoma adenocarcinoma of the duodenum duodenum cancer SBC
	OS	osteosarcoma osteogenic sarcoma primary osteosarcoma OS
	ULMS	leiomyosarcoma uterine leiomyosarcoma leiomyosarcoma of the uterus ULMS
	AMPCA	ampullary carcinoma carcinoma of the ampulla of Vater ampullary adenocarcinoma AMPCA
	MGCT	mixed germ cell tumor mixed germ cell neoplasm germ cell tumor, mixed type MGCT
	WT	Wilms' tumor nephroblastoma renal embryonal tumor WT
	OCS	ovarian carcinosarcoma malignant mixed mesodermal tumor mixed mesodermal tumor of the ovary ovarian mixed tumor OCS
	AODG	anaplastic oligodendroglioma oligodendroglioma anaplastic oligodendroglioma WHO grade III AODG
	ES	Ewing sarcoma Ewing's sarcoma primitive neuroectodermal tumor (PNET) ES
	ALUCA	atypical lung carcinoid atypical carcinoid tumor lung carcinoid tumor (atypical) atypical neuroendocrine tumor of the lung ALUCA
	LUCA	lung carcinoid carcinoid tumor of the lung pulmonary carcinoid LUCA
	EPM	ependymoma ependymal tumor central nervous system ependymoma EPM
	LUAS	adenosquamous carcinoma lung adenosquamous carcinoma adenosquamous cell carcinoma of the lung LUAS

Task	Class	Class names
OT108	UCCC	clear cell carcinoma uterine clear cell carcinoma clear cell carcinoma of the uterus UCCC
	MXOV	mixed ovarian carcinoma mixed epithelial ovarian carcinoma ovarian mixed carcinoma MXOV
	PLBMESO	pleural mesothelioma biphasic mesothelioma biphasic pleural mesothelioma pleural biphasic mesothelioma PLBMESO
	DES	desmoid tumor aggressive fibromatosis desmoid fibromatosis extra-abdominal desmoid tumor desmoid-type fibromatosis DES
	SYNS	synovial sarcoma synovial sarcoma with biphasic morphology monophasic synovial sarcoma synovial sarcoma, high grade SYNS
	SFT	solitary fibrous tumor hemangiopericytoma solitary fibrous tumor of the pleura hemangiopericytoma of the soft tissue SFT
	MAAP	mucinous adenocarcinoma of the appendix appendiceal mucinous adenocarcinoma mucinous carcinoma of the appendix MAAP
	ECAD	endocervical adenocarcinoma adenocarcinoma of the cervix cervical adenocarcinoma ECAD
	MYCF	mycosis fungoides cutaneous T-cell lymphoma mycosis fungoides/Sezary syndrome MF
	CHS	chondrosarcoma primary chondrosarcoma secondary chondrosarcoma dedifferentiated chondrosarcoma chondrosarcoma of bone CHS
	ANGS	angiosarcoma vascular sarcoma hemangiosarcoma angiosarcoma of soft tissue ANGS
	PAST	pilocytic astrocytoma juvenile pilocytic astrocytoma cystic astrocytoma PAST
	MOV	mucinous ovarian cancer mucinous cystadenocarcinoma mucinous neoplasm of the ovary mucinous ovarian carcinoma MOV
	ACYC	adenoid cystic carcinoma cylindroma adenoid cystic adenocarcinoma ACC

Task	Class	Class names
OT108	SCHW	schwannoma neurilemmoma peripheral nerve sheath tumor schwannoma tumor SCHW
	UMEC	mixed endometrial carcinoma uterine mixed endometrial carcinoma mixed carcinoma of the uterine corpus endometrial carcinoma, mixed subtype UMEC
	MPNST	malignant peripheral nerve sheath tumor malignant schwannoma peripheral nerve sheath tumor MPNST
	SBOV	serous borderline ovarian tumor serous borderline tumor borderline serous ovarian neoplasm SBOV
	LUNE	large cell neuroendocrine carcinoma large cell neuroendocrine tumor neuroendocrine carcinoma, large cell type large cell carcinoma with neuroendocrine features LCNEC
	CLLSLL	chronic lymphocytic leukemia small lymphocytic lymphoma chronic lymphocytic leukemia/small lymphocytic lymphoma CLL / SLL
	GRCT	granulosa cell tumor granulosa cell neoplasm granulosa tumor granulosa cell tumor of the ovary GRCT
	THME	medullary thyroid cancer medullary thyroid carcinoma thyroid medullary carcinoma medullary carcinoma of the thyroid MTC
	VSC	squamous cell carcinoma of the vulva squamous cell carcinoma of the vagina vulvar squamous cell carcinoma vaginal squamous cell carcinoma VSC
	THAP	anaplastic thyroid carcinoma anaplastic thyroid cancer undifferentiated thyroid carcinoma THAP
	PGNG	paraganglioma extra-adrenal paraganglioma head and neck paraganglioma carotid body tumor glomus tumor PGNG
	SSRCC	signet ring cell carcinoma signet ring cell carcinoma of the stomach gastric signet ring cell carcinoma signet ring cell gastric cancer SSRCC

Task	Class	Class names
OT108	PECOMA	perivascular epithelioid cell tumor PEComa epithelioid smooth muscle tumor angiomyolipoma clear cell sugar tumor
	WDLS	well-differentiated liposarcoma differentiated liposarcoma liposarcoma, well-differentiated WDLS
	ATM	atypical meningioma meningioma WHO grade II atypical meningeal tumor atypical tumor of the meninges ATM
	ROCY	oncocytoma renal oncocytoma oncocytic tumor of the kidney kidney oncocytoma ROCY
	ERMS	embryonal rhabdomyosarcoma rhabdomyosarcoma, embryonal type embryonal rhabdomyoblastoma ERMS
OT108 & TCGA-OT	ACC	adrenocortical carcinoma adrenal cortical carcinoma adrenal cortex carcinoma ACC
	ASTR	astrocytoma diffuse astrocytoma fibrillary astrocytoma anaplastic astrocytoma grade II astrocytoma grade III astrocytoma ASTR
	BLCA	urothelial carcinoma bladder urothelial carcinoma transitional cell carcinoma bladder cancer BLCA
	CCRCC	clear cell carcinoma renal clear cell carcinoma clear cell renal cell carcinoma clear cell RCC CCRCC
	CHRC	chromophobe renal cell carcinoma chromophobe RCC chromophobe carcinoma renal cell carcinoma, chromophobe type CHRC
	COAD	colon adenocarcinoma adenocarcinoma of the colon colorectal adenocarcinoma COAD
	DDL	dedifferentiated liposarcoma dedifferentiated liposarcoma variant liposarcoma, dedifferentiated DDL

Task	Class	Class names
OT108 & TCGA-OT	COAD	colon adenocarcinoma adenocarcinoma of the colon colorectal adenocarcinoma COAD
	DDLS	dedifferentiated liposarcoma dedifferentiated liposarcoma variant liposarcoma, dedifferentiated DDLS
	ESCA	esophageal adenocarcinoma adenocarcinoma of the esophagus esophageal cancer, adenocarcinoma type ESCA
	ESCC	esophageal squamous cell carcinoma esophageal SCC squamous cell carcinoma of the esophagus SCC of the esophagus ESCC
	GBM	glioblastoma multiforme glioblastoma GBM multiforme glioblastoma grade IV astrocytoma
	HCC	hepatocellular carcinoma liver cancer hepatoma HCC
	HGSOC	high-grade serous ovarian cancer high-grade serous carcinoma HGSOC serous papillary carcinoma serous ovarian carcinoma
	HNSC	head and neck squamous cell carcinoma HNSCC head and neck SCC oropharyngeal squamous cell carcinoma laryngeal squamous cell carcinoma hypopharyngeal squamous cell carcinoma nasopharyngeal squamous cell carcinoma oral cavity squamous cell carcinoma HNSC
	IDC	invasive ductal carcinoma breast invasive ductal carcinoma ductal carcinoma, no special type IDC
	ILC	invasive lobular carcinoma breast invasive lobular carcinoma invasive lobular carcinoma of the breast lobular carcinoma breast ILC
	LMS	leiomyosarcoma smooth muscle sarcoma leiomyosarcoma of the soft tissue LMS
	LUAD	lung adenocarcinoma adenocarcinoma of the lung pulmonary adenocarcinoma peripheral lung adenocarcinoma LUAD

Task	Class	Class names
OT108 & TCGA-OT	LUSC	squamous cell carcinoma lung squamous cell carcinoma squamous carcinoma of the lung LUSC
	MEL	acral melanoma melanoma acral lentiginous melanoma MEL
	MFH	undifferentiated pleomorphic sarcoma malignant fibrous histiocytoma high-grade spindle cell sarcoma MFH
	PAAD	pancreatic adenocarcinoma adenocarcinoma of the pancreas pancreas adenocarcinoma PAAD
	PLEMESO	pleural mesothelioma epithelioid mesothelioma epithelioid pleural mesothelioma pleural mesothelioma, epithelioid type PLEMESO
	PRAD	prostate adenocarcinoma adenocarcinoma of the prostate prostatic adenocarcinoma PRAD
	PRCC	papillary renal cell carcinoma renal cell carcinoma, papillary type papillary RCC PRCC
	READ	rectal adenocarcinoma adenocarcinoma of the rectum rectal cancer READ
	STAD	diffuse type stomach adenocarcinoma diffuse gastric adenocarcinoma diffuse-type gastric cancer gastric adenocarcinoma, diffuse type STAD
	THPA	papillary thyroid carcinoma papillary thyroid cancer papillary thyroid neoplasm thyroid papillary carcinoma PTC
	UCS	uterine carcinosarcoma uterine malignant mixed Müllerian tumor malignant mixed Müllerian tumor carcinosarcoma of the uterus UCS
	UEC	endometrioid carcinoma uterine endometrioid carcinoma endometrial endometrioid carcinoma endometrial carcinoma, endometrioid type UEC
	USC	uterine serous carcinoma uterine papillary serous carcinoma serous papillary carcinoma of the uterus serous carcinoma USC

Task	Class	Class names
OT108 & TCGA-OT	THFO	follicular thyroid carcinoma follicular thyroid cancer follicular carcinoma of the thyroid thyroid follicular cancer THFO
	AASTR	anaplastic astrocytoma astrocytoma, anaplastic grade III astrocytoma AASTR
	CESC	squamous cell carcinoma of the cervix cervical squamous cell carcinoma cervical SCC CESC
	ODG	oligodendroglioma oligodendroglial tumor oligodendroglioma grade II oligodendroglioma grade III ODG
	MACR	mucinous adenocarcinoma mucinous adenocarcinoma of the colon mucinous adenocarcinoma of the rectum mucinous colorectal adenocarcinoma MACR
	SEM	seminoma testicular seminoma pure seminoma classic seminoma seminomatous germ cell tumor SEM
	MFS	myxofibrosarcoma myxoid fibrosarcoma myxofibrosarcomatosis MFS
TCGA-OT	THYM	thymoma thymic tumor thymic carcinoma thymic epithelial neoplasm THYM
	NSGCT	non-seminomatous germ cell tumor germ cell tumor, non-seminomatous mixed germ cell tumor embryonal carcinoma yolk sac tumor teratoma NSGCT
	OAST	oligoastrocytoma oligoastrocytic tumor oligodendroglial-astrocytic tumor OAST
	PHC	pheochromocytoma chromaffin cell tumor adrenal pheochromocytoma paraganglioma PHC
	DSTAD	diffuse type adenocarcinoma of the stomach diffuse stomach adenocarcinoma diffuse gastric adenocarcinoma stomach adenocarcinoma, diffuse type DSTAD

Task	Class	Class names
TCGA-OT	AOAST	anaplastic oligoastrocytoma oligoastrocytoma anaplastic mixed glioma AOAST
	UM	uveal melanoma uvea melanoma ocular melanoma choroidal melanoma ciliary body melanoma iris melanoma UM
	SKCM	cutaneous melanoma skin melanoma melanoma of the skin malignant melanoma SKCM
	TSTAD	tubular stomach adenocarcinoma tubular adenocarcinoma of the stomach stomach tubular adenocarcinoma gastric tubular adenocarcinoma TSTAD

Supplementary Table 92: Class prompts for OT-108 and TCGA-OncoTree subtyping.

Class	Class names
Adrenocortical carcinoma	adrenocortical carcinoma adrenal cortex cancer adrenal cortical carcinoma ACC
Bladder Urothelial Carcinoma	bladder urothelial carcinoma bladder cancer urothelial carcinoma of the bladder BUC
Brain Lower Grade Glioma	brain lower grade glioma low grade glioma brain glioma with low grade BLGG
Breast invasive carcinoma	breast invasive carcinoma breast cancer invasive carcinoma of the breast BIC
Cervical squamous cell carcinoma and endocervical adenocarcinoma	cervical squamous cell carcinoma cervical cancer endocervical adenocarcinoma cervical carcinoma
Cholangiocarcinoma	cholangiocarcinoma bile duct cancer cholangiocellular carcinoma CCA
Colon adenocarcinoma	colon adenocarcinoma colon cancer adenocarcinoma in the colon COAD
Esophageal carcinoma	esophageal carcinoma esophageal cancer esophageal squamous cell carcinoma ESCA
Glioblastoma multiforme	glioblastoma multiforme GBM brain tumor glioblastoma
Head and Neck squamous cell carcinoma	head and neck squamous cell carcinoma head and neck cancer HNSCC
Kidney Chromophobe	kidney chromophobe chromophobe renal cell carcinoma KICH
Kidney renal clear cell carcinoma	kidney renal clear cell carcinoma clear cell renal cell carcinoma KIRC CCRCC
Kidney renal papillary cell carcinoma	kidney renal papillary cell carcinoma papillary renal cell carcinoma KIRP PRCC
Liver hepatocellular carcinoma	liver hepatocellular carcinoma hepatocellular carcinoma hepatocellular carcinoma in the liver LIHC HCC
Lung adenocarcinoma	lung adenocarcinoma adenocarcinoma of the lung LUAD
Lung squamous cell carcinoma	lung squamous cell carcinoma squamous cell carcinoma of the lung LUSC

Class	Class names
Lymphoid Neoplasm Diffuse Large B-cell Lymphoma	lymphoid neoplasm diffuse large B-cell lymphoma diffuse large B-cell lymphoma DLBCL DLBC
Mesothelioma	mesothelioma cancer in the mesothelium MESO
Ovarian serous cystadenocarcinoma	ovarian serous cystadenocarcinoma serous cystadenocarcinoma OV
Pancreatic adenocarcinoma	pancreatic adenocarcinoma adenocarcinoma in the pancreas pancreatic cancer PAAD PDAC
Pheochromocytoma and Paraganglioma	pheochromocytoma and paraganglioma pheochromocytoma paraganglioma PCPG
Prostate adenocarcinoma	prostate adenocarcinoma prostate cancer adenocarcinoma in the prostate PRAD
Rectum adenocarcinoma	rectum adenocarcinoma rectal cancer rectal adenocarcinoma READ
Sarcoma	sarcoma soft tissue sarcoma bone sarcoma SARC
Skin Cutaneous Melanoma	skin cutaneous melanoma cutaneous melanoma skin cancer SKCM
Stomach adenocarcinoma	stomach adenocarcinoma gastric adenocarcinoma gastric cancer STAD
Testicular Germ Cell Tumors	testicular germ cell tumors testicular cancer germ cell tumors TGCT
Thymoma	thymoma thymic carcinoma thymus cancer THYM
Thyroid carcinoma	thyroid carcinoma thyroid cancer carcinoma of the thyroid gland THCA
Uterine Carcinosarcoma	uterine carcinosarcoma carcinosarcoma UCS
Uterine Corpus Endometrial Carcinoma	uterine corpus endometrial carcinoma endometrial carcinoma UCEC
Uveal Melanoma	uveal melanoma eye melanoma ocular melanoma UVM

Supplementary Table 93: Class prompts for TCGA UniformTumor subtyping.

Class	Class names
Glioblastoma, IDH-wildtype	glioblastoma, IDH-wildtype glioblastoma without IDH mutation glioblastoma with retained IDH glioblastoma, IDH retained
Transitional meningioma	transitional meningioma meningioma, transitional type meningioma of transitional type meningioma, transitional
Anaplastic meningioma	anaplastic meningioma meningioma, anaplastic type meningioma of anaplastic type meningioma, anaplastic
Pituitary adenoma	pituitary adenoma adenoma of the pituitary gland pituitary gland adenoma pituitary neuroendocrine tumor neuroendocrine tumor of the pituitary neuroendocrine tumor of the pituitary gland
Oligodendroglioma, IDH-mutant and 1p/19q codeleted	oligodendroglioma, IDH-mutant and 1p/19q codeleted oligodendroglioma oligodendroglioma with IDH mutation and 1p/19q codeletion
Haemangioma	hemangioma haemangioma of the CNS hemangioma of the CNS haemangioma of the central nervous system hemangioma of the central nervous system
Ganglioglioma	gangliocytoma glioneuronal tumor circumscribed glioneuronal tumor
Schwannoma	schwannoma Antoni A Antoni B neurilemoma
Anaplastic oligodendroglioma, IDH-mutant, 1p/19q codeleted	anaplastic oligodendroglioma, IDH-mutant and 1p/19q codeleted anaplastic oligodendroglioma anaplastic oligodendroglioma with IDH mutation and 1p/19q codeletion
Anaplastic astrocytoma, IDH-wildtype	anaplastic astrocytoma, IDH-wildtype anaplastic astrocytoma without IDH mutation anaplastic astrocytoma, IDH retained anaplastic astrocytoma with retained IDH
Pilocytic astrocytoma	pilocytic astrocytoma juvenile pilocytic astrocytoma spongioblastoma pilomyxoid astrocytoma
Angiomatous meningioma	angiomatous meningioma meningioma, angiomatous type meningioma of angiomatous type meningioma, angiomatous
Haemangioblastoma	haemangioblastoma capillary haemangioblastoma lindau tumor angioblastoma
Gliosarcoma	gliosarcoma gliosarcoma variant of glioblastoma
Adamantinomatous craniopharyngioma	adamantinomatous craniopharyngioma craniopharyngioma
Anaplastic astrocytoma, IDH-mutant	anaplastic astrocytoma, IDH-mutant anaplastic astrocytoma with IDH mutation anaplastic astrocytoma with mutant IDH anaplastic astrocytoma with mutated IDH
Ependymoma	ependymoma subependymoma myxopapillary ependymoma

Class	Class names
Anaplastic ependymoma	anaplastic ependymoma ependymoma, anaplastic ependymoma, anaplastic type
Glioblastoma, IDH-mutant	glioblastoma, IDH-mutant glioblastoma with IDH mutation glioblastoma with mutant IDH glioblastoma with mutated IDH
Atypical meningioma	atypical meningioma meningioma, atypical type meningioma of atypical type meningioma, atypical
Metastatic tumours	metastatic tumors metastases to the brain metastatic tumors to the brain brain metastases brain metastatic tumors
Meningothelial meningioma	meningothelial meningioma meningioma, meningothelial type meningioma of meningothelial type meningioma, meningothelial
Langerhans cell histiocytosis	langerhans cell histiocytosis histiocytosis X eosinophilic granuloma Hand-Schüller-Christian disease Hashimoto-Pritzker disease Letterer-Siwe disease
Diffuse large B-cell lymphoma of the CNS	diffuse large B-cell lymphoma of the CNS DLBCL DLBCL of the CNS DLBCL of the central nervous system
Diffuse astrocytoma, IDH-mutant	diffuse astrocytoma, IDH-mutant diffuse astrocytoma with IDH mutation diffuse astrocytoma with mutant IDH diffuse astrocytoma with mutated IDH
Secretory meningioma	secretory meningioma meningioma, secretory type meningioma of secretory type meningioma, secretory
Haemangiopericytoma	haemangiopericytoma solitary fibrous tumor hemangiopericytoma angioblastic meningioma
Fibrous meningioma	fibrous meningioma meningioma, fibrous type meningioma of fibrous type meningioma, fibrous
Lipoma	lipoma CNS lipoma lipoma of the CNS lipoma of the central nervous system
Medulloblastoma, non-WNT/non-SHH	medulloblastoma, non-WNT/non-SHH medulloblastoma medulloblastoma group 3 medulloblastoma group 4

Supplementary Table 94: Class prompts for EBRAINS subtyping.

Task	Class	Class names
Antibody-mediated Rejection (AMR)	AMR	antibody-mediated rejection AMR in kidney transplant acute antibody-mediated rejection chronic antibody-mediated rejection graft rejection caused by donor-specific antibodies complement-mediated kidney allograft rejection kidney transplant rejection with microvascular inflammation C4d-positive antibody-mediated rejection
	no AMR	no antibody-mediated rejection absence of AMR in kidney transplant no evidence of donor-specific antibody-mediated rejection absence of C4d deposition in kidney allograft no signs of complement activation or C4d deposition
T-Cell Mediated Rejection (TCMR)	TCMR	T cell-mediated rejection TCMR in kidney transplant acute T cell-mediated rejection chronic T cell-mediated rejection kidney transplant rejection caused by T cells cellular-mediated rejection inflammatory rejection involving T cells kidney allograft rejection with tubulitis kidney transplant rejection with interstitial inflammation
	no TCMR	no T cell-mediated rejection absence of TCMR in kidney transplant kidney transplant without T cell-mediated rejection no evidence of cellular-mediated rejection absence of tubulitis or interstitial inflammation absence of T cell involvement in kidney transplant rejection

Supplementary Table 95: Class prompts for renal allograft rejection.

Task	Class	Class names
Cellular-mediated Rejection (CMR)	CMR	antibody-mediated rejection CMR in heart transplant acute cellular-mediated rejection cellular rejection detected in endomyocardial biopsy heart transplant rejection involving T cells lymphocytic infiltration in the myocardium interstitial inflammation in the heart tissue rejection driven by cellular immune response
	no CMR	no cellular-mediated rejection absence of CMR in heart transplant no evidence of cellular rejection in endomyocardial biopsy heart tissue with no signs of cellular-mediated rejection absence of interstitial inflammation or lymphocytic infiltration normal endomyocardial biopsy findings without rejection no cellular immune response in the myocardium

Supplementary Table 96: Class prompts for cellular-mediated heart allograft rejection.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	<u>0.536</u> $\pm$ 0.0061	<u>0.599</u> $\pm$ 0.0055	<u>0.966</u> $\pm$ 0.0010
TITAN	0.761 $\pm$ 0.0063	0.798 $\pm$ 0.0043	0.989 $\pm$ 0.0006

Supplementary Table 97: Zero-shot results for tumor subtype ($C = 32$) prediction on TCGA-UT-8K. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	<u>0.459</u> $\pm$ 0.0192	<u>0.537</u> $\pm$ 0.0137	<u>0.973</u> $\pm$ 0.0023
TITAN	0.616 $\pm$ 0.0178	0.713 $\pm$ 0.0127	0.985 $\pm$ 0.0014

Supplementary Table 98: Zero-shot results for OncoTree code ($C = 46$) prediction on TCGA-OT. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	<u>0.330</u> $\pm$ 0.0098	<u>0.296</u> $\pm$ 0.0116	<u>0.959</u> $\pm$ 0.0021
TITAN	0.477 $\pm$ 0.0108	0.452 $\pm$ 0.0133	0.980 $\pm$ 0.0015

Supplementary Table 99: Zero-shot results for OncoTree code ($C = 108$) prediction on OT108. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	<u>0.278</u> $\pm$ 0.0173	<u>0.262</u> $\pm$ 0.0198	<u>0.899</u> $\pm$ 0.0054
TITAN	0.543 $\pm$ 0.0201	0.365 $\pm$ 0.0210	0.968 $\pm$ 0.0025

Supplementary Table 100: Zero-shot results for tumor type ($C = 30$) prediction on EBRAINS. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	<u>0.565</u> $\pm$ 0.0124	<u>0.724</u> $\pm$ 0.0234	<u>0.886</u> $\pm$ 0.0225
TITAN	0.940 $\pm$ 0.0220	0.917 $\pm$ 0.0368	0.985 $\pm$ 0.0154

Supplementary Table 101: Zero-shot results for OncoTree code ($C = 3$) prediction on TCGA-RCC. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	<u>0.435</u> $\pm$ 0.0155	<u>0.862</u> $\pm$ 0.0136	<u>0.839</u> $\pm$ 0.0173
TITAN	0.966 $\pm$ 0.0064	0.940 $\pm$ 0.0074	0.993 $\pm$ 0.0018

Supplementary Table 102: Zero-shot results for OncoTree code ($C = 3$) prediction on CPTAC-CCRCC and DHMC-RCC. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	<u>0.517</u> $\pm$ 0.0507	<u>0.390</u> $\pm$ 0.0460	0.909 $\pm$ 0.0167
TITAN	0.585 $\pm$ 0.0199	0.489 $\pm$ 0.0466	<u>0.859</u> $\pm$ 0.0238

Supplementary Table 103: Zero-shot results for histological pattern ($C = 5$) prediction on DHMC-LUAD. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	0.918 $\pm$ 0.0192	0.918 $\pm$ 0.0194	<u>0.978</u> $\pm$ 0.0062
TITAN	<u>0.907</u> $\pm$ 0.0196	<u>0.906</u> $\pm$ 0.0196	0.985 $\pm$ 0.0039

Supplementary Table 104: Zero-shot results for tumor subtype ($C = 2$) prediction on TCGA-NSCLC. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	0.938 $\pm$ 0.0069	0.936 $\pm$ 0.0072	0.982 $\pm$ 0.0037
TITAN	<u>0.919</u> $\pm$ 0.0078	<u>0.916</u> $\pm$ 0.0083	<u>0.981</u> $\pm$ 0.0044

Supplementary Table 105: Zero-shot results for tumor subtype ($C = 2$) prediction on CPTAC-NSCLC. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	<u>0.894</u> $\pm$ 0.0135	<u>0.895</u> $\pm$ 0.0213	<u>0.944</u> $\pm$ 0.0146
TITAN	0.895 $\pm$ 0.0254	0.903 $\pm$ 0.0216	0.952 $\pm$ 0.0167

Supplementary Table 106: Zero-shot results for tumor subtype ($C = 2$) prediction on TCGA-BRCA. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	0.612 $\pm$ 0.0127	0.569 $\pm$ 0.0183	<u>0.699</u> $\pm$ 0.0165
TITAN	<u>0.603</u> $\pm$ 0.0103	<u>0.528</u> $\pm$ 0.0193	0.801 $\pm$ 0.0136

Supplementary Table 107: Zero-shot results for cellular rejection ($C = 2$) prediction on CRANE. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	<u>0.562</u> $\pm$ 0.0144	<u>0.610</u> $\pm$ 0.0194	<u>0.627</u> $\pm$ 0.0193
TITAN	0.737 $\pm$ 0.0159	0.732 $\pm$ 0.0153	0.784 $\pm$ 0.0154

Supplementary Table 108: Zero-shot results for cellular rejection ($C = 2$) prediction on Renal allograft rejection. The best result is marked in bold and the second best is underlined.

Encoder	Bal. acc.	Weighted F1	AUROC
PRISM	<u>0.584</u> $\pm$ 0.0179	<u>0.573</u> $\pm$ 0.0163	<u>0.576</u> $\pm$ 0.0210
TITAN	0.693 $\pm$ 0.0148	0.633 $\pm$ 0.0166	0.762 $\pm$ 0.0159

Supplementary Table 109: Zero-shot results for antibody-mediated rejection ($C = 2$) prediction on Renal allograft rejection. The best result is marked in bold and the second best is underlined.

Encoder	S1	S2	S3	Logistic regression		SimpleShot		20-nearest neighbors	
				Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V	✓			0.820 $\pm$ 0.0055	0.870 $\pm$ 0.0037	0.818 $\pm$ 0.0053	0.864 $\pm$ 0.0039	0.812 $\pm$ 0.0050	0.842 $\pm$ 0.0038
TITAN	✓	✓		<u>0.827</u> $\pm$ 0.0056	<u>0.875</u> $\pm$ 0.0038	0.817 $\pm$ 0.0057	0.866 $\pm$ 0.0039	0.822 $\pm$ 0.0060	0.839 $\pm$ 0.0041
TITAN	✓		✓	0.832 $\pm$ 0.0055	0.881 $\pm$ 0.0036	0.821 $\pm$ 0.0057	0.864 $\pm$ 0.0039	0.829 $\pm$ 0.0053	<u>0.857</u> $\pm$ 0.0039
TITAN _L		✓	✓	<u>0.827</u> $\pm$ 0.0053	0.873 $\pm$ 0.0038	<u>0.822</u> $\pm$ 0.0053	<u>0.867</u> $\pm$ 0.0038	<u>0.834</u> $\pm$ 0.0057	0.848 $\pm$ 0.0040
MH-ABMIL _L		✓	✓	0.815 $\pm$ 0.0054	0.862 $\pm$ 0.0038	0.801 $\pm$ 0.0056	0.850 $\pm$ 0.0040	0.823 $\pm$ 0.0059	0.833 $\pm$ 0.0040
TITAN	✓	✓	✓	0.832 $\pm$ 0.0056	0.881 $\pm$ 0.0036	0.828 $\pm$ 0.0052	0.875 $\pm$ 0.0037	0.843 $\pm$ 0.0056	0.865 $\pm$ 0.0037

Supplementary Table 110: Ablation study of vision-language design. Linear probing results for tumor subtype ($C = 32$) prediction on TCGA-UT-8K. The best result is marked in bold and the second best is underlined.

Encoder	S1	S2	S3	Logistic regression		SimpleShot		20-nearest neighbors	
				Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V	✓			0.690 $\pm$ 0.0196	0.758 $\pm$ 0.0123	0.639 $\pm$ 0.0149	0.744 $\pm$ 0.0124	0.706 $\pm$ 0.0183	0.775 $\pm$ 0.0116
TITAN	✓	✓		0.651 $\pm$ 0.0163	0.733 $\pm$ 0.0127	0.646 $\pm$ 0.0162	0.716 $\pm$ 0.0130	0.674 $\pm$ 0.0190	0.723 $\pm$ 0.0123
TITAN	✓		✓	<u>0.693</u> $\pm$ 0.0161	0.752 $\pm$ 0.0119	0.666 $\pm$ 0.0177	0.756 $\pm$ 0.0120	0.755 $\pm$ 0.0159	<u>0.801</u> $\pm$ 0.0107
TITAN _L		✓	✓	0.685 $\pm$ 0.0156	<u>0.761</u> $\pm$ 0.0120	0.699 $\pm$ 0.0159	0.775 $\pm$ 0.0121	0.731 $\pm$ 0.0168	0.799 $\pm$ 0.0111
MH-ABMIL _L		✓	✓	0.663 $\pm$ 0.0160	0.760 $\pm$ 0.0123	0.636 $\pm$ 0.0176	0.740 $\pm$ 0.0125	0.719 $\pm$ 0.0173	0.773 $\pm$ 0.0116
TITAN	✓	✓	✓	0.704 $\pm$ 0.0192	0.764 $\pm$ 0.0116	<u>0.685</u> $\pm$ 0.0183	<u>0.774</u> $\pm$ 0.0119	<u>0.744</u> $\pm$ 0.0152	0.802 $\pm$ 0.0108

Supplementary Table 111: Ablation study of vision-language design. Linear probing results for OncoTree code ($C = 46$) prediction on TCGA-OT. The best result is marked in bold and the second best is underlined.

Encoder	S1	S2	S3	Logistic regression		SimpleShot		20-nearest neighbors	
				Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V	✓			0.558±0.0104	0.536±0.0127	0.464±0.0105	0.430±0.0128	0.524±0.0106	0.517±0.0129
TITAN	✓	✓		0.539±0.0108	0.519±0.0131	0.452±0.0101	0.413±0.0130	0.508±0.0109	0.501±0.0130
TITAN	✓		✓	<u>0.564</u> ±0.0103	<u>0.540</u> ±0.0128	0.498±0.0103	0.458±0.0134	0.553±0.0108	0.542±0.0130
TITAN _L		✓	✓	0.559±0.0107	0.538±0.0130	<u>0.515</u> ±0.0101	<u>0.475</u> ±0.0135	<u>0.569</u> ±0.0108	<u>0.557</u> ±0.0135
MH-ABMIL _L		✓	✓	0.557±0.0109	0.535±0.0130	0.491±0.0102	0.452±0.0131	0.550±0.0109	0.540±0.0136
TITAN	✓	✓	✓	0.587 ±0.0103	0.563 ±0.0130	0.527 ±0.0101	0.489 ±0.0132	0.580 ±0.0103	0.567 ±0.0129

Supplementary Table 112: Ablation study of vision-language design. Linear probing results for OncoTree code ($C = 108$) prediction on OT108. The best result is marked in bold and the second best is underlined.

Encoder	S1	S2	S3	Logistic regression		SimpleShot		20-nearest neighbors	
				Bal. acc.	Weighted F1	Bal. acc.	Weighted F1	Bal. acc.	Weighted F1
TITAN _V	✓			0.732±0.0208	0.785±0.0175	0.656±0.0187	0.709±0.0199	<u>0.742</u> ±0.0192	<u>0.727</u> ±0.0182
TITAN	✓	✓		0.707±0.0212	0.766±0.0187	0.596±0.0211	0.664±0.0213	0.654±0.0216	0.634±0.0203
TITAN	✓		✓	<u>0.734</u> ±0.0212	0.791 ±0.0169	<u>0.685</u> ±0.0202	<u>0.739</u> ±0.0197	0.725±0.0208	0.721±0.0191
TITAN _L		✓	✓	0.725±0.0206	0.771±0.0178	0.682±0.0196	0.733±0.0198	0.712±0.0214	0.704±0.0192
MH-ABMIL _L		✓	✓	0.724±0.0204	0.779±0.0189	0.642±0.0204	0.706±0.0210	0.711±0.0217	0.707±0.0189
TITAN	✓	✓	✓	0.735 ±0.0204	<u>0.786</u> ±0.0182	0.695 ±0.0196	0.746 ±0.0200	0.754 ±0.0203	0.748 ±0.0182

Supplementary Table 113: Ablation study of vision-language design. Linear probing results for tumor type ($C = 30$) prediction on EBRAINS. The best result is marked in bold and the second best is underlined.

OncoTreeCode	# samples
AASTR	214
ACC	256
AM	31
ANM	46
ANSC	57
AODG	30
ASTR	167
ATM	83
CCM	13
CCOV	59
CEMU	17
CHOL	34
CHOM	12
CHRCC	131
ECAD	24
EMBCA	35
EOV	61
ESCC	135
FM	57
GBC	59
IHCH	32
LNET	11
LUCA	59
LUNE	26
MBC	13
MGM	104
MM	21
MPNST	27
ODG	256
PAAD	248
PANET	71
PAST	34
PGNG	31
PLBMESO	19
PSM	26
SM	41
SYNS	20
THAP	28
THFO	135
THME	34
USC	171
UTUC	58
WT	53

Supplementary Table 114: Overview of the dataset Rare-Cancers with 43 OncoTree codes.

Oncotree code	#samples
AASTR	164
ACC	227
AM	31
ANM	46
ASTR	104
ATM	83
CCM	13
CEMU	17
CHOM	12
CH RCC	109
ECAD	24
EMBCA	35
ESCC	92
FM	57
IHCH	32
MBC	13
MGM	104
MM	21
MPNST	27
ODG	203
PAAD	194
PANET	8
PGNG	31
PLBMESO	19
PSM	26
SM	41
SYNS	20
THFO	109
USC	120

Supplementary Table 115: Overview of the dataset Rare-Cancers-Public with 29 OncoTree codes.

Tissue Site	Oncotree code	#samples
Ovary	GRCT	5
	MOV	4
	CCOV	5
	EOV	4
	OCS	2
	LGSOC	1
	MXOV	1
Soft Tissue	SFT	5
	DDLS	6
	SYNS	4
	PECOMA	1
	LMS	1

Supplementary Table 116: Overview of the dataset Rare-Cancers-External with 12 OncoTree codes grouped by two tissue sites, collected at Department of Pathology, Kanagawa Cancer Center Hospital, Japan.

Encoder	Top-1 acc.	Top-3 acc.	MV@3 acc.	Top-5 acc.	MV@5 acc.
GigaPath	0.384±0.0102	0.574±0.0086	0.486±0.0050	0.669±0.0108	0.465±0.0065
PRISM	0.449±0.0135	0.634±0.0216	0.540±0.0174	0.717±0.0238	0.519±0.0201
CHIEF	0.333±0.0166	0.523±0.0139	0.446±0.0135	0.618±0.0090	0.430±0.0138
TITAN _v	0.520±0.0184	<u>0.711</u> ±0.0097	0.607±0.0143	<u>0.791</u> ±0.0094	0.594±0.0090
TITAN	0.539 ±0.0100	0.725 ±0.0125	0.631 ±0.0221	0.804 ±0.0099	0.620 ±0.0156

Supplementary Table 117: Slide retrieval results for rare cancer retrieval ($C = 43$) prediction on Rare-Cancer. The best result is marked in bold and the second best is underlined.

Encoder	Top-1 acc.	Top-3 acc.	MV@3 acc.	Top-5 acc.	MV@5 acc.	Top-10 acc.	MV@10 acc.
GigaPath	0.051±0.0000	0.103±0.0000	0.103±0.0000	0.149±0.0103	0.123±0.0103	0.231±0.0000	0.072±0.0103
PRISM	0.000±0.0000	0.021±0.0103	0.021±0.0103	0.026±0.0000	0.021±0.0103	0.051±0.0000	0.021±0.0103
CHIEF	0.000±0.0000	0.000±0.0000	0.000±0.0000	0.021±0.0103	0.021±0.0103	0.021±0.0103	0.000±0.0000
TITAN _V	0.456 ±0.0103	0.682 ±0.0126	0.559 ±0.0103	0.754 ±0.0205	0.610 ±0.0103	0.754 ±0.0205	0.513 ±0.0000
TITAN	<u>0.359</u> ±0.0000	<u>0.518</u> ±0.0103	<u>0.415</u> ±0.0192	<u>0.585</u> ±0.0103	<u>0.390</u> ±0.0192	<u>0.631</u> ±0.0126	<u>0.436</u> ±0.0000

Supplementary Table 118: Slide retrieval results for rare cancer retrieval ($C = 12$) prediction on Rare-Cancer-External. The best result is marked in bold and the second best is underlined.

Encoder	Top-1 acc.	Top-3 acc.	MV@3 acc.	Top-5 acc.	MV@5 acc.
GigaPath	0.420±0.0285	0.618±0.0258	0.507±0.0273	0.713±0.0141	0.481±0.0313
PRISM	0.482±0.0353	0.663±0.0334	0.547±0.0375	0.757±0.0372	0.530±0.0327
CHIEF	0.380±0.0336	0.563±0.0455	0.470±0.0197	0.654±0.0357	0.446±0.0202
TITAN _V	<u>0.549</u> ±0.0236	<u>0.743</u> ±0.0269	<u>0.614</u> ±0.0301	<u>0.814</u> ±0.0273	<u>0.601</u> ±0.0370
TITAN	0.555 ±0.0289	0.754 ±0.0126	0.647 ±0.0244	0.832 ±0.0192	0.636 ±0.0187

Supplementary Table 119: Slide retrieval results for rare cancer retrieval ($C = 29$) prediction on Rare-Cancer-Public. The best result is marked in bold and the second best is underlined.

Encoder	Top-1 acc.	Top-3 acc.	MV@3 acc.	Top-5 acc.	MV@5 acc.
Mean pool (CONCHv1.5)	0.776±0.0047	0.866±0.0038	0.807±0.0044	0.893±0.0035	0.804±0.0044
GigaPath	0.605±0.0053	0.728±0.0049	0.645±0.0052	0.784±0.0047	0.646±0.0054
PRISM	0.754±0.0046	0.854±0.0037	0.788±0.0044	0.888±0.0033	0.787±0.0044
CHIEF	0.552±0.0054	0.690±0.0050	0.609±0.0053	0.755±0.0046	0.613±0.0054
TITAN _V	<u>0.838</u> ±0.0041	<u>0.898</u> ±0.0034	<u>0.857</u> ±0.0039	<u>0.920</u> ±0.0030	<u>0.864</u> ±0.0038
TITAN	0.854 ±0.0039	0.912 ±0.0032	0.875 ±0.0036	0.931 ±0.0028	0.876 ±0.0036

Supplementary Table 120: Slide retrieval results for tumor subtype ($C = 32$) prediction on TCGA-UT-8K. The best result is marked in bold and the second best is underlined.

Encoder	Top-1 acc.	Top-3 acc.	MV@3 acc.	Top-5 acc.	MV@5 acc.
Mean pool (CONCHv1.5)	0.649±0.0133	0.803±0.0108	0.712±0.0125	0.864±0.0095	0.711±0.0125
GigaPath	0.483±0.0135	0.666±0.0123	0.572±0.0129	0.732±0.0118	0.565±0.0136
PRISM	0.697±0.0126	0.836±0.0098	0.755±0.0116	0.878±0.0086	0.749±0.0116
CHIEF	0.479±0.0136	0.669±0.0124	0.602±0.0132	0.742±0.0118	0.573±0.0134
TITAN _V	<u>0.732</u> ±0.0123	<u>0.852</u> ±0.0096	<u>0.773</u> ±0.0115	<u>0.902</u> ±0.0080	<u>0.766</u> ±0.0118
TITAN	0.775 ±0.0112	0.880 ±0.0086	0.807 ±0.0103	0.910 ±0.0078	0.808 ±0.0106

Supplementary Table 121: Slide retrieval results for OncoTree code ($C = 46$) prediction on TCGA-OT. The best result is marked in bold and the second best is underlined.

Encoder	Top-1 acc.	Top-3 acc.	MV@3 acc.	Top-5 acc.	MV@5 acc.
Mean pool (CONCHv1.5)	0.402±0.0123	0.546±0.0126	0.494±0.0128	0.619±0.0123	0.473±0.0127
GigaPath	0.293±0.0115	0.450±0.0124	0.414±0.0121	0.535±0.0122	0.429±0.0119
PRISM	0.452±0.0125	0.636±0.0126	0.547±0.0127	0.708±0.0119	0.519±0.0128
CHIEF	0.264±0.0112	0.442±0.0131	0.400±0.0129	0.519±0.0127	0.386±0.0126
TITAN _V	<u>0.490</u> ±0.0124	<u>0.666</u> ±0.0122	<u>0.587</u> ±0.0125	<u>0.730</u> ±0.0113	<u>0.556</u> ±0.0130
TITAN	0.537 ±0.0129	0.707 ±0.0116	0.621 ±0.0126	0.768 ±0.0108	0.606 ±0.0126

Supplementary Table 122: Slide retrieval results for OncoTree code ($C = 108$) prediction on OT108. The best result is marked in bold and the second best is underlined.

Encoder	Top-1 acc.	Top-3 acc.	MV@3 acc.	Top-5 acc.	MV@5 acc.
Mean pool (CONCHv1.5)	0.633±0.0203	0.813±0.0163	0.719±0.0190	0.873±0.0140	0.710±0.0193
GigaPath	0.593±0.0206	0.806±0.0163	0.733±0.0180	0.860±0.0142	0.705±0.0189
PRISM	0.648±0.0196	0.811±0.0160	0.751±0.0177	0.867±0.0143	0.720±0.0188
CHIEF	0.479±0.0207	0.713±0.0181	0.631±0.0193	0.776±0.0169	0.625±0.0197
TITAN _V	<u>0.687</u> ±0.0191	<u>0.848</u> ±0.0150	<u>0.776</u> ±0.0180	<u>0.904</u> ±0.0123	<u>0.763</u> ±0.0181
TITAN	0.750 ±0.0185	0.865 ±0.0147	0.809 ±0.0168	0.911 ±0.0123	0.811 ±0.0167

Supplementary Table 123: Slide retrieval results for tumor type ($C = 30$) prediction on EBRAINS. The best result is marked in bold and the second best is underlined.

Encoder	Top-1 acc.	Top-3 acc.	MV@3 acc.	Top-5 acc.	MV@5 acc.
Mean pool (CONCHv1.5)	0.672±0.0158	0.884±0.0113	0.689±0.0155	0.945±0.0079	0.699±0.0158
GigaPath	0.608±0.0170	0.857±0.0116	0.630±0.0162	0.938±0.0082	0.636±0.0162
PRISM	0.644±0.0171	<u>0.887</u> ±0.0107	0.666±0.0167	0.942±0.0080	0.691±0.0157
CHIEF	0.621±0.0167	0.848±0.0119	0.646±0.0162	0.943±0.0077	0.632±0.0164
TITAN _v	<u>0.712</u> ±0.0160	0.881±0.0113	<u>0.723</u> ±0.0157	<u>0.949</u> ±0.0076	<u>0.756</u> ±0.0153
TITAN	0.789 ±0.0147	0.919 ±0.0094	0.785 ±0.0146	0.963 ±0.0066	0.791 ±0.0144

Supplementary Table 124: Slide retrieval results for antibody-mediated rejection ($C = 2$) prediction on Renal allograft rejection. The best result is marked in bold and the second best is underlined.

Tissue Site	Oncotree code	#samples
Adrenal Gland	ACC	221
	PHC	155
	MNET	1
Biliary tract	IHCH	30
	PHCH	4
	EHCH	2
	CHOL	1
Bladder	BLCA	424
Bone	LMS	3
	DLBCLNOS	1
Bowel	COAD	347
	READ	149
	MACR	53
	DLBCLNOS	5
	COADREAD	3
	DDLS	3
Brain	GBM	521
	OAST	203
	ODG	184
	AASTR	153
	AOAST	148
	ASTR	96
Breast	IDC	788
	ILC	203
	MDLC	27
	IMMC	16
	MBC	12
	BRCA	6
	PD	3
	MPT	2
	SPC	2
	BRCNOS	1
	BCC	1
	ACBC	1
	DLBCLNOS	1
Cervix	CESC	219
	ECAD	21
	CEMU	13
	CEAS	4
	CEEN	3
Eye	UM	64
	PHC	1
Head and neck	HNSC	464
	PGNG	2
	LMS	1
	DLBCLNOS	1
Heart	PGNG	1
Kidney	CCRCC	504
	PRCC	284
	CHRC	108
	SYNS	5
	MFH	2
Liver	HCC	326
	HCCIHCH	7
	FLC	3
Lung	LUAD	500
	LUSC	476
	PLEMESO	1
Lymph	DLBCLNOS	25
	PGNG	1

Supplementary Table 125: Overview of the dataset TCGA-Slide-Reports with 89 OncoTree codes grouped by 30 tissue sites.

Encoder	Recall@1	Recall@3	Recall@5	Recall@10	Mean recall
PRISM	<u>0.674</u> ±0.0048	<u>0.818</u> ±0.0039	<u>0.857</u> ±0.0035	<u>0.910</u> ±0.0028	<u>0.815</u> ±0.0032
TITAN	0.784 ±0.0042	0.906 ±0.0029	0.938 ±0.0024	0.972 ±0.0017	0.900 ±0.0023

Supplementary Table 126: Cross-modal retrieval results (report-to-slide) on TCGA-Slide-Reports. The best result is marked in bold and the second best is underlined.

Encoder	Recall@1	Recall@3	Recall@5	Recall@10	Mean recall
PRISM	<u>0.552</u> ± 0.0051	<u>0.693</u> ± 0.0046	<u>0.744</u> ± 0.0043	<u>0.807</u> ± 0.0039	<u>0.699</u> ± 0.0040
TITAN	0.752 ± 0.0042	0.838 ± 0.0037	0.871 ± 0.0033	0.908 ± 0.0028	0.842 ± 0.0031

Supplementary Table 127: Cross-modal retrieval results (slide-to-report) on TCGA-Slide-Reports. The best result is marked in bold and the second best is underlined.