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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☐	☒	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	To collect and process histopathological images, Python (version 3.13.5) was used along with the following libraries and tools: Aslide (https://github.com/MrPeterJin/ASlide) to handle various WSI formats, CLAM (https://github.com/mahmoodlab/CLAM) for tissue segmentation, and PyTorch (version 2.8.0) for model development.
Data analysis	We utilized Python (version 3.13.5) and PyTorch (version 2.8.0) to conduct model pretraining and downstream task evaluation. For compared foundation models, we strictly adhered to the original implementations as described in their respective publications to extract generalizable features. For task agnostic pretraining, we used 8 NVIDIA H800 GPUs, while downstream task training and evaluation were performed on NVIDIA 3090 GPUs. The vision transformer architecture was implemented using the timm library (version 1.0.16), and its weights were initialized with those from Virchow2. The peft library (version 0.15.2) was employed to implement LoRA modules. The weights and codes of compared foundation model were obtained from Hugging Face (https://huggingface.co/). Data analysis was conducted in R version 4.2.1 (2022-06-23) and Python 3.13.5 usint the numpy (version 2.2.3), scipy (version 1.15.3) and scikit-learn (version 1.7.0) packages.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The TCGA whole-slide images and associated clinical data can be accessed through the NIH Genomic Data Commons (https://portal.gdc.cancer.gov). Whole-slide images and clinical data from the internal and external cohorts are not publicly available owing to institutional policies and patient privacy regulations, but were collected under Institutional Review Board approvals. Access to these datasets for non-commercial academic use may be requested from the corresponding author. All other data supporting the findings of this study are available within the article and its Supplementary Information files.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	Sex and gender characteristics of the study are available in Supplementary Tables S1.1-1.11. Sex or gender was not included as a covariate at any stage of our experimental analysis.
Reporting on race, ethnicity, or other socially relevant groupings	Race, ethnicity and other socially relevant groupings were not collected from the patients and were unrelated to model implementation or deployment.
Population characteristics	Population characteristics of this study are available in Supplementary Tables S1.1-1.11.
Recruitment	Recruitment was not necessary for the retrospective datasets in this study. For the prospective real-world deployment study of CRISP, patients undergoing thyroid, breast, or lung surgery with intraoperative consultation at Sun Yat-sen University Cancer Center were recruited between November 2024 and July 2025, representing the most common sites for intraoperative consultation.
Ethics oversight	This study was approved by the Ethics Committee of Sun Yat-sen University Cancer Center (Approval No. SL-B2024-708-03) and carried out in compliance with the Declaration of Helsinki.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	For model pre-training, we utilized 81,667 frozen section slides , generating over 50 million pathological image patches. An additional 20,129 slides were used for retrospective and prospective performance validation, resulting in a total of 101,796 frozen section slides. The sample size was determined by data availability.
Data exclusions	Cases were excluded if they met any of the following: (1) no available intraoperative frozen section; (2) absence of identifiable tissue on the slide; (3) presence of scanning artifacts such as defocus or blurring; or (4) incomplete diagnostic or clinical information.
Replication	Additional replication was unnecessary, as the models were validated using five independent medical center cohorts and one prospective cohort, demonstrating consistent performance across all validation sets.
Randomization	Samples were randomly split into development and validation datasets. The splits were stratified by class to ensure similar class proportions across splits. For patients with multiple slides, all slides from the same patient were assigned to the same dataset to maintain patient-level independence.
Blinding	All data were anonymized prior to processing to ensure the removal of any patient-identifiable information.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	The study was registered in the Chinese Clinical Trial Registry (ChiCTR; http://www.chictr.org.cn/) under the registration number ChiCTR2500106350.
Study protocol	Study protocols can be found in http://www.chictr.org.cn/.
Data collection	For the prospective real-world deployment study of CRISP, patients undergoing thyroid, breast, or lung surgery with intraoperative consultation at Sun Yat-sen University Cancer Center were recruited between November 2024 and July 2025, representing the most common sites for intraoperative consultation. Inclusion criteria were: (1) at least one available intraoperative frozen section; (2) presence of identifiable tissue on the slide; (3) absence of scanning artifacts such as defocus or blurring; (4) complete diagnostic and clinical information; (5) age ≥18 years at the time of surgery; and (6) documented informed consent. Following screening, a total of 2,071 patients with 4,143 intraoperative frozen sections were included. Based on the tissue site, patients were assigned to three prospective cohorts: PCS-THYR (n=1,330), PCS-BREA (n=391), and PCS-LUNG (n=350).
Outcomes	The primary outcome of this study was the patients' diagnostic information. The diagnostic reference standard for each patient was established based on the postoperative FFPE pathology report in combination with immunohistochemistry and molecular test results, and independently verified by a board-certified pathologist blinded to the study.

Plants

Seed stocks	NA
Novel plant genotypes	NA
Authentication	NA