Predicting Endometrial Cancer Subtypes and Molecular Features from Histopathology Images Using Multi-resolution Deep Learning Models

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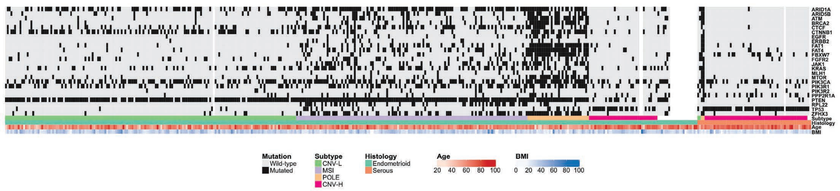
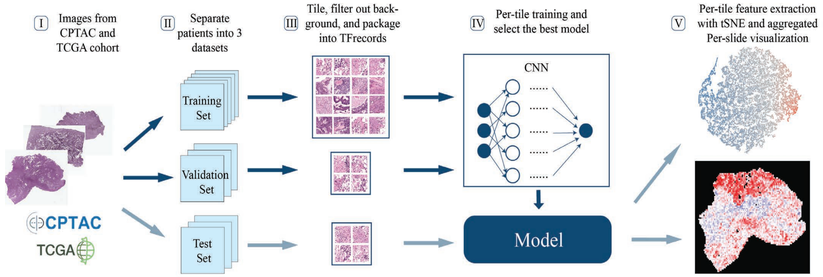
ABSTRACT

The determination of endometrial carcinoma histological subtypes, molecular subtypes, and mutation status is a critical diagnostic process that directly affects patients' prognosis and treatment options. Compared to the histopathological approach, however, the availability of molecular subtyping is limited as it can only be obtained by genomic sequencing, which may be cost prohibitive. Here, we implemented a customized multi-resolution deep convolutional neural network model, Panoptes, that predicts not only the histological subtypes, but also molecular subtypes and 18 common gene mutations based on digitized H&E stained pathological images with high accuracy. Our models achieved an area under the receiver operating characteristic curve (AUROC) of 0.969 in predicting histological subtype and 0.934 to 0.958 in predicting the copy number high (CNV-H) molecular subtype. The prediction tasks of 4 mutations and microsatellite high (MSI-H) molecular subtype also achieved a high performance with AUROC ranging from 0.781 to 0.873. Feature extraction and visualization revealed that the model relied on human-interpretable patterns. Our results suggest that Panoptes can help pathologists determine molecular subtypes and mutations of endometrial carcinoma without sequencing, and our models are generalizable to independent datasets.

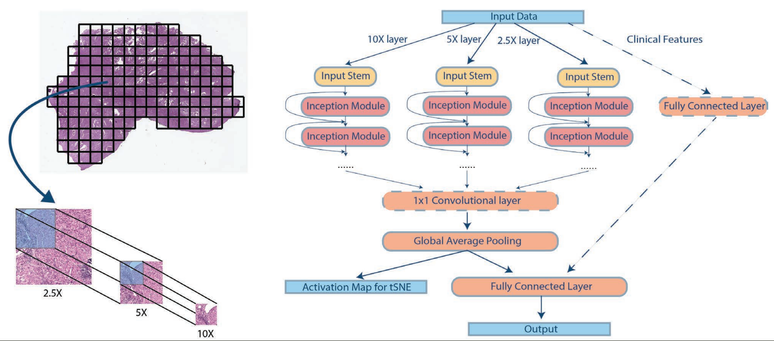
DATA



WORKFLOW

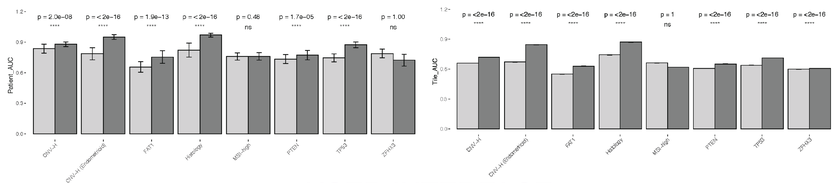


ARCHITECTURE

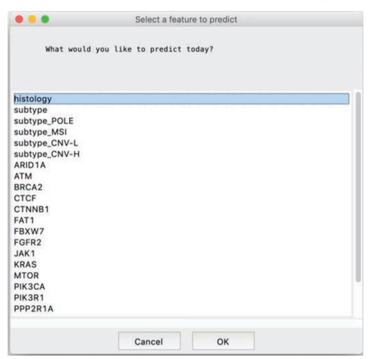


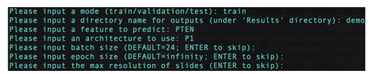
PREDICTION

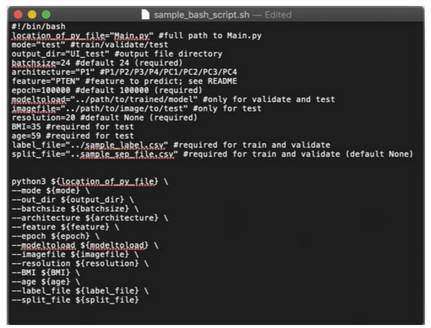
	Best Architecture	Per-patient AUROC	Per-tile AUROC
Histology	Panoptes2	**0.969 (0.905-1)**	**0.870 (0.866-0.874)**
CNV-H from endometrioid	Panoptes1	**0.958 (0.886-1)**	**0.864 (0.859-0.870)**
CNV-H	Panoptes4	**0.934 (0.851-1)**	0.731 (0.728-0.734)
TP53	Panoptes2	**0.873 (0.768-0.977)**	0.713 (0.709-0.717)
FAT1	Panoptes2 with clinical	**0.835 (0.666-1)**	0.639 (0.635-0.642)
MSI-High	InceptionResnetV1	**0.827 (0.705-0.948)**	0.638 (0.635-0.641)
ZFHX3	InceptionResnetV1	**0.824 (0.689-0.959)**	0.637 (0.634-0.640)
PTEN	InceptionV2	**0.781 (0.579-0.984)**	0.623 (0.620-0.627)
FGFR2	Panoptes4 with clinical	**0.755 (0.540-0.970)**	0.550 (0.545-0.554)
MTOR	Panoptes1	0.724 (0.496-0.951)	0.674 (0.670-0.678)
CTCF	Panoptes4	0.724 (0.518-0.931)	0.571 (0.568-0.575)
PIK3R1	InceptionResnetV1	0.702 (0.524-0.880)	0.596 (0.593-0.599)
PIK3CA	Panoptes4	0.689 (0.532-0.847)	0.526 (0.523-0.530)
ARID1A	InceptionResnetV2	0.683 (0.513-0.853)	0.542 (0.538-0.545)
JAK1	Panoptes2 with clinical	0.662 (0.410-0.940)	0.612 (0.605-0.618)
CTNNB1	InceptionResnetV2	0.648 (0.439-0.858)	0.619 (0.616-0.622)
KRAS	Panoptes2 with clinical	0.638 (0.404-0.871)	0.515 (0.510-0.519)
FBXW7	InceptionV3	0.629 (0.366-0.892)	0.606 (0.602-0.609)
RPL22	InceptionV3	0.632 (0.395-0.868)	0.517 (0.512-0.522)
BRCA2	InceptionResnetV1	0.613 (0.318-0.908)	0.624 (0.620-0.629)



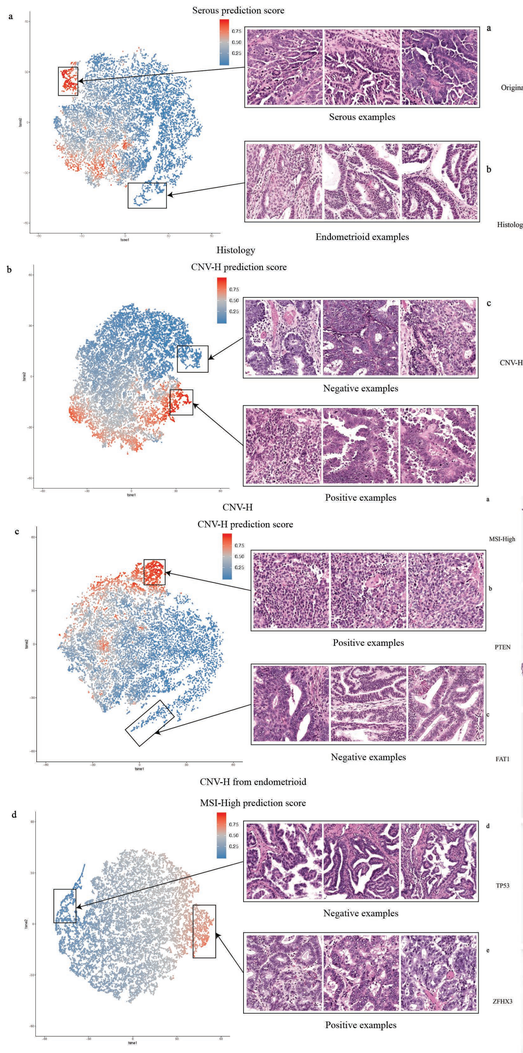
USER INTERFACE

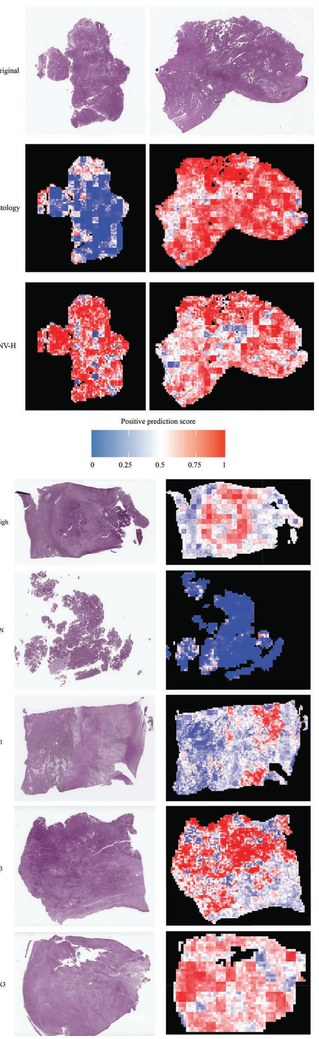






VISUALIZATION





MORE INFORMATION

bioRxiv

GitHub

PyPI

References:
1. Szegedy, Christian, et al. "Inception-v4, inception-resnet and the impact of residual connections on learning." AAAI. Vol. 4. 2017.
2. Cooper, Lee AD, et al. "PanCancer insights from The Cancer Genome Atlas: the pathologist's perspective." The Journal of pathology 244.5 (2018): 512-524.
3. Coudray, N. et al. Classification and mutation prediction from non–small cell lung cancer histopathology images using deep learning. Nat. Med. 24, 1559–1567 (2018).
4. Morice, P., Leary, A., Creutzberg, C., Abu-Rustum, N. & Darai, E. Endometrial cancer. Lancet 387, 1094–1108 (2016).

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