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영문제목	Cytology-Specific Foundation Models for Predicting BRAF Mutation Status in Thyroid Fine-Needle Aspiration Cytology

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Object The BRAF V600E mutation shapes diagnosis, prognosis, and targeted treatment in thyroid carcinoma, yet cytological examination alone cannot establish mutation status, so a separate molecular assay is required. This adds cost and delay, particularly for indeterminate aspirates. We investigated whether mutation status can be inferred directly from digitised fine-needle aspiration (FNA) cytology slides, and whether a foundation model pretrained on cytology rather than tissue sections offers an advantage.

Methods Two institutions contributed 263 thyroid FNA cytology whole-slide images (245 BRAF-positive, 18 BRAF-negative), scanned with extended z-stacking to capture cells across focal planes. Patch features were extracted with four Vision Foundation Models: the cytology-pretrained CytoFM and three histopathology-pretrained models (UNI2-h, UNI, Virchow2). Clustering-constrained attention multiple-instance learning performed slide-level classification using mutation labels only, without cell- or patch-level annotation. Because positives outnumbered negatives 13.6 to 1, we combined feature-space interpolation, bag-level class weighting, and patch dropout, and tuned hyperparameters by Bayesian search under stratified five-fold cross-validation.

Results The cytology-pretrained model outperformed every histopathology-pretrained counterpart, reaching an AUROC of 0.784 against 0.715 for the strongest alternative, with non-overlapping 95% confidence intervals. Attention maps highlighted dense, architecturally atypical cell clusters while assigning low weight to background and preparation artefact, indicating that the model attended to diagnostically meaningful material.

Conclusions BRAF mutation status can be predicted from thyroid FNA cytology with weak supervision alone, and domain-matched cytology pretraining contributes materially to that performance. The approach may help triage which indeterminate aspirates warrant molecular testing, reducing both

cost and time to diagnosis.

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