

Using Deep Learning to Predict and Visualize STK11 Mutation in LUAD with Histopathological Slides from CPTAC

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Method

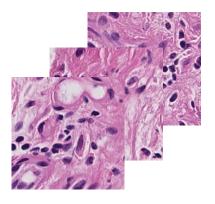
- Maximum image resolution is 20X; 324 slides from 110 patients
- Cutting each slide into 299x299 pixel tiles, excluding background and contaminants
- 80% slides for training; 10% slides for validation; 10% slides for testing. (patient-level separation)

Original image



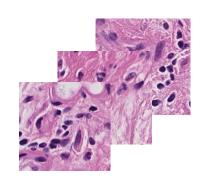
80000x90750 7.26 Billion Pixels

Tile



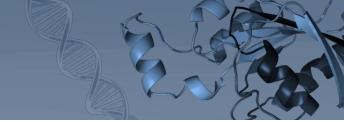
299x299 89400 Pixels 1/81208 of original image

Unique area of each tile

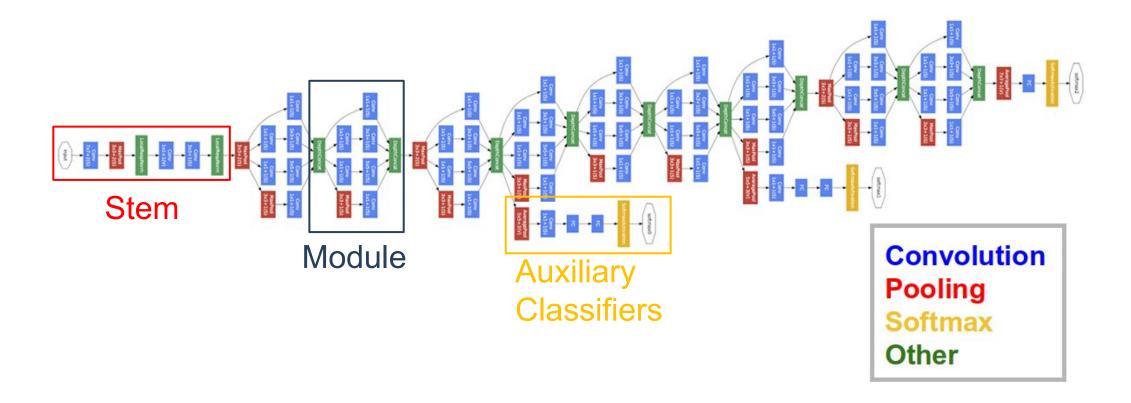


250x250 62500 Pixels 1/116160 of original image

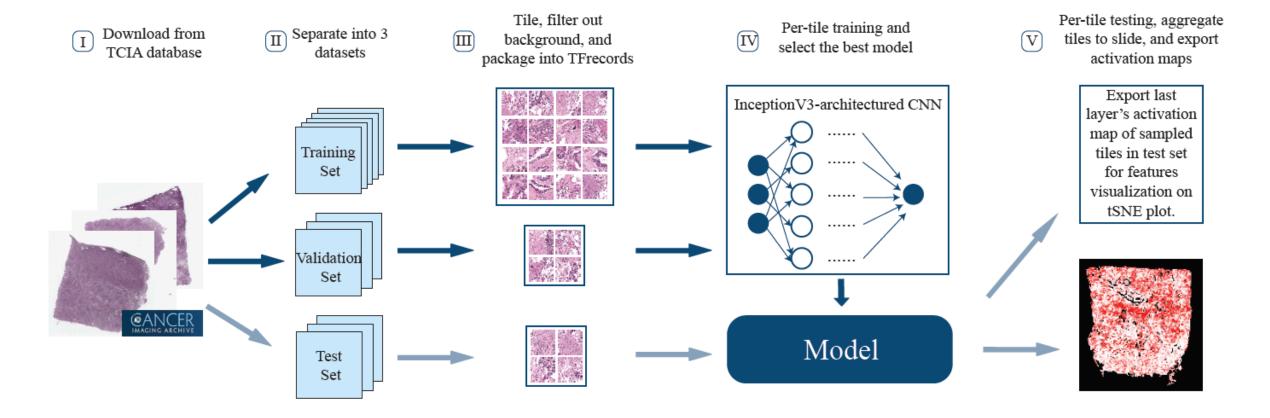
Inception Architecture



InceptionV3

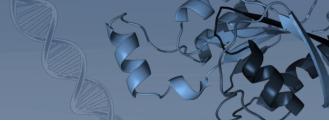


Workflow

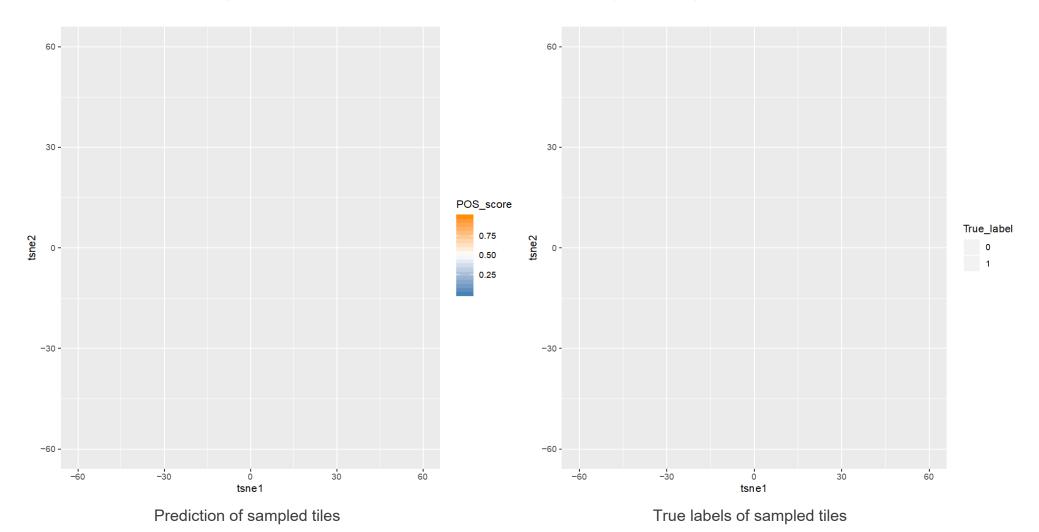


VI Metrics of test set	STK11-mutated count	WT count	AUROC	AUPRC	Accuracy
Per-slide level	5	31	0.961 (0.891-1.000)	0.860	0.944 (0.813-0.993)
Per-tile level	21507	116483	0.892 (0.890-0.894)	0.667	0.873 (0.871-0.875)

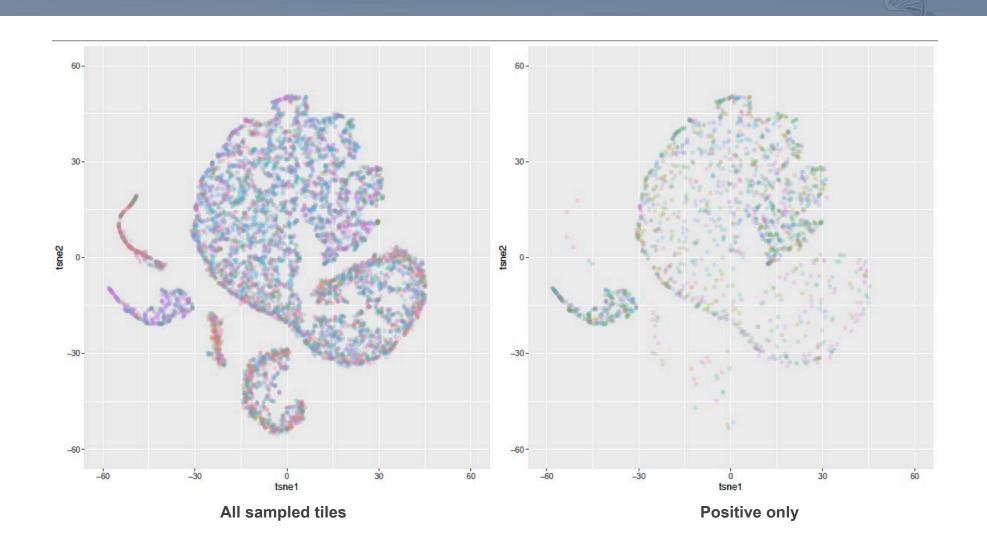
tSNE of Last CONV layer activation



Sampled 10000 tiles (2000 positive and 8000 negative) from test set of 36 slides

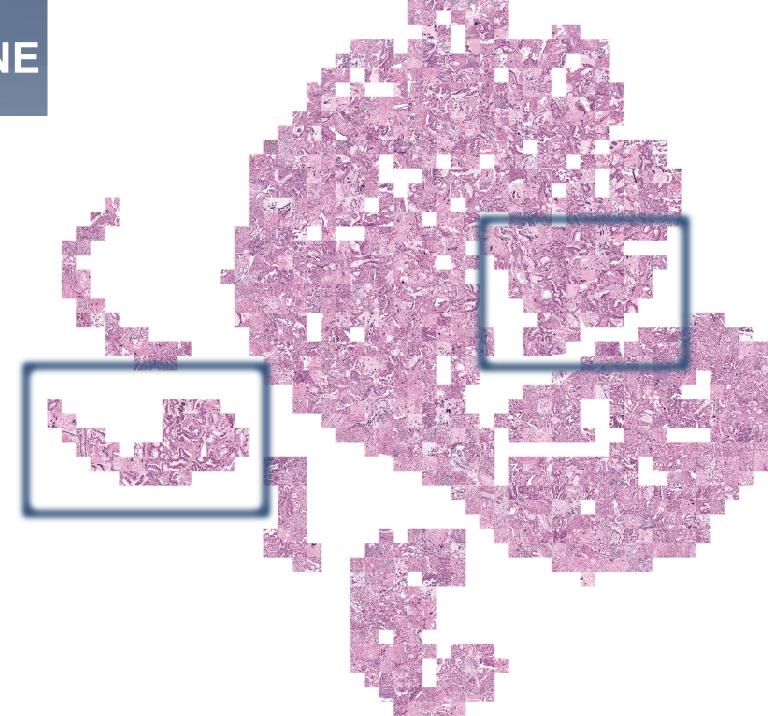


Tiles labeled by corresponding slides that they belong to



Tile visualization on tSNE

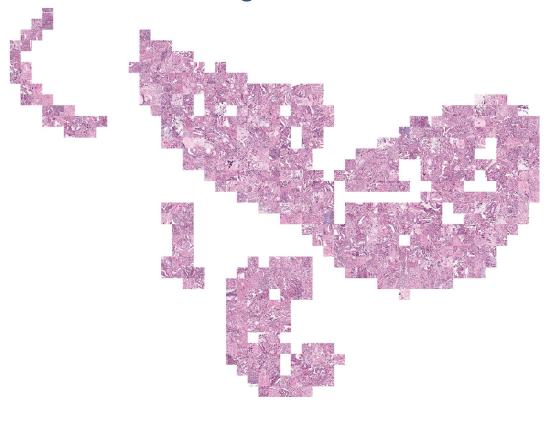
- Binned on tSNE space and sample 1 tile in each bin to represent their relative position on tSNE plot.
- 2 STK11 positive areas are boxed.



Positive clusters

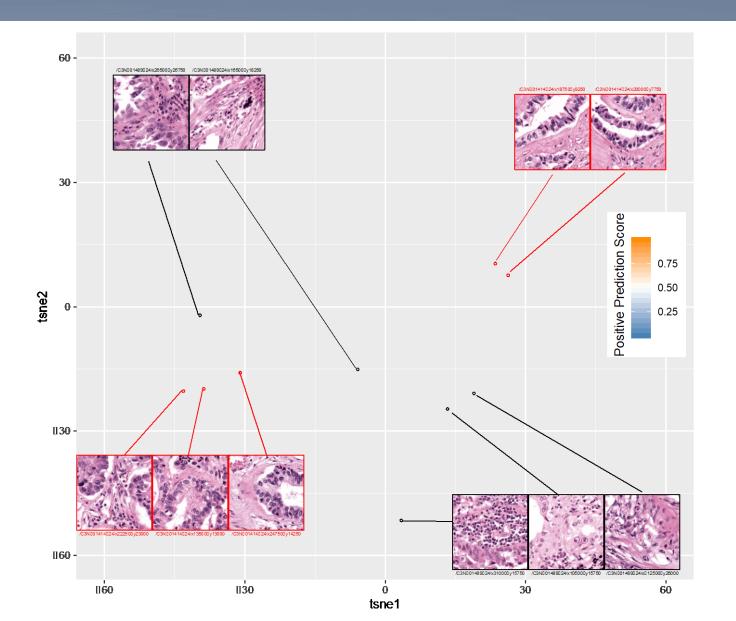
"Cancer cells, with no inflammatory cells"

Negative clusters

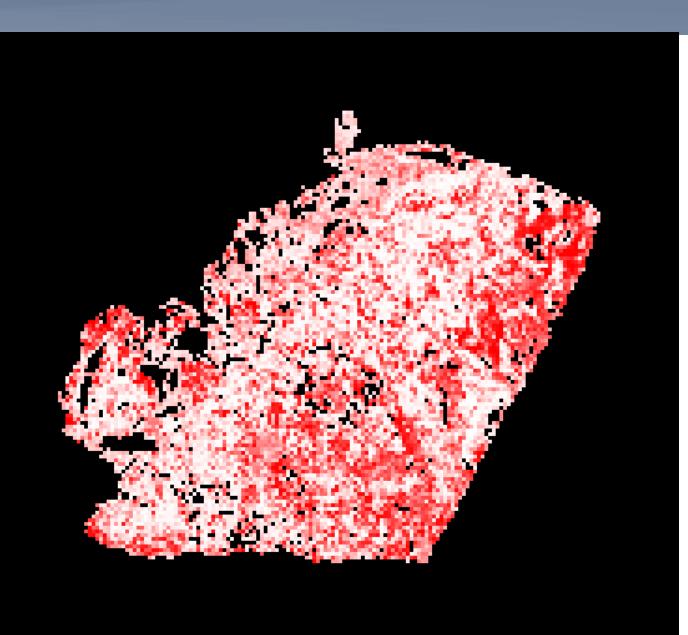


"Inflammatory cells, with some cancer cells nearby"

Corresponds to the findings of STK11 mutation in immune responses of LUAD patients



Visualization



Each "pixel" represents 1 tile; The more red the more likely to be STK11 mutated

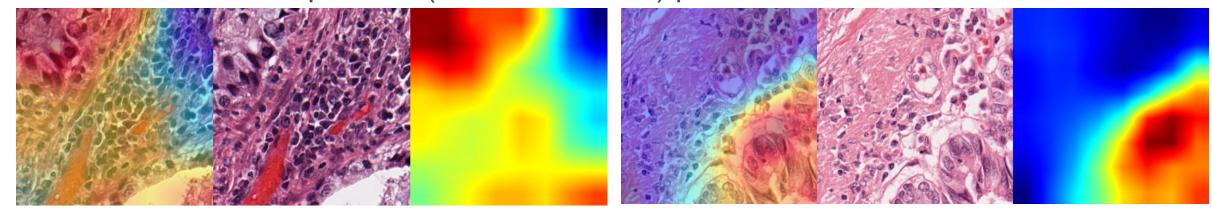




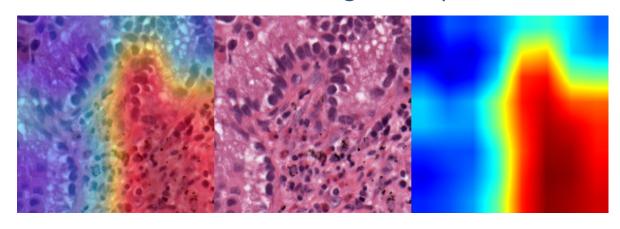
Class Activation Mapping: Open the "Black Box"

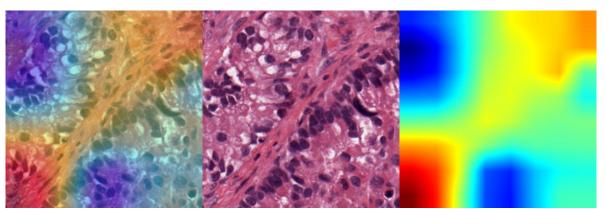


Some tiles with >0.8 positive (STK11 Mutated) prediction score.

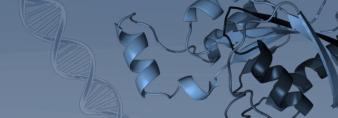


Some tiles with >0.8 negative (**NOT** STK11 Mutated) prediction score.





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