

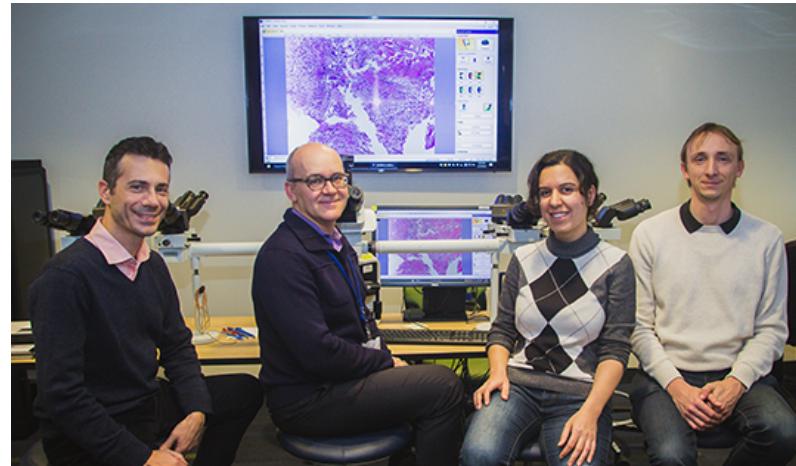
Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning

Nicolas Coudray  ^{1,2,9}, Paolo Santiago Ocampo ^{3,9}, Theodore Sakellaropoulos ⁴, Navneet Narula ³, Matija Snuderl ³, David Fenyö ^{5,6}, Andre L. Moreira ^{3,7}, Narges Razavian  ^{8*} and Aristotelis Tsirigos  ^{1,3*}

The team

Lung cancer project

- Paolo Santiago Ocampo
- Narges Razavian
- Andre L. Moreira
- Theodore Sakellaropoulos
- Navneet Narula
- David Fenyö
- Matija Snuderl
- Aristotelis Tsirigos



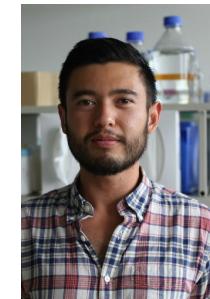
Aris
Tsirigos

Andre
Moreira

Narges
Razavian
Nicolas
Coudray

NYU Shared Resources

- HPC (High-Performance Computing)
- CBRD (Center for Biospecimens Research & Development)
- ABL (Applied Bioinformatics Laboratories)



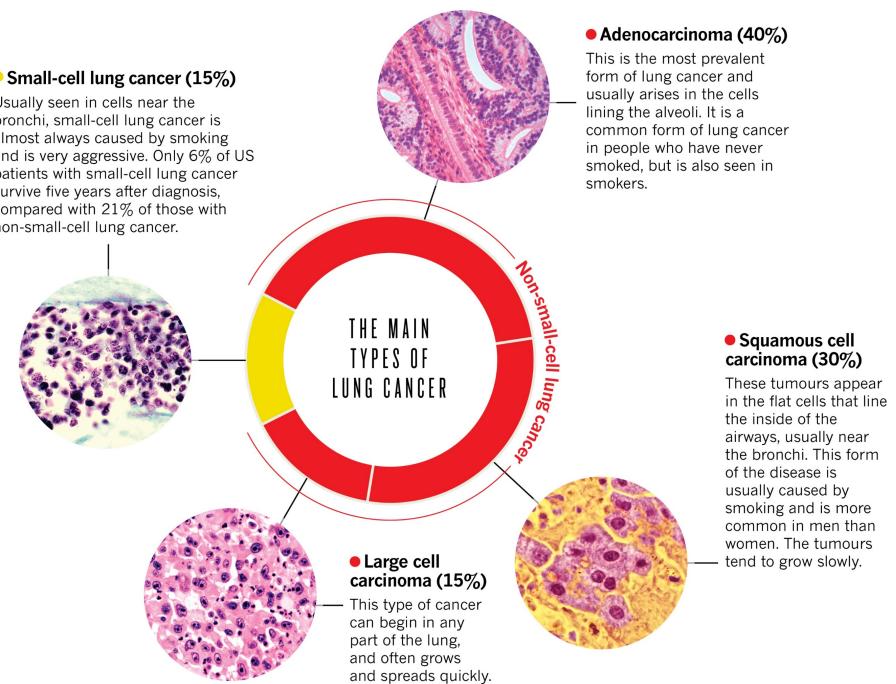
Paolo
Ocampo

Funding

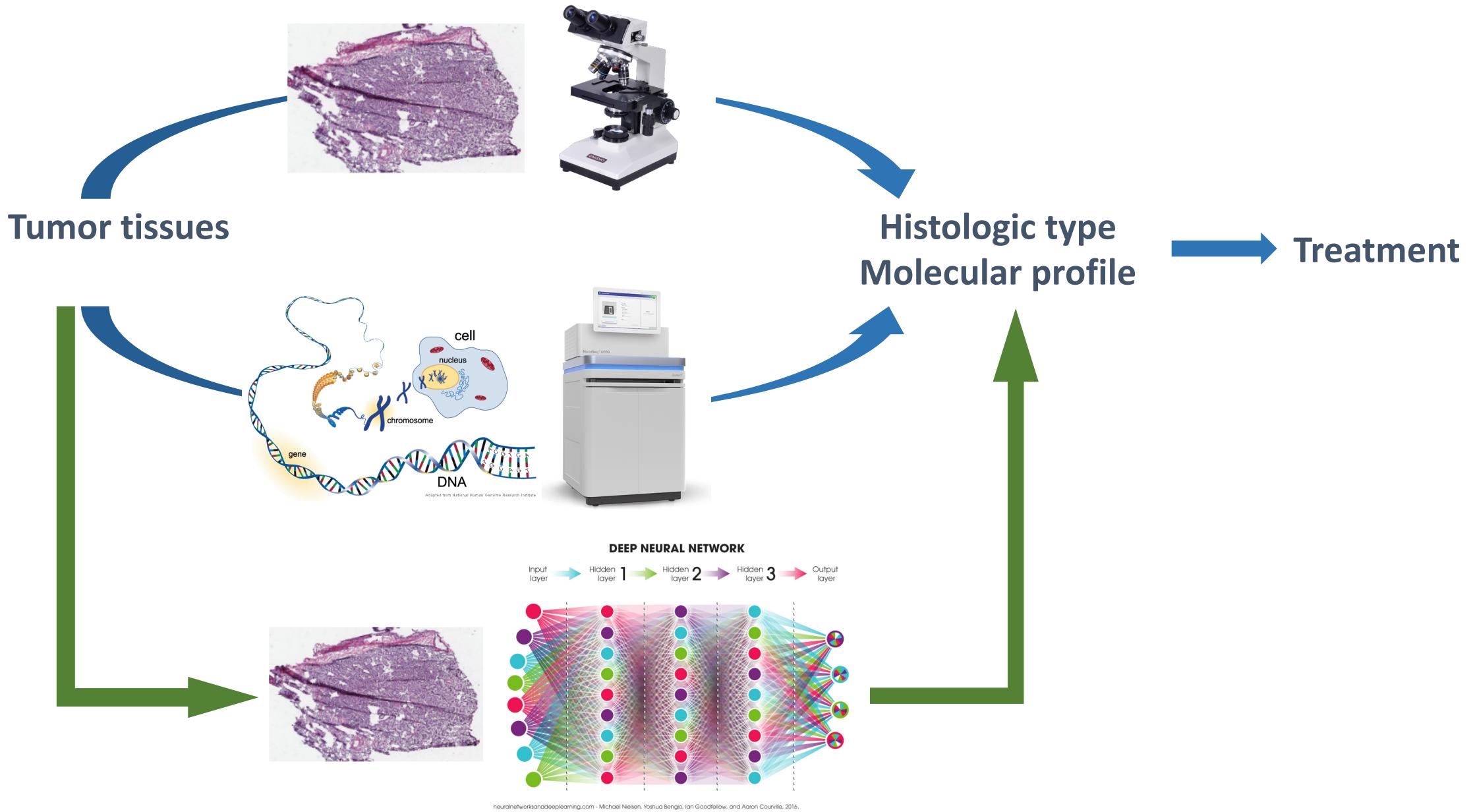


Overview

- Can we use machine learning to accurately classify histopathology images?
- How does an AI algorithm compare to pathologists?
- Is there any additional information we can extract from these images?



Toward lung cancer automated diagnosis...

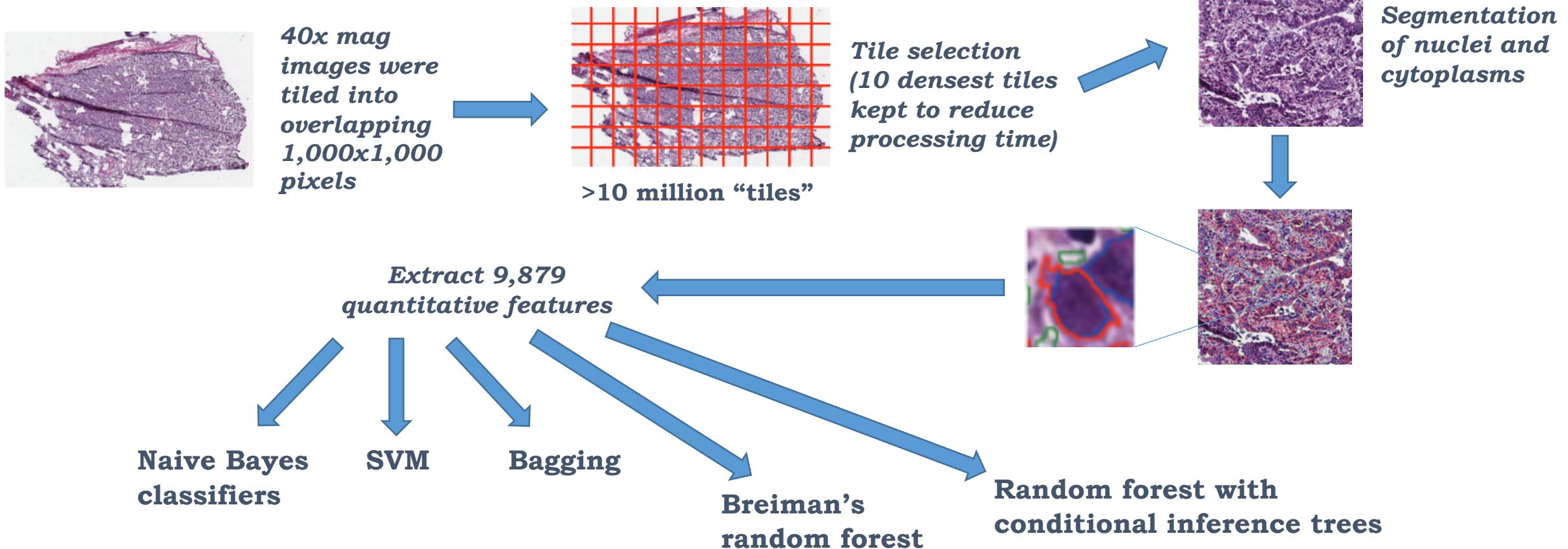


Automation – state of the art

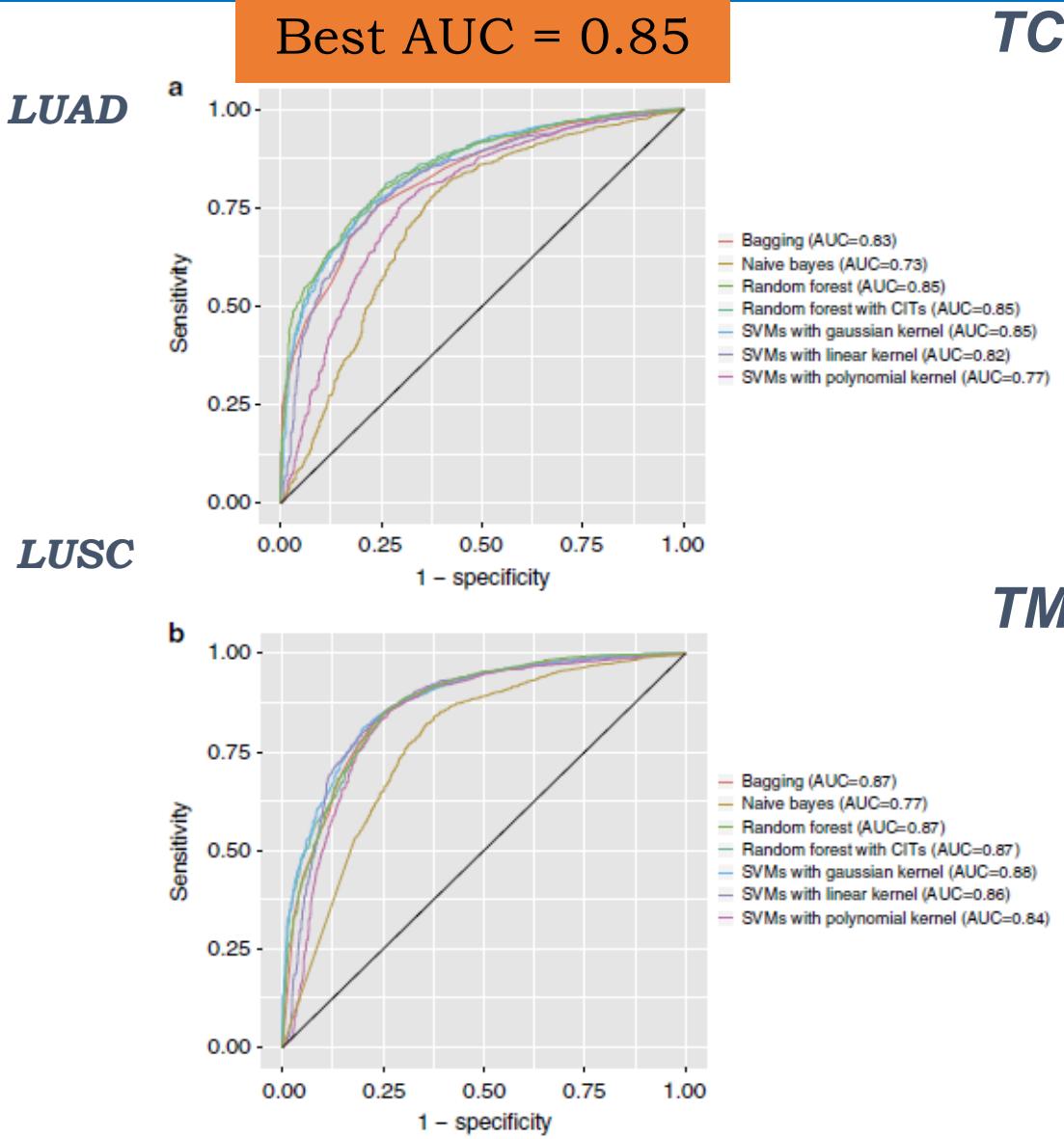
Predicting non-small cell lung cancer prognosis by fully automated microscopic pathology image features

Nature Communications 7:12474 · August 2016

Kun-Hsing Yu^{1,2}, Ce Zhang³, Gerald J. Berry⁴, Russ B. Altman¹, Christopher Ré³, Daniel L. Rubin^{1,*}
& Michael Snyder^{2,*}

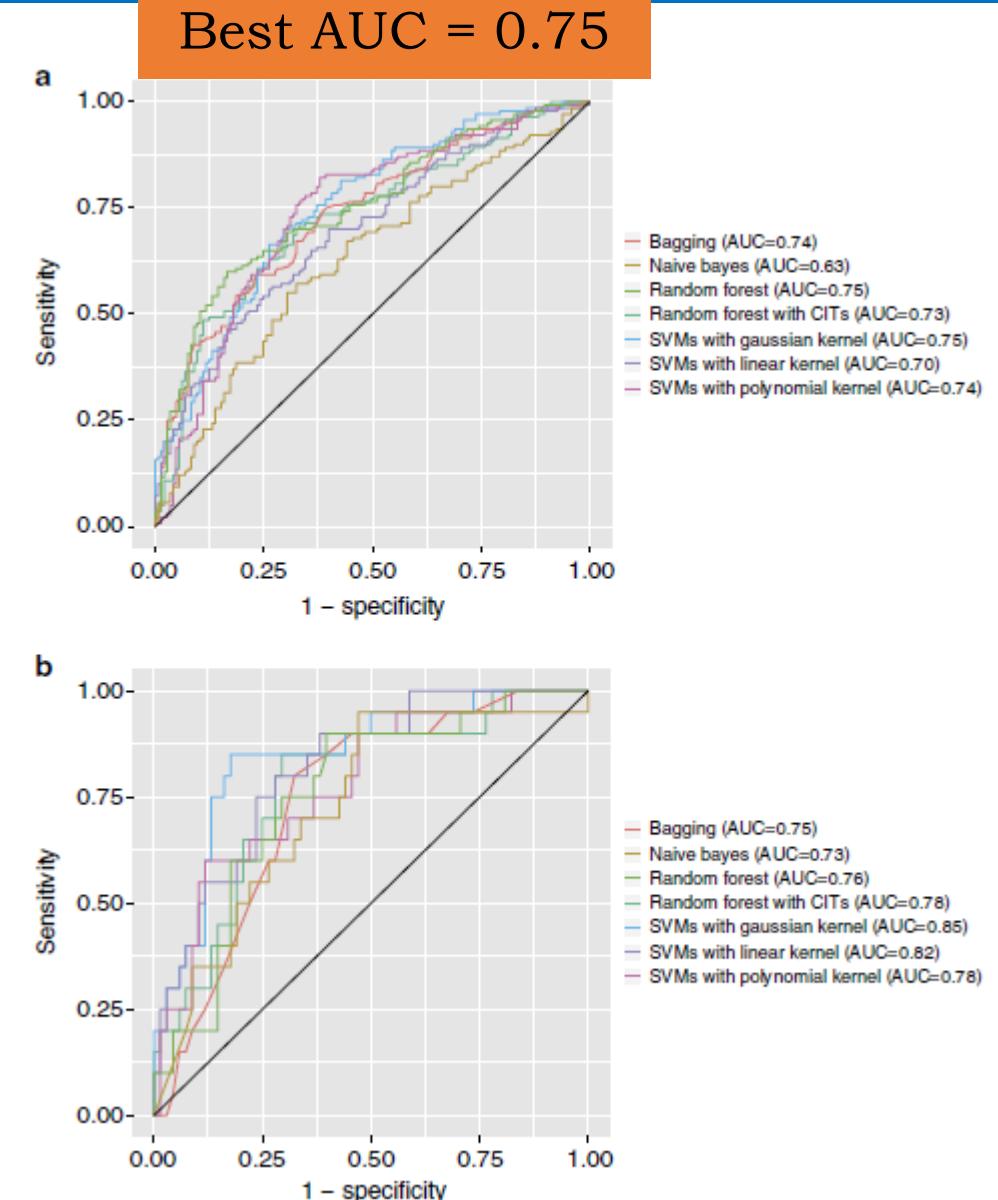


Distinguish malignancy vs normal adjacent tissues

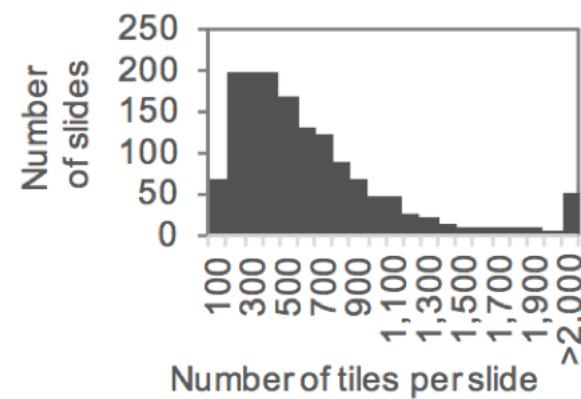
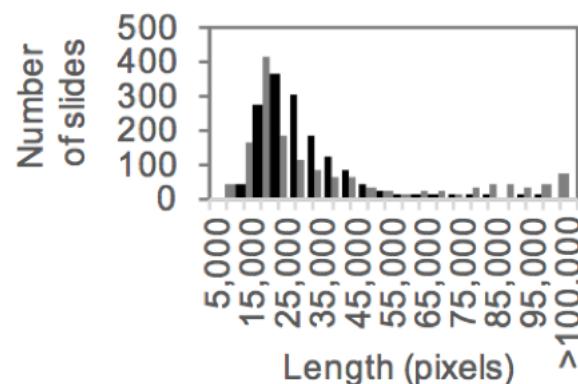
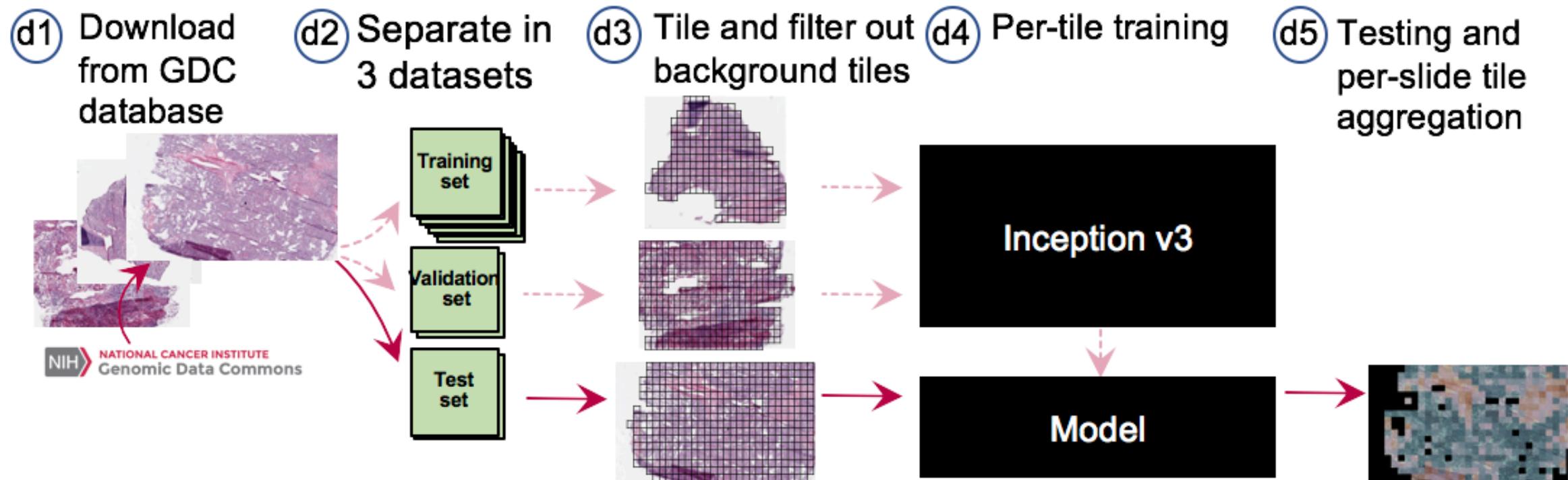


Classification with top 80 features

Distinguish LUAD vs LUSC tissues

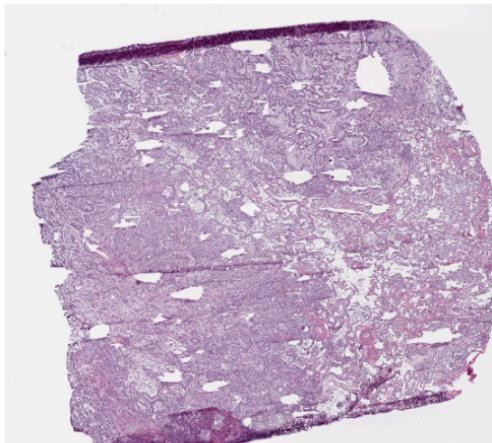


Strategy

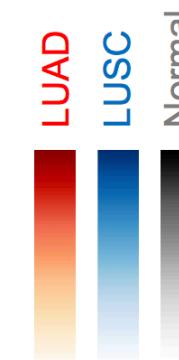
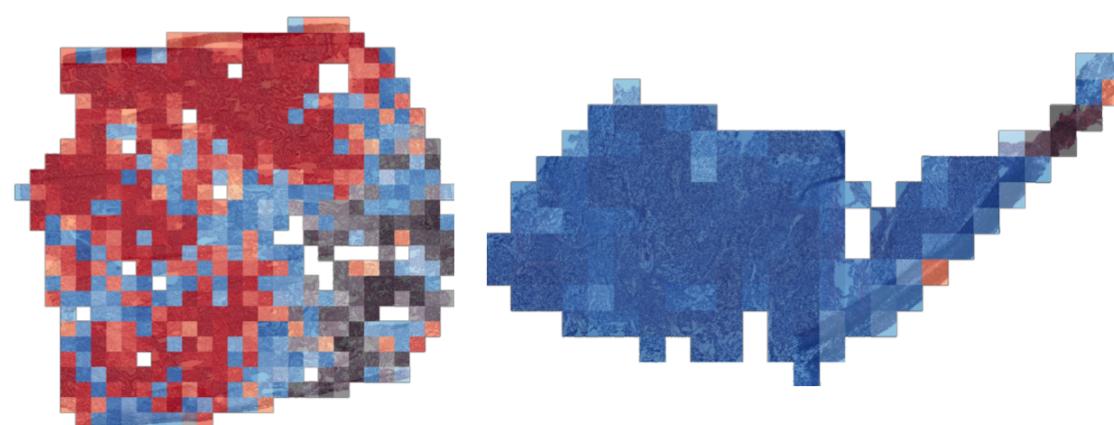
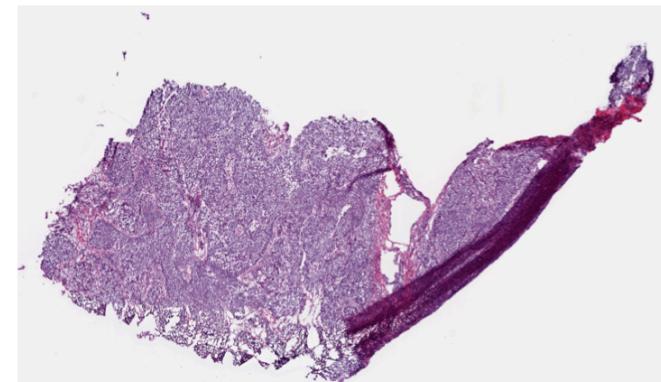


Heatmap view allows assessment of slide heterogeneity

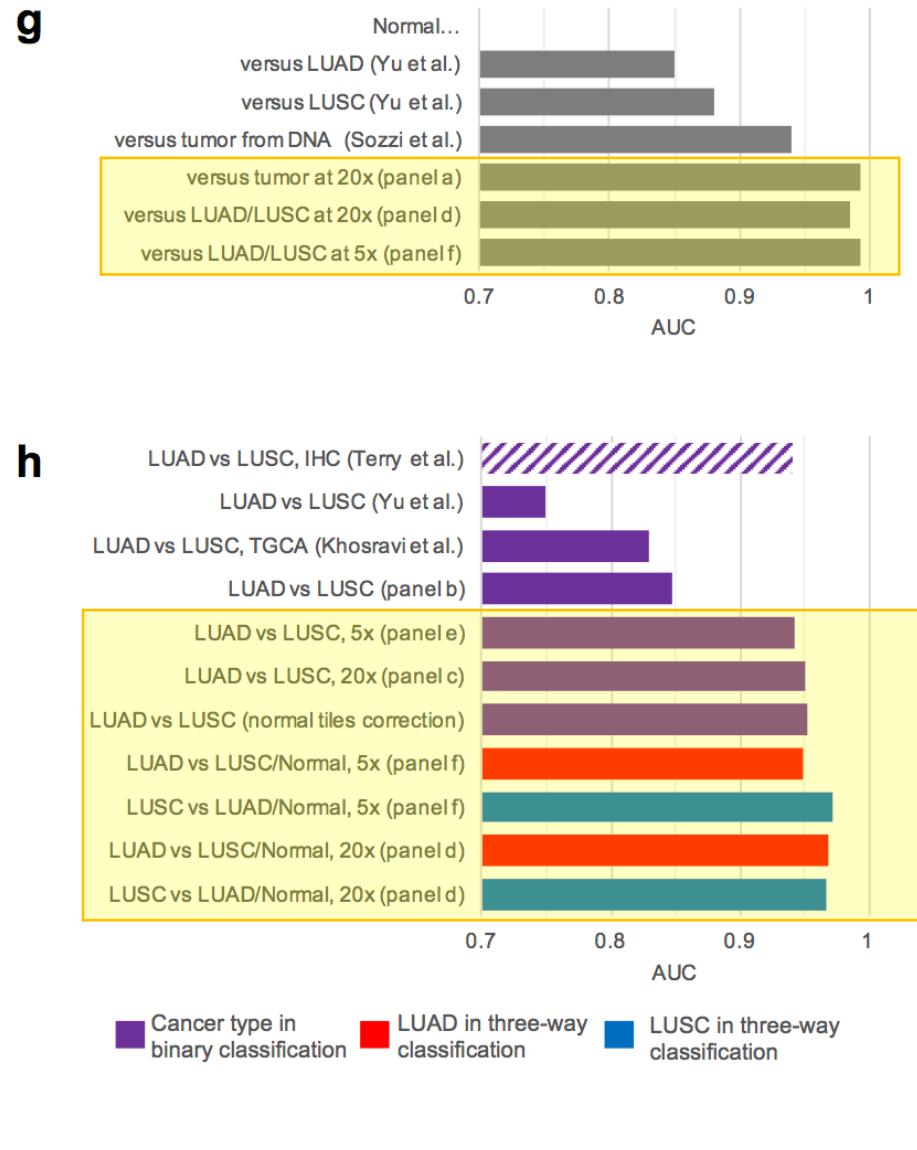
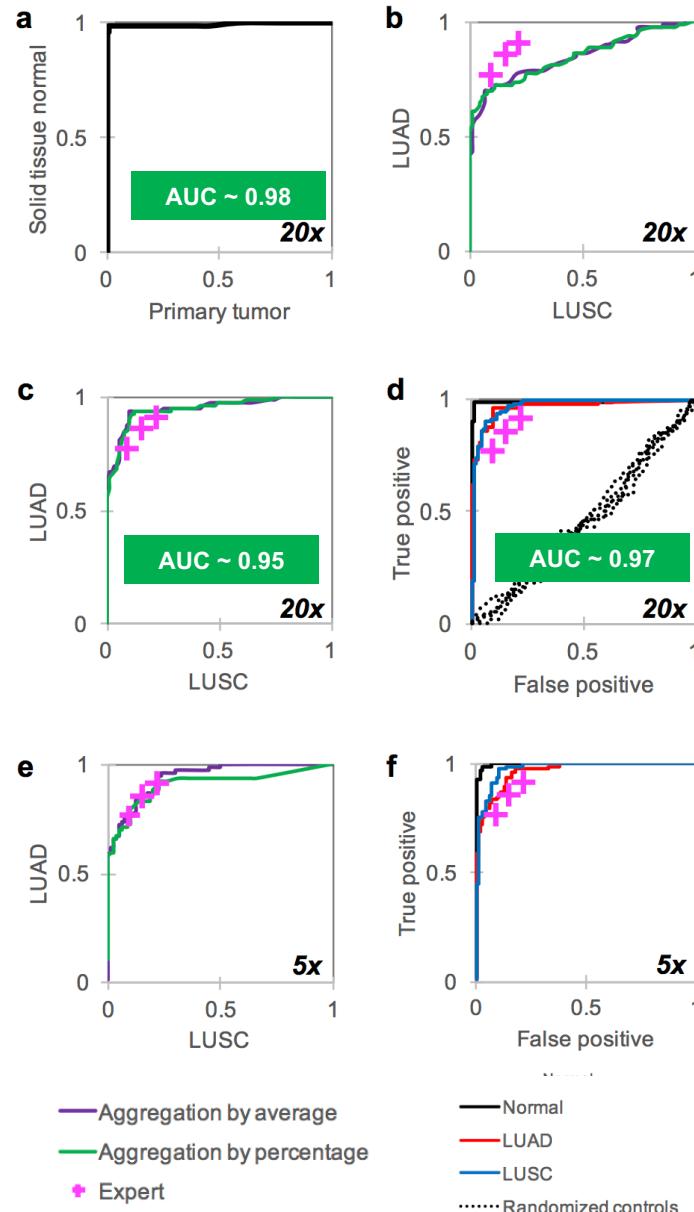
LUAD slide



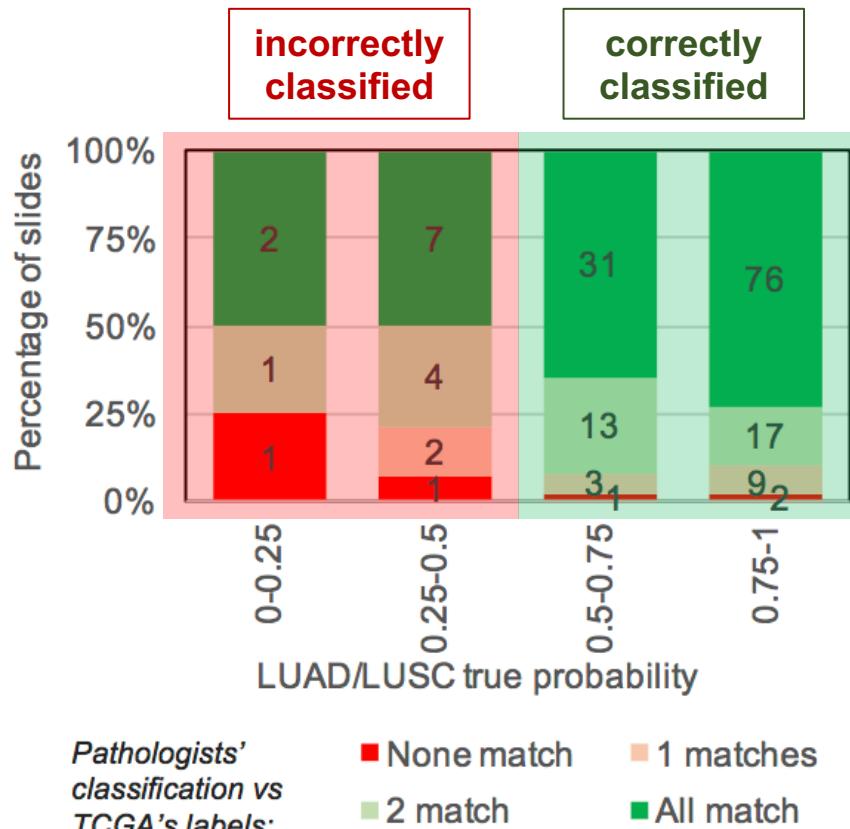
LUSC slide



Performance overview



Comparison with classification by experts



Cohen's kappa statistics:

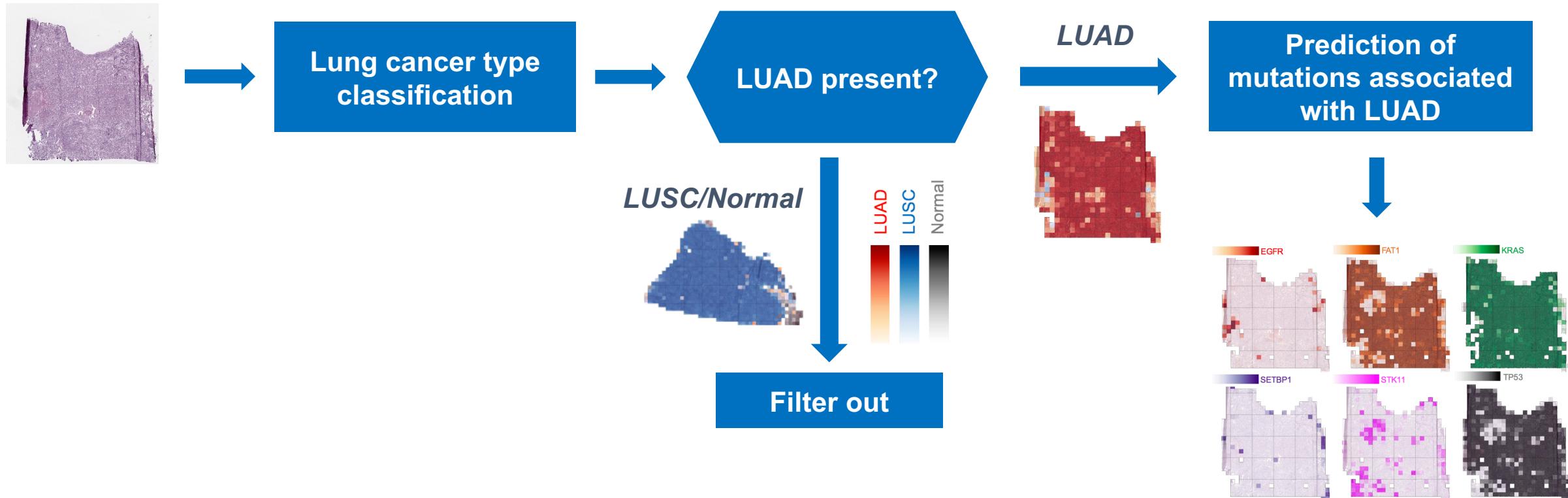
- ❖ AI vs TCGA 0.82
- ❖ Pathologists vs TCGA 0.67, 0.70, 0.70 (p-values: 0.035, 0.091, 0.090)
- ❖ Consensus vs TCGA 0.78 (p-value: 0.549)
- ❖ Inter-pathologist 0.52-0.78

Cohen's kappa measures the agreement between two raters who each classify N items into C mutually exclusive categories.

Time efficiency:

Takes ~20 seconds to diagnose a slide on a single Tesla K20m GPU

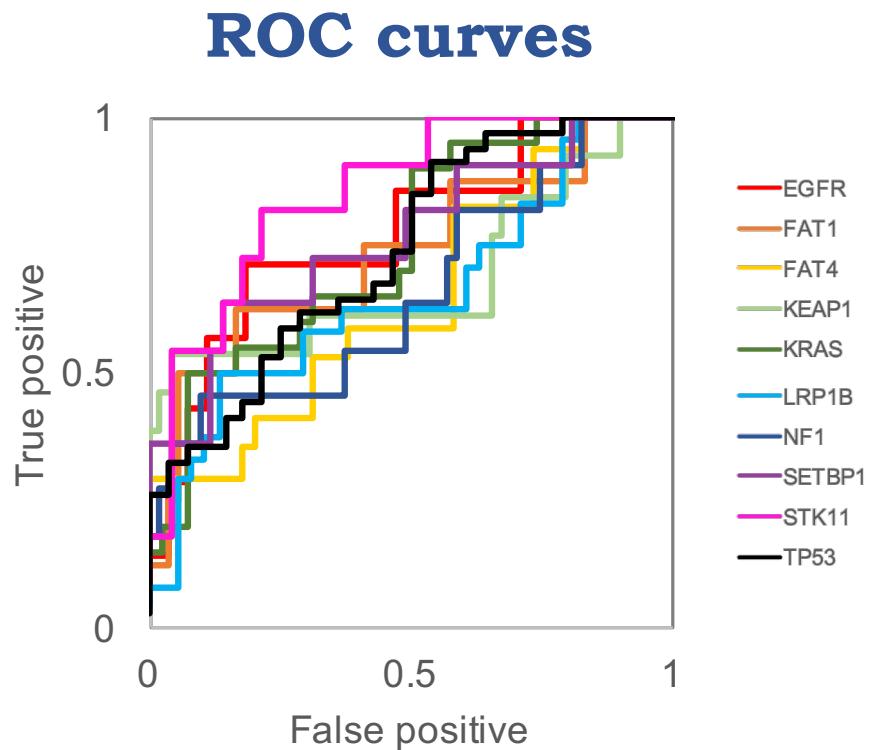
Workflow for the detection of LUAD mutations



Mutation prediction for LUAD

- * CNN modified for multi-output classification
- * Test set: ~44,000 tiles from 62 LUAD slides

Mutations	Per slide AUC after aggregation by...	
	... average predicted probability	... percentage of positively classified tiles
STK11	0.856 [0.709-0.964]	0.842 [0.683-0.967]
EGFR	0.826 [0.628-0.979]	0.782 [0.516-0.979]
SETBP1	0.775 [0.595-0.931]	0.752 [0.550-0.927]
TP53	0.760 [0.626-0.872]	0.754 [0.627-0.870]
FAT1	0.750 [0.512-0.940]	0.750 [0.491-0.946]
KRAS	0.733 [0.580-0.857]	0.716 [0.552-0.854]
KEAP1	0.675 [0.466-0.865]	0.659 [0.440-0.856]
LRP1B	0.656 [0.513-0.797]	0.657 [0.512-0.799]
FAT4	0.642 [0.470-0.799]	0.640 [0.440-0.856]
NF1	0.640 [0.419-0.845]	0.632 [0.405-0.845]



Testing on independent NYU cohort

Testing EGFR-mutant prediction performance on independent NYU cohorts:

- * Total of 63 FFPE images were tested:

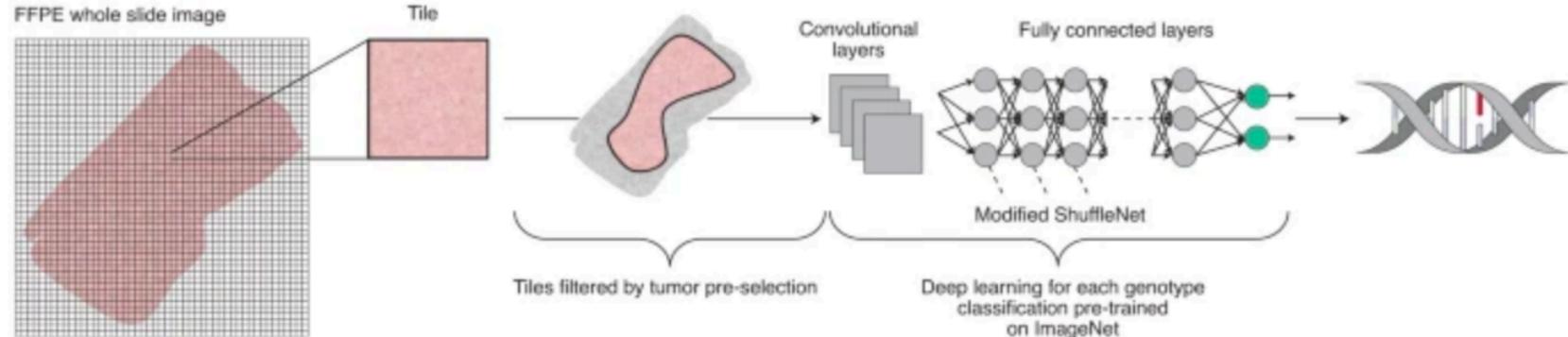
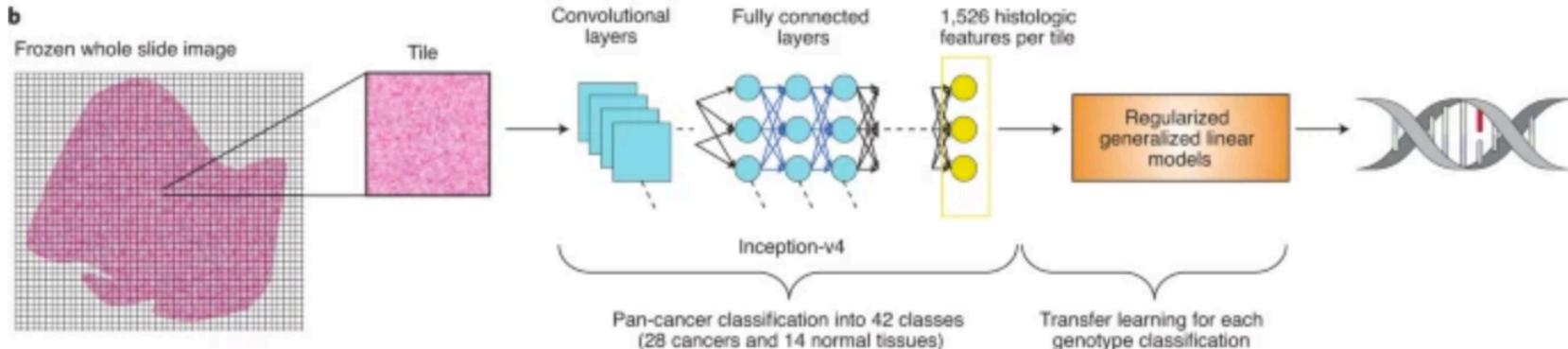
AUC = 0.687

- * 41 out of 63 analyzed by IHC (*L858R* and *E746_A75-del* only):

AUC = 0.659

- * 22 out of 63 analyzed by sequencing:

AUC = 0.750

a**b**

Nature Cancer | Article

Pan-cancer image-based detection of clinically actionable genetic alterations

Jakob Nikolas Kather, Lara R. Heij [...] & Tom Luedde

Nature Cancer | Article

Pan-cancer computational histopathology reveals mutations, tumor composition and prognosis

Yu Fu, Alexander W. Jung [...] & Moritz Gerstung