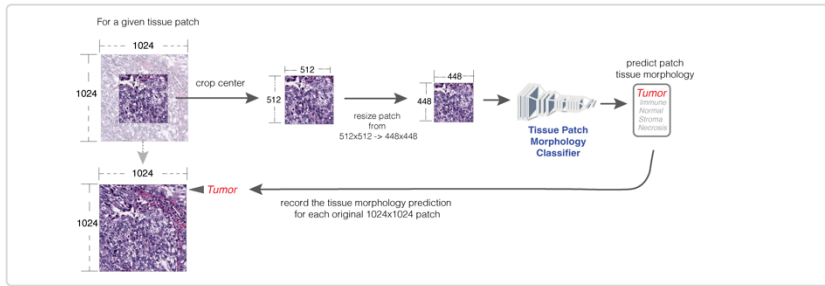
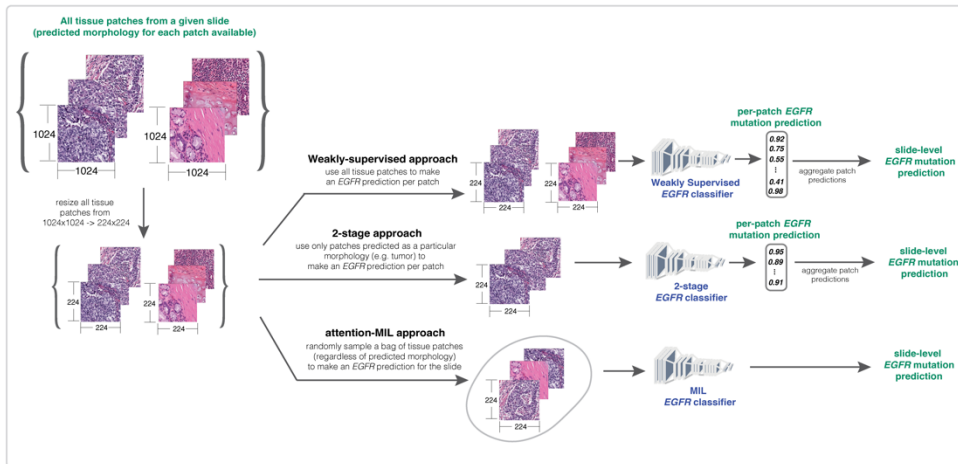


**Supplementary Figure 1. Overall bag aggregation scores of high-attention patches for numerical variables for 49 pathologist reviewed bags.**

**(a)** Mean aggregate values of the high-attention patches. **(b)** Standard deviation of the scores for the high-attention patches, with wild-type predictions having a higher standard deviation of tumor nuclei fraction than mutant calls ( $p=0.028$ ). **(c)** Maximum aggregate value of the high-attention patches, with predicted wild-type bags having a significantly higher maximum peritumoral immune infiltration fraction than bags predicted to be mutant ( $p=0.041$ ). **(d)** Minimum aggregate value of high-attention patches, with significantly higher minimum tumor nuclei fraction across high-attention patches for mutant predictions than wild-type predictions ( $p=0.037$ )

**A****Tissue Morphology Prediction****B****EGFR Mutation Prediction**

**Supplementary Figure 2. Patch processing overview of tissue morphology prediction for full patch dataset and procedure for training *EGFR* mutation prediction models.**

**(a)** Procedure for using the trained tissue morphology prediction model to classify each patch within the full dataset by taking the raw 1024x1024 patch and center cropping out a 512x512 patch, resizing that center crop patch to 448x448, making the morphology classification and then recording the classification for the raw 1024x1024 patch. **(b)** Procedure of resizing all 1024x1024 patches for which morphology predictions have been performed to 224x224 and inputting these patches into the various *EGFR* mutation prediction models, including the weakly-supervised model that uses all tissue patches from a slide, the 2-stage models that use only patches predicted to be a particular morphology type, and the MIL model that uses a random sampling of all tissue patches from the slide and for which the tissue morphology predictions may be used post-hoc to analyze learned model attention.

**Supplementary Table 1. Significance statistics of pathologist-reviewed categories relative to predicted *EGFR* mutation status for high attention patches within bags.**

category	statistic	pvalue	rank	qvalue (practical)
tumor nuclei percentage_std	-2.2667706	0.02815071	1	0.20275584
tumor nuclei percentage_min	2.14441798	0.03731603	2	0.20275584
peritumoral immune percentage_max	-2.1075396	0.04055117	3	0.20275584
peritumoral immune percentage_std	-1.9727147	0.05455574	4	0.20458402
tumor nuclei percentage_mean	1.04516634	0.30140746	5	0.76205232
peritumoral immune percentage_min	0.95833333	0.34290476	6	0.76205232
necrosis percentage_mean	-0.8391513	0.40572434	7	0.76205232
intratumoral immune percentage_min	-0.8247776	0.41375449	8	0.76205232
necrosis percentage_std	-0.733626	0.46689946	9	0.76205232
tumor nuclei percentage_max	-0.6534834	0.5166981	10	0.76205232
intratumoral immune percentage_max	0.52140926	0.60458314	11	0.76205232
intratumoral immune percentage_std	0.47176191	0.63932689	12	0.76205232
necrosis percentage_max	-0.4421601	0.66044535	13	0.76205232
peritumoral immune percentage_mean	-0.3339032	0.73997008	14	0.79282508
intratumoral immune percentage_mean	-0.0527459	0.95816281	15	0.95816281

**Supplementary Table 2. Association rules mining statistics using pathologist-generated categorical descriptions for high-attention patches within bags with *EGFR* predictions.**

Antecedents	Consequents	Antecedent support	Consequent support	Support	Confidence	Lift	Leverage	Conviction
(fibrosis, lepidic_m, hobnail)	(EGFR+)	0.041667	0.520833	0.041667	1	1.92	0.019965	inf
(fibrosis, acinar_p, hobnail)	(EGFR+)	0.041667	0.520833	0.041667	1	1.92	0.019965	inf
(other,lepidic_p, hobnail)	(EGFR+)	0.041667	0.520833	0.041667	1	1.92	0.019965	inf
(columnar,acinar_p,inflammation)	(EGFR+)	0.083333	0.520833	0.0625	0.75	1.44	0.019097	1.916667
(lepidic_m,lepidic_p,hobnail)	(EGFR+)	0.083333	0.520833	0.0625	0.75	1.44	0.019097	1.916667
(columnar, papillary_p,other)	(EGFR+)	0.0625	0.520833	0.041667	0.666667	1.28	0.021701	1.4375
(lepidic_p,inflammation,hobnail)	(EGFR+)	0.0625	0.520833	0.041667	0.666667	1.28	0.021701	1.4375
Antecedents	Consequents	Antecedent support	Consequent support	Support	Confidence	Lift	Leverage	Conviction
(inflammation, hobnail, solid_m)	(EGFR-)	0.0625	0.479167	0.0625	1	2.086957	0.032552	inf
(inflammation, acinar_p, hobnail)	(EGFR-)	0.0625	0.479167	0.0625	1	2.086957	0.032552	inf
(acinar_p, hobnail, solid_m)	(EGFR-)	0.041667	0.479167	0.041667	1	2.086957	0.021701	inf

(acinar_p, inflammation, hobnail, solid_m)	(EGFR-)	0.041667	0.479167	0.041667	1	2.086957	0.021701	inf
(mucinous_p, mucinous, other)	(EGFR-)	0.083333	0.479167	0.0625	0.75	1.565217	0.022569	2.083333
(acinar_p, inflammation, solid_m)	(EGFR-)	0.0625	0.479167	0.041667	0.666667	1.391304	0.011719	1.5625