Option 1 - Epithelioid tumour							
	Topic	Options					
1	Predominant architectural growth pattern	Tubular	Papillary	Trabecular	Adenomaotoid	Solid	Micropapillary
2	Second most predominant pattern	Tubular	Papillary	Trabecular	Adenomaotoid	Solid	Micropapillary
3	Nuclear atypia	Mild	Moderate	Severe			
4	Inflammation*	None-sparse	Mild-moderate	Marked			
5	Necrosis**	None	Some	Universal			
6	Stroma:Tumour ratio	More stroma	Roughly equal	More tumour			
7	Stromal cellularity***	Low	Moderate	High			
8	^Biphasic features?	No	Yes				
9	Other notable features or comments	free text/annotations					
	^By biphasic, we refer to mixed epithelioid and spindled morphology within individual tiles rather than within the cluster						

Option 2 - Spindle cells / extracellular matrix				
	Topic	Options		
1	Cellularity	Low	Medium	High
2	Architecture	Orderly (parallel)	Less orderly (eg wavy)	Disorderly (random/storiform)
3	Presence of desmoplastic sarcomatoid morphology	Present	Absent	
4	Nuclear atypia	None/mild	Moderate	Severe
5	Inflammation*	None-sparse	Mild-moderate	Marked
6	Necrosis**	None	Some	Universal
7	^Biphasic features?	No	Yes	
8	Other notable features or comments	free text/annotations		
	^By biphasic, we refer to mixed epithelioid and spindled morphology within individual tiles rather than within the cluster			

Option 3 - Non-tumour								
Topic	Options							
Tiles contain mostly (by area)	Normal/near-normal lung			Collagenosis	Haemorrhage	Vessels (wall or lumen)	Airway	Cartilage
Second most common feature (by area)	Normal/near-normal lung	Non-neoplastic pathological lung	Elastosis	Collagenosis	Haemorrhage	Vessels (wall or lumen)	Airway	Cartilage
Inflammation*	None-sparse	Mild-moderate	Marked					
Necrosis**	None	Some	Universal					
Other notable features or comments	free text/annotations							
Inflammation*	None-sparse	Mild-moderate	Marked					

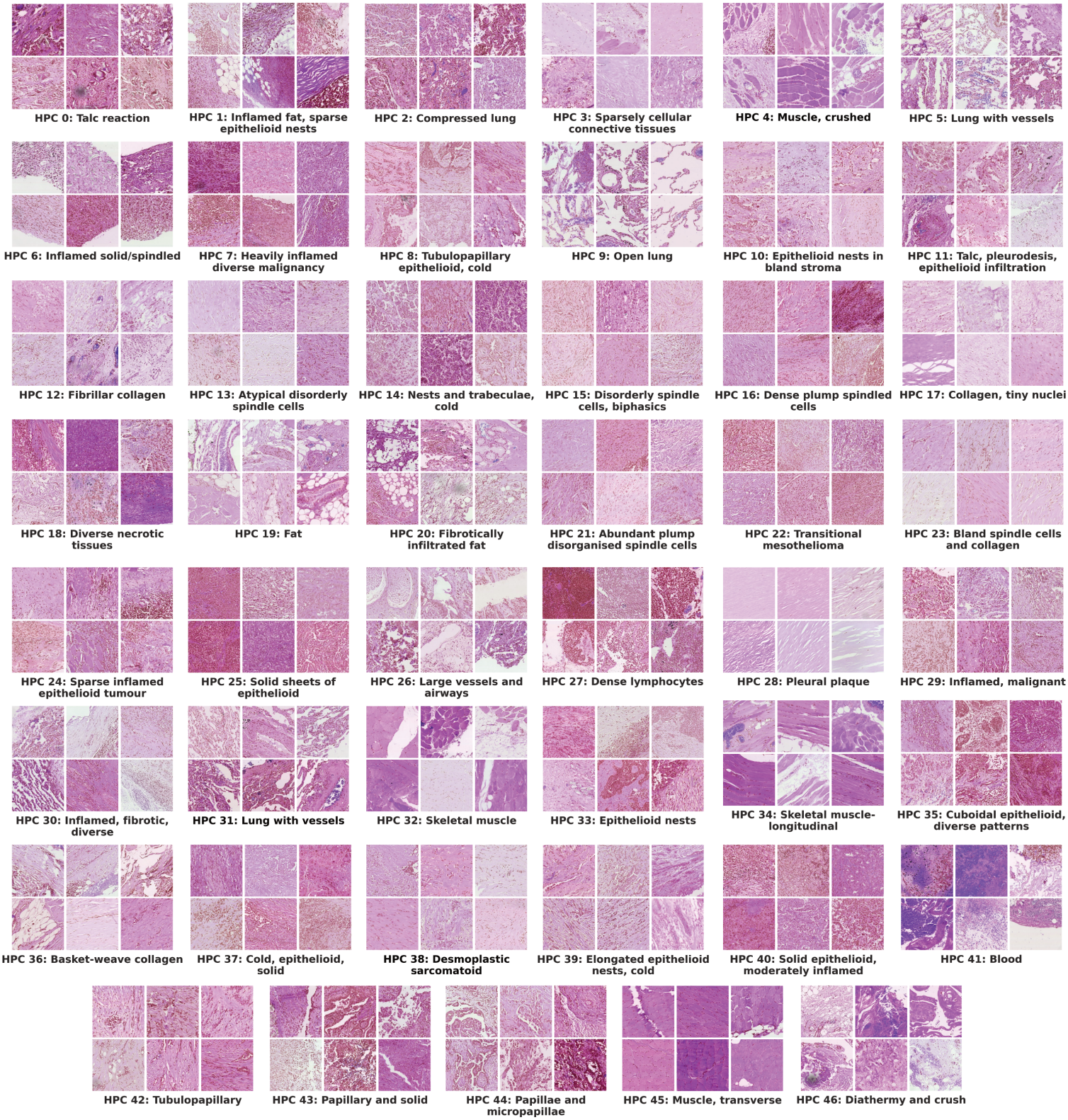
Supplementary Table 1: Pathologist Annotation Sheet Criteria

Leiden Resolution	Dataset	AUC	Precision Score	Sensitivity	Specificity
2.0	LATTICe-M	86.9 ± 0.04	62.3 ± 0.15	**80.6 ± 0.12**	72.9 ± 0.11
4.0		**87.2 ± 0.03**	63.1 ± 0.15	80.2 ± 0.11	74.5 ± 0.08
7.0		86.5 ± 0.03	**65.0 ± 0.15**	77.8 ± 0.09	**76.9 ± 0.09**
2.0	TCGA	76.5 ± 0.04	62.1 ± 0.08	61.9 ± 0.1	75.3 ± 0.1
4.0		**80.5 ± 0.03**	68.3 ± 0.1	**69.8 ± 0.08**	**79.4 ± 0.09**
7.0		78.2 ± 0.06	**65.3 ± 0.16**	63.8 ± 0.11	78.7 ± 0.1

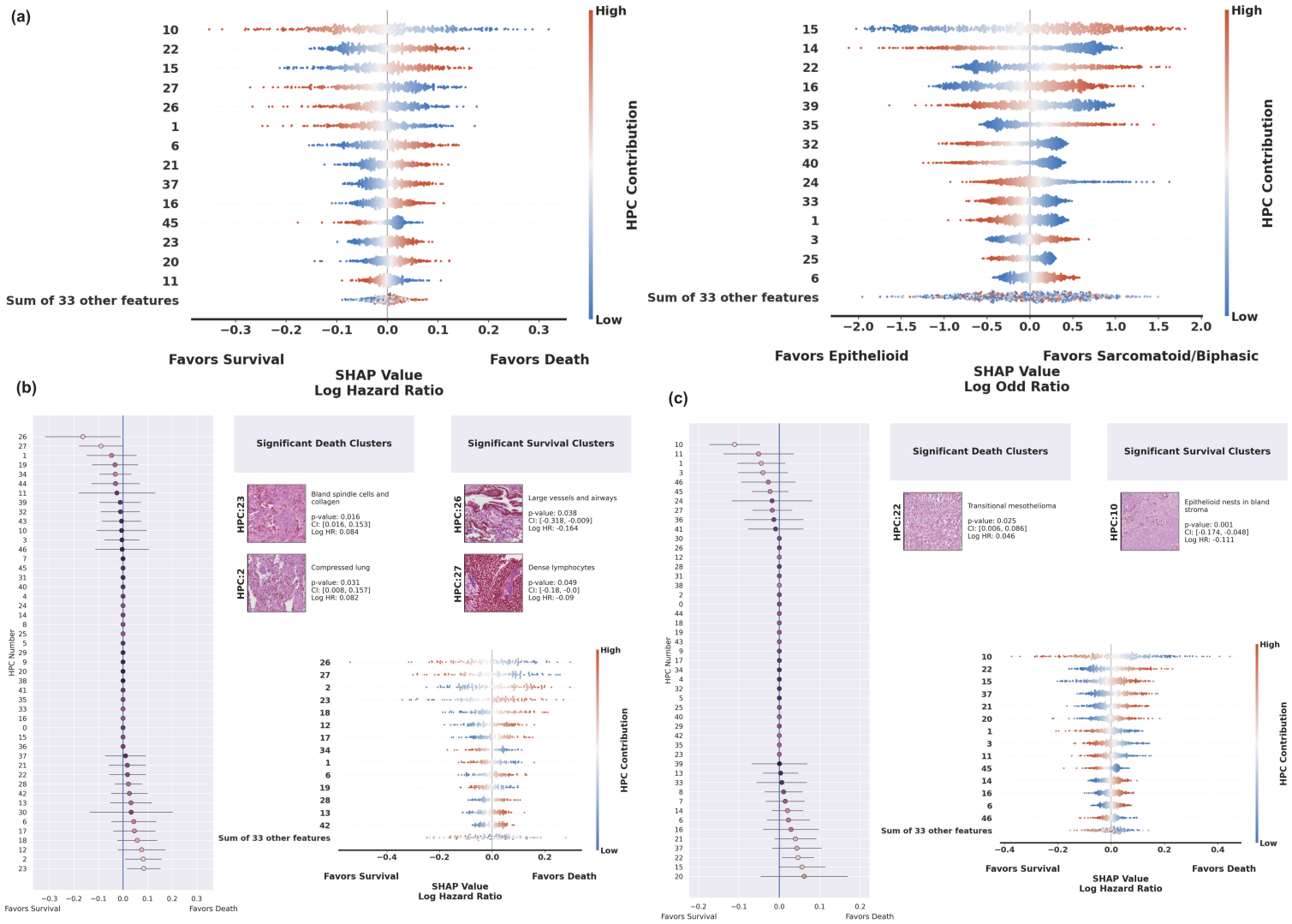
Supplementary Table 2: Area under the curve (AUC), Precision, Sensitivity, Specificity scores for the mesothelioma subtype classification task on LATTICe-M (primary) and TCGA (additional) cohorts across different Leiden clustering algorithm resolutions. The scores are averaged over 5-fold cross-validation and after undersampling using the edited nearest neighbour model (ENN).

	HPCs			Clinical and HPCs	
Leiden Resolutions	Train	Test	TCGA	Train	Test
2.0	0.67 ± 0.0	0.65 ± 0.03	0.65 ± 0.01	0.68 ± 0.01	0.66 ± 0.03
4.0	0.69 ± 0.0	**0.66 ± 0.03**	0.66 ± 0.02	0.7 ± 0.0	0.66 ± 0.03
7.0	0.7 ± 0.01	0.65 ± 0.04	**0.66 ± 0.01**	0.71 ± 0.01	0.66 ± 0.04
9.0	0.7 ± 0.01	0.66 ± 0.04	0.65 ± 0.02	0.71 ± 0.01	**0.67 ± 0.04**

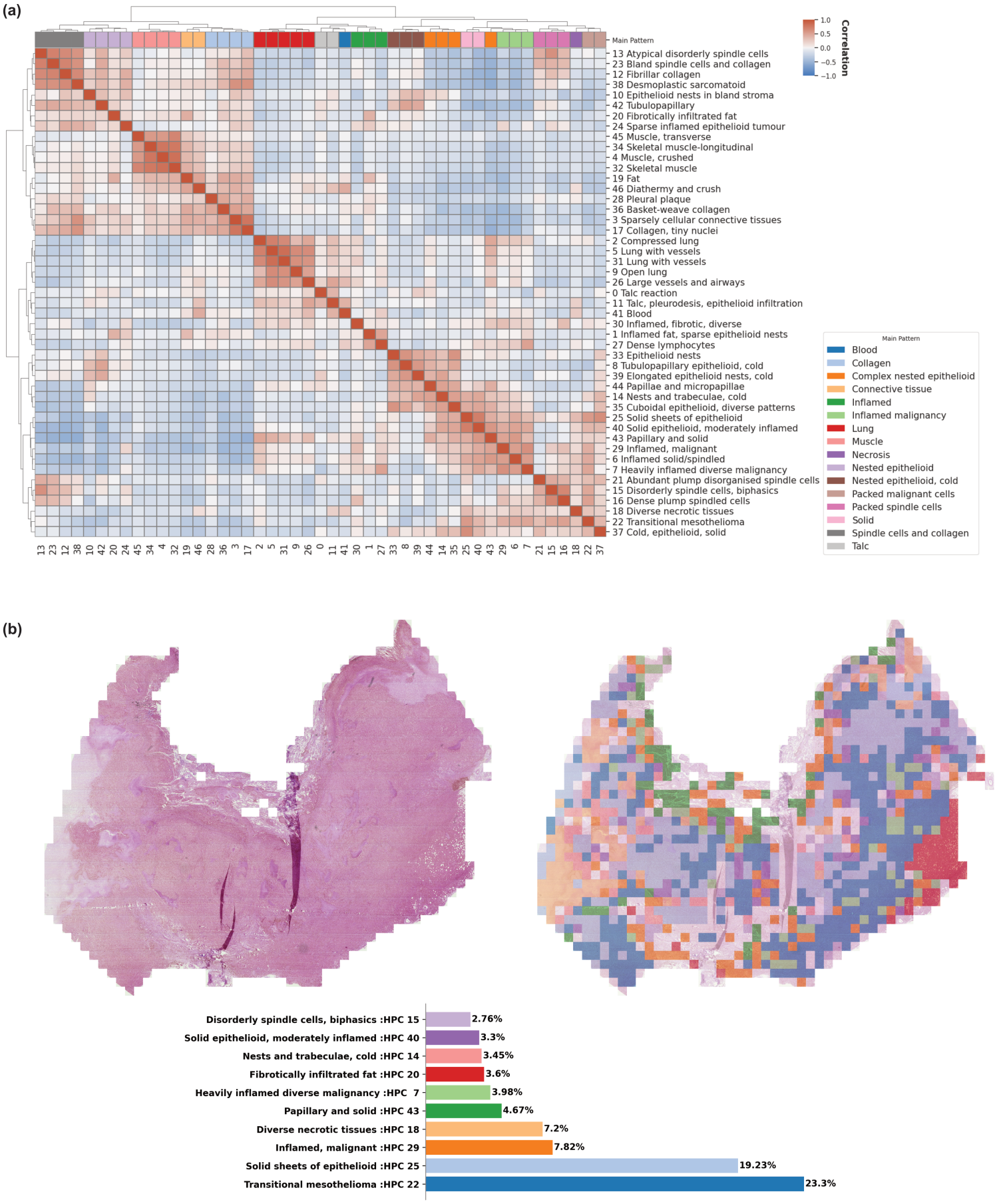
Supplementary Table 3: Patient outcome prediction using Cox proportional hazard ratio model C-indices in train, test (LATTICe-M), and additional (TCGA) datasets across different Leiden resolutions with 5-fold cross-validated scores. Clinical information, including subtype, TNM stage, and age, was added to the patient vectors derived from HPL for the primary dataset only.



Supplementary Figure 1: Examples of tiles from LATTICe-M Dataset assigned to All HPCs



Supplementary Figure 2: **(a)** SHAP plots showing the impact of HPCs on predictive survival (left) and subtype (right) models, in order. **(b),(c)** SHAP and Forest plots from Cox models trained and tested separately on each mesothelioma subtype group cases, displaying HPC significance within each subtype. The plots are organised with Sarcomatoid/Biphasic on the left and Epithelioid on the right.



Supplementary Figure 3: **(a)**HPC Pearson correlation heatmap; annotations were independently provided by a pathologist after examination of representative sets of tile images (100 random tiles per HPC). The main pattern row displays supercluster annotations, confirming the model's clustering performance, as nearly identical HPCs within a supercluster are grouped together in the correlation matrix. **(a)**An epithelioid sample case characterised mostly by transitional mesothelioma HPC.