

## Supplements

### 1. Performance metrics plots NSCLC vs. MET

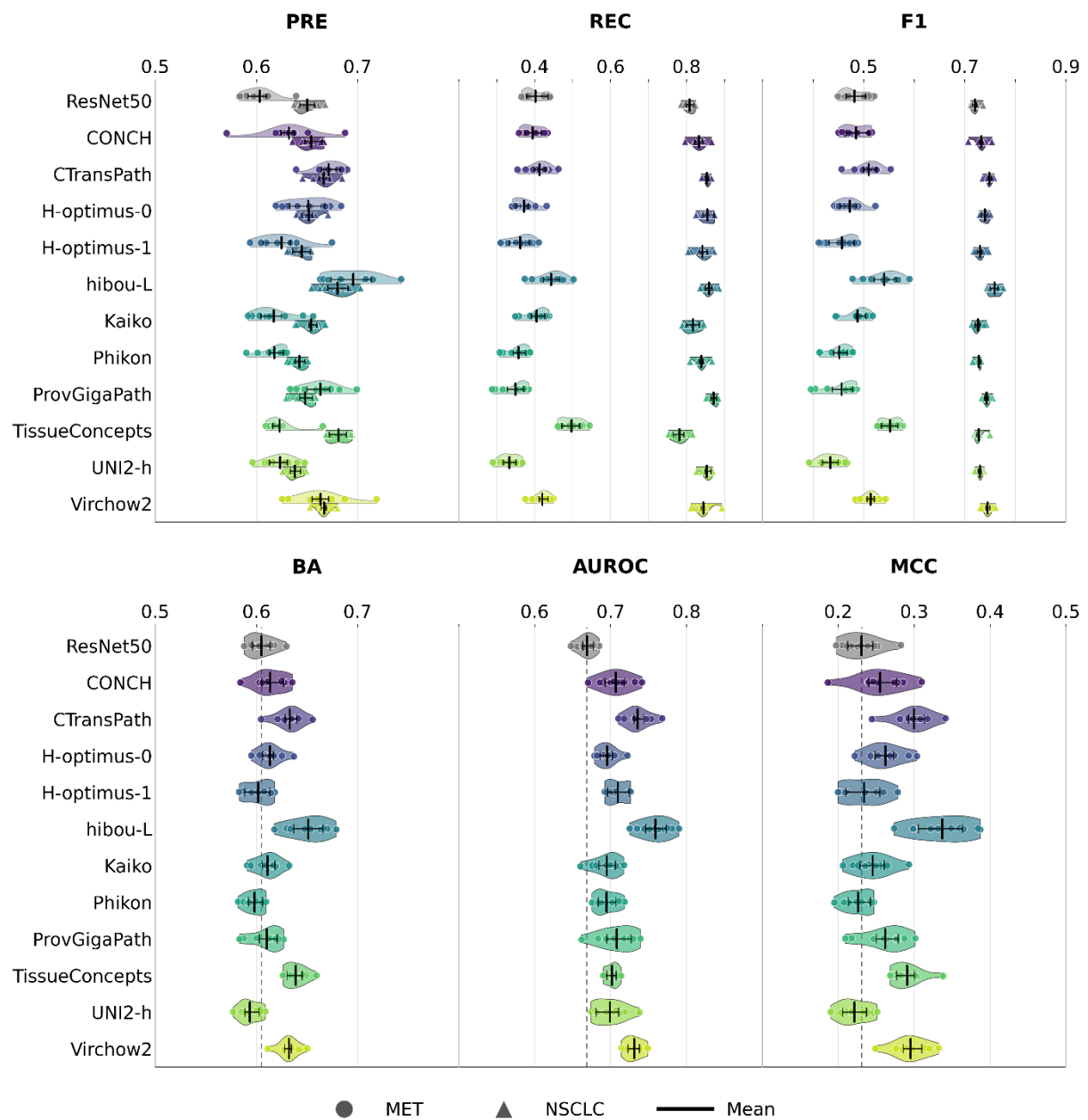


Figure S1: Logistic regression: Patch-level performance metrics NSCLC vs. MET.

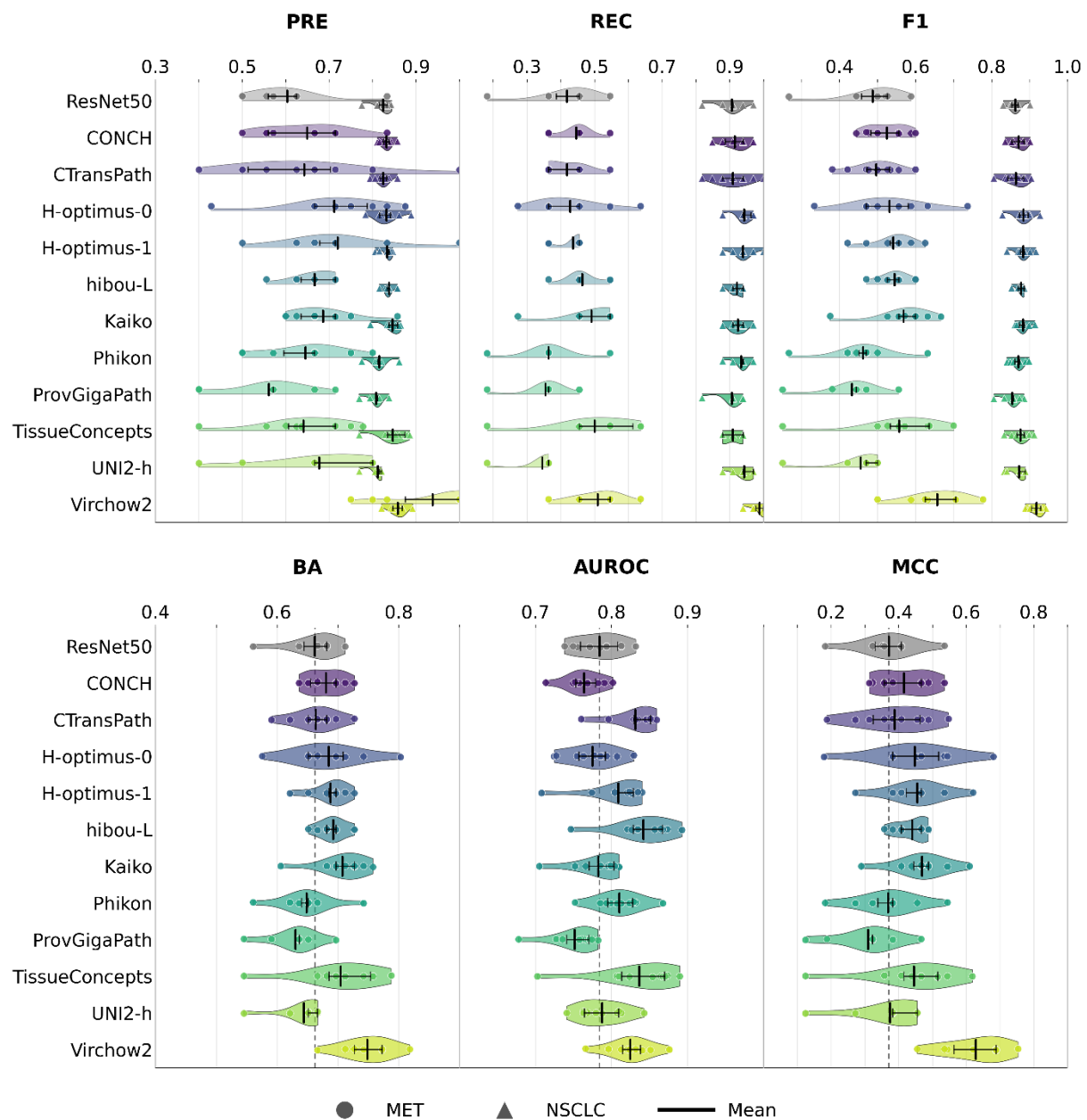


Figure S2: Logistic regression: Slide-level performance metrics NSCLC vs. MET.

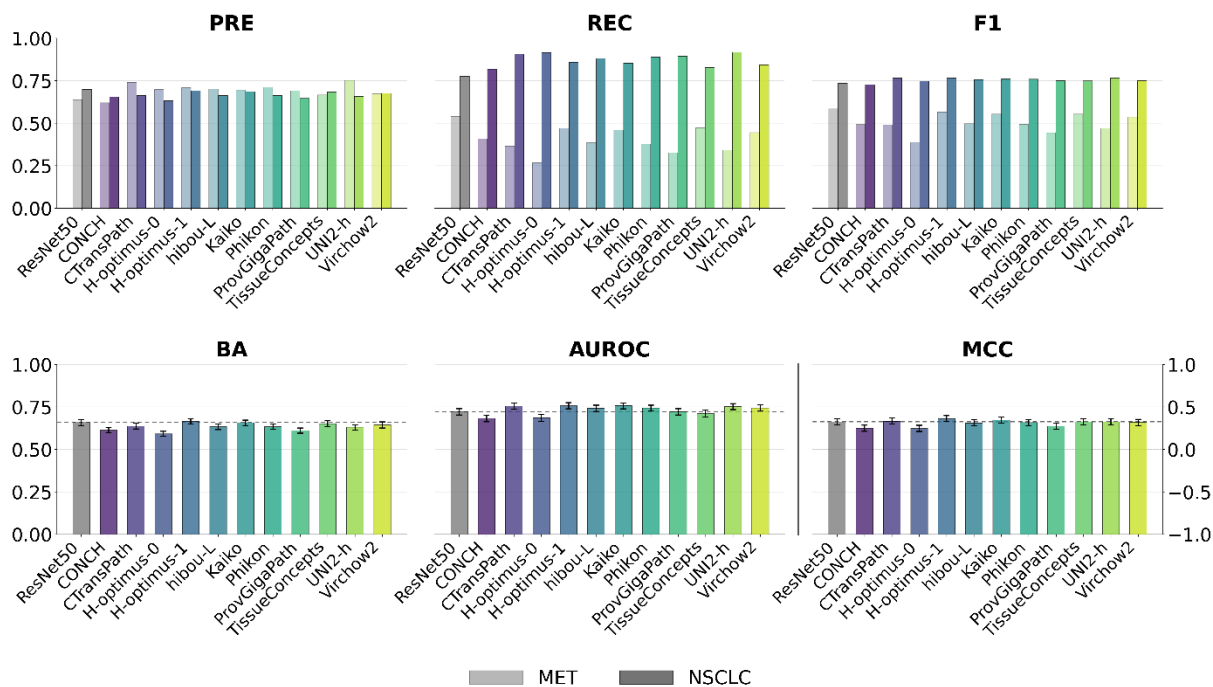


Figure S3: MLP: Patch-level performance metrics NSCLC vs. MET.

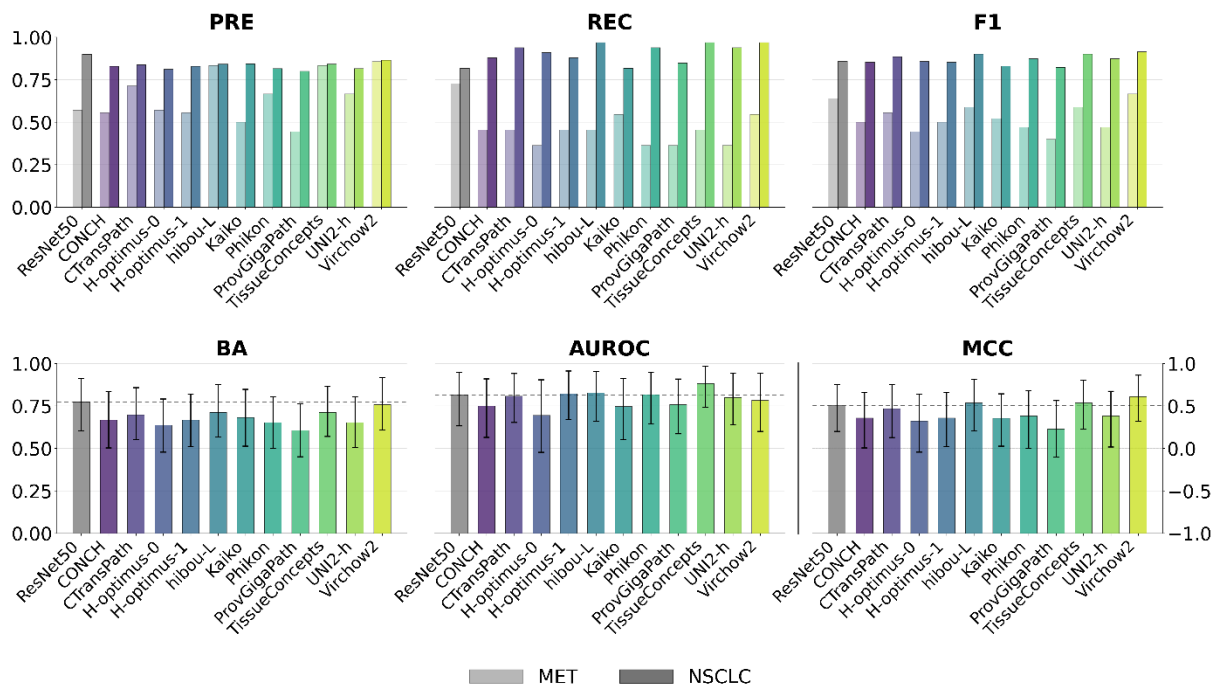


Figure S4: MLP: Slide-level performance metrics NSCLC vs. MET.

## 2. Performance metrics plots AC vs. SCC

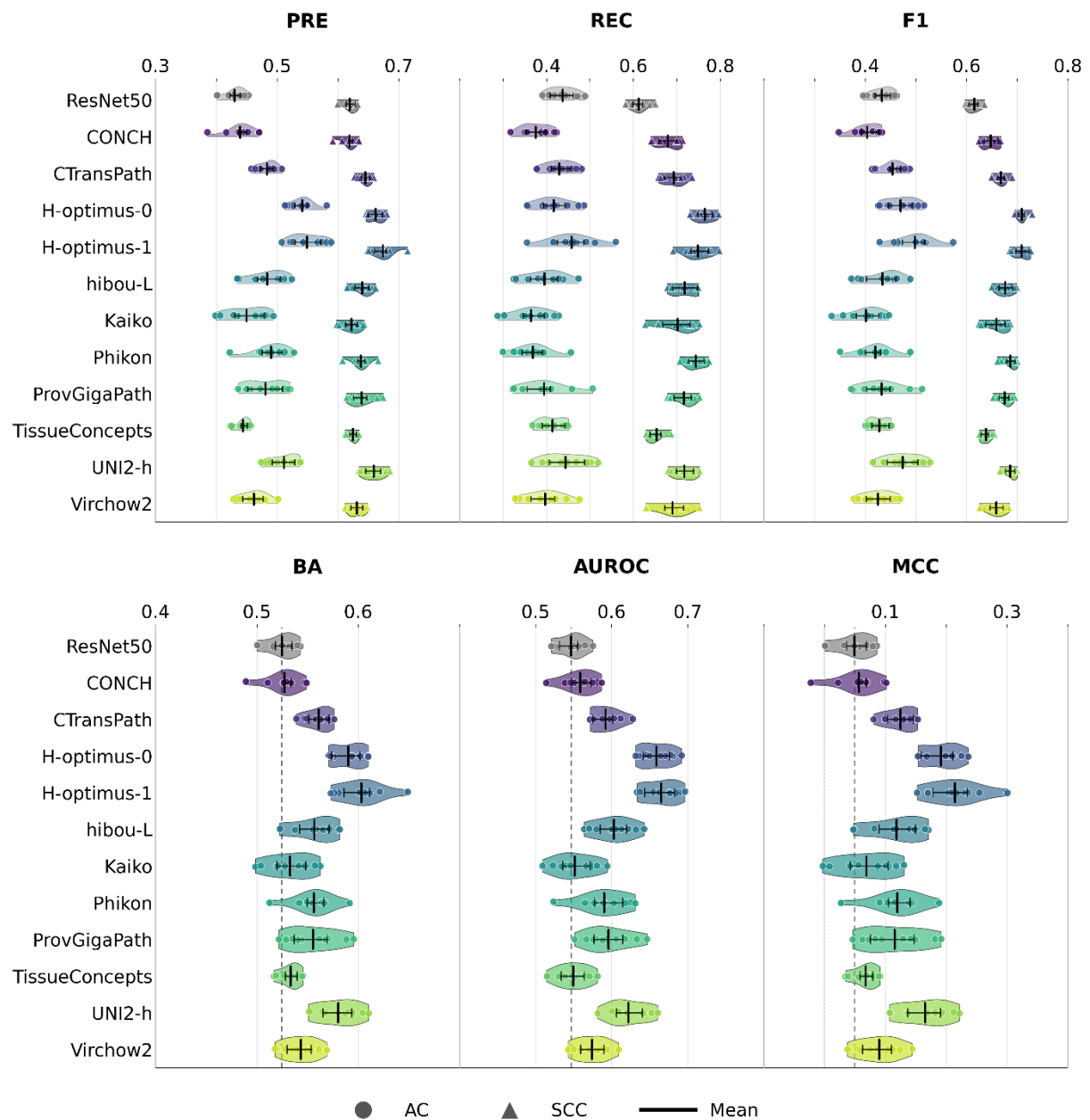


Figure S5: Logistic regression: Patch-level performance metrics AC vs. SCC.

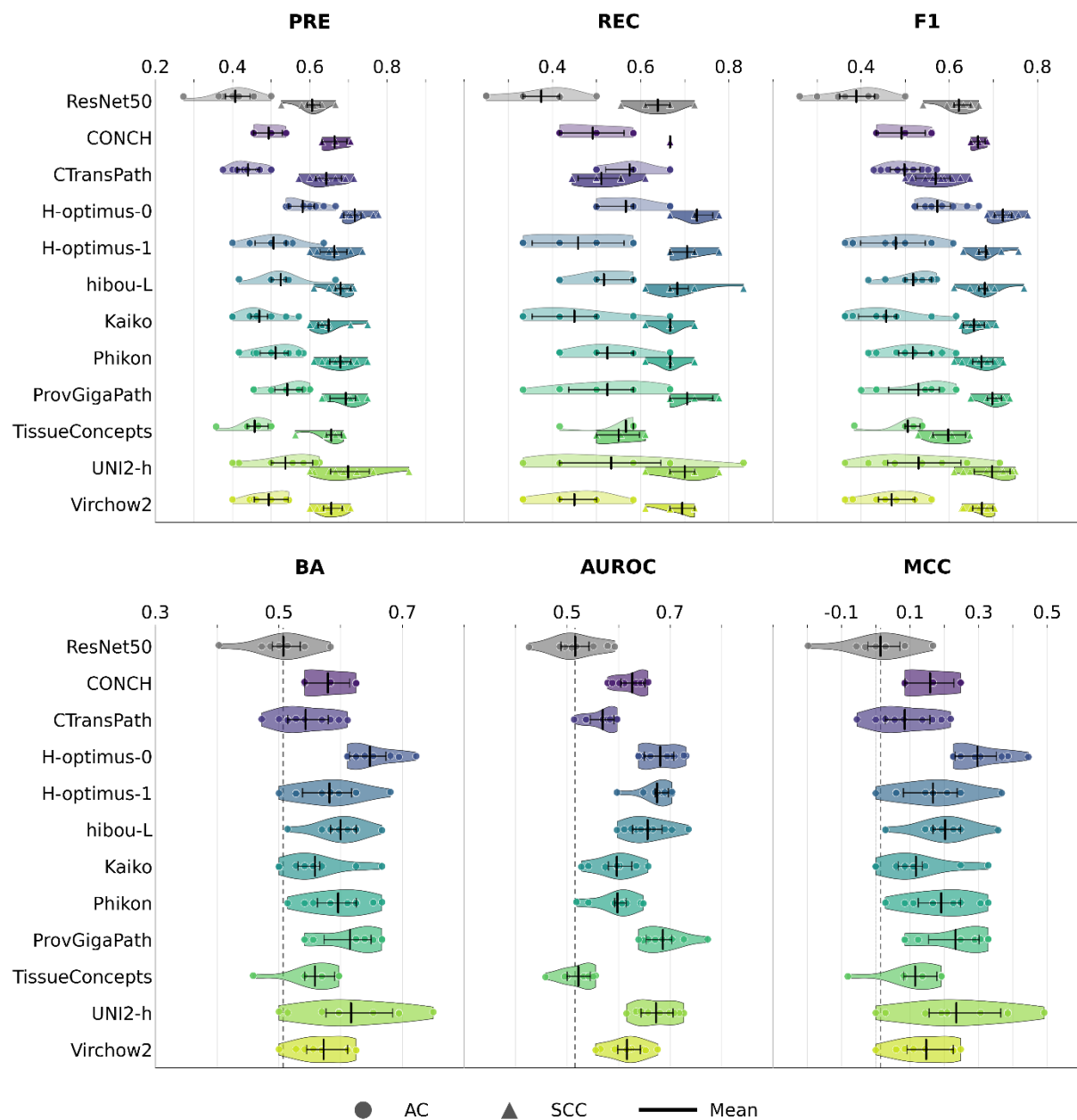


Figure S6: Logistic regression: Slide-level performance metrics AC vs. SCC.

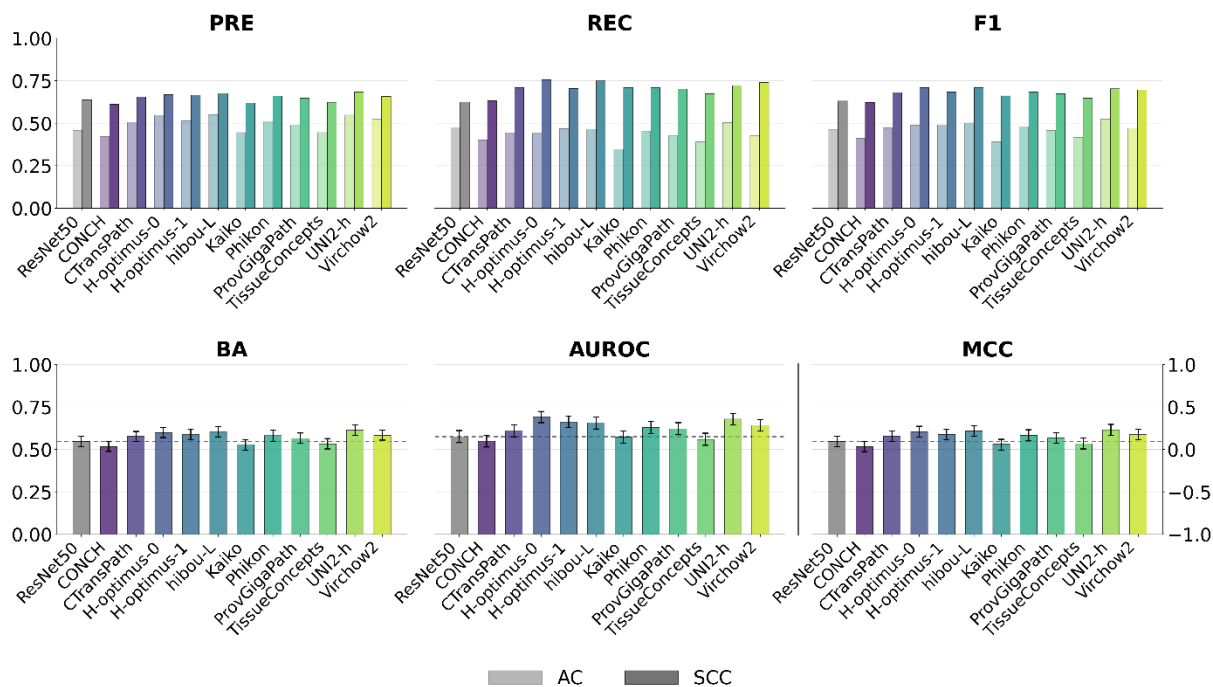


Figure S7: MLP: Patch-level performance metrics AC vs. SCC.

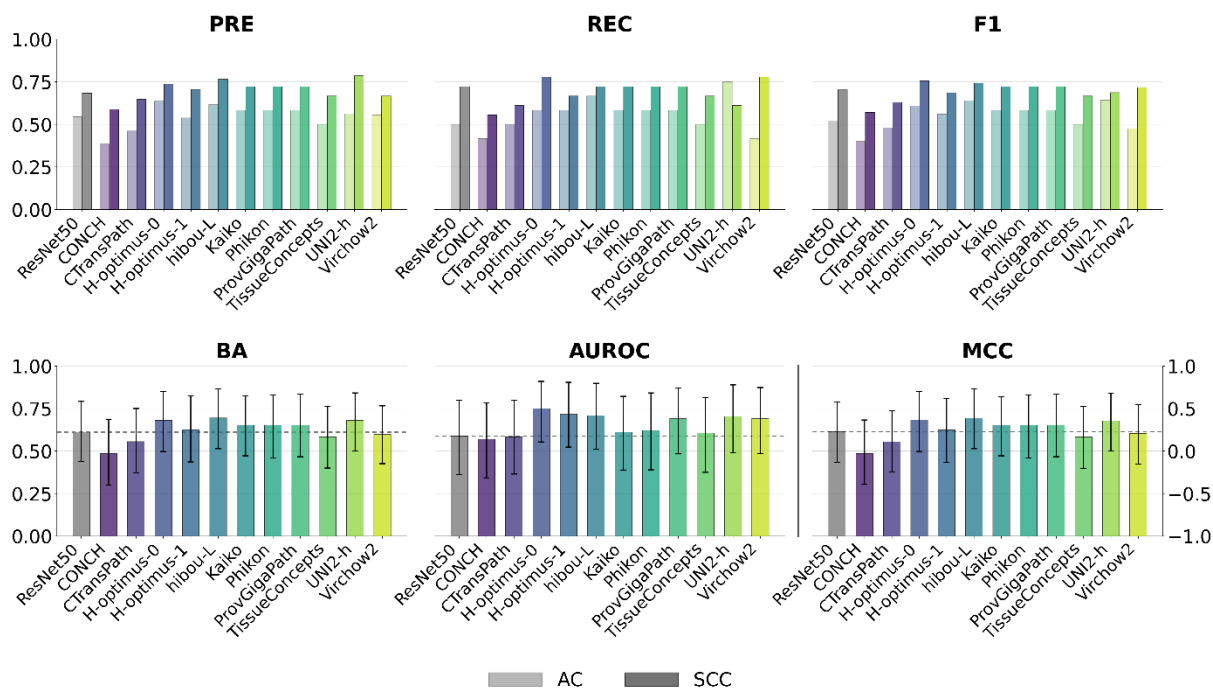


Figure S8: MLP: Slide-level performance metrics AC vs. SCC.

### 3. Performance metrics tables NSCLC vs. MET

Table S1: Logistic regression on CONCH embeddings: Patch-level performance metrics NSCLC vs. MET.

| Fold           | Class | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------|-------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1         | MET   | 0.6289                 | 0.3668                 | 0.4634                 | 0.6047                 | 0.6902                 | 0.2402                 |
|                | NSCLC | 0.6467                 | 0.8426                 | 0.7318                 |                        |                        |                        |
| Fold 2         | MET   | 0.6508                 | 0.4227                 | 0.5125                 | 0.6289                 | 0.7317                 | 0.2855                 |
|                | NSCLC | 0.6655                 | 0.8351                 | 0.7407                 |                        |                        |                        |
| Fold 3         | MET   | 0.5705                 | 0.3720                 | 0.4503                 | 0.5842                 | 0.6702                 | 0.1863                 |
|                | NSCLC | 0.6356                 | 0.7964                 | 0.7070                 |                        |                        |                        |
| Fold 4         | MET   | 0.6376                 | 0.4338                 | 0.5164                 | 0.6273                 | 0.7188                 | 0.2780                 |
|                | NSCLC | 0.6660                 | 0.8207                 | 0.7353                 |                        |                        |                        |
| Fold 5         | MET   | 0.6318                 | 0.3582                 | 0.4572                 | 0.6032                 | 0.7002                 | 0.2391                 |
|                | NSCLC | 0.6451                 | 0.8482                 | 0.7329                 |                        |                        |                        |
| Fold 6         | MET   | 0.6876                 | 0.4046                 | 0.5095                 | 0.6355                 | 0.7413                 | 0.3099                 |
|                | NSCLC | 0.6668                 | 0.8663                 | 0.7536                 |                        |                        |                        |
| Fold 7         | MET   | 0.6358                 | 0.3780                 | 0.4741                 | 0.6103                 | 0.7105                 | 0.2514                 |
|                | NSCLC | 0.6507                 | 0.8426                 | 0.7343                 |                        |                        |                        |
| Fold 8         | MET   | 0.6229                 | 0.3789                 | 0.4712                 | 0.6060                 | 0.6860                 | 0.2399                 |
|                | NSCLC | 0.6485                 | 0.8332                 | 0.7294                 |                        |                        |                        |
| Fold 9         | MET   | 0.6190                 | 0.4021                 | 0.4875                 | 0.6111                 | 0.7038                 | 0.2461                 |
|                | NSCLC | 0.6536                 | 0.8201                 | 0.7274                 |                        |                        |                        |
| Fold 10        | MET   | 0.6367                 | 0.4261                 | 0.5106                 | 0.6247                 | 0.7160                 | 0.2737                 |
|                | NSCLC | 0.6636                 | 0.8232                 | 0.7349                 |                        |                        |                        |
| Mean $\pm$ std | MET   | 0.6322<br>$\pm 0.0290$ | 0.3943<br>$\pm 0.0271$ | 0.4853<br>$\pm 0.0253$ | 0.6136<br>$\pm 0.0155$ | 0.7069<br>$\pm 0.0215$ | 0.2550<br>$\pm 0.0339$ |
|                | NSCLC | 0.6542<br>$\pm 0.0108$ | 0.8329<br>$\pm 0.0191$ | 0.7327<br>$\pm 0.0116$ |                        |                        |                        |

Table S2: Logistic regression on CONCH embeddings: Slide-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.5714            | 0.3636            | 0.4444            | 0.6364            | 0.7135            | 0.3229            |
|                   | NSCLC        | 0.8108            | 0.9091            | 0.8571            |                   |                   |                   |
| Fold 2            | MET          | 0.8333            | 0.4545            | 0.5882            | 0.7121            | 0.8017            | 0.5353            |
|                   | NSCLC        | 0.8421            | 0.9697            | 0.9014            |                   |                   |                   |
| Fold 3            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.7493            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 4            | MET          | 0.5000            | 0.4545            | 0.4762            | 0.6515            | 0.7686            | 0.3131            |
|                   | NSCLC        | 0.8235            | 0.8485            | 0.8358            |                   |                   |                   |
| Fold 5            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.7548            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 6            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.7906            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 7            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.7576            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 8            | MET          | 0.6667            | 0.5455            | 0.6000            | 0.7273            | 0.7824            | 0.4880            |
|                   | NSCLC        | 0.8571            | 0.9091            | 0.8824            |                   |                   |                   |
| Fold 9            | MET          | 0.5556            | 0.4545            | 0.5000            | 0.6667            | 0.7521            | 0.3578            |
|                   | NSCLC        | 0.8286            | 0.8788            | 0.8529            |                   |                   |                   |
| Fold 10           | MET          | 0.5556            | 0.4545            | 0.5000            | 0.6667            | 0.7686            | 0.3578            |
|                   | NSCLC        | 0.8286            | 0.8788            | 0.8529            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6492<br>±0.1017 | 0.4455<br>±0.0516 | 0.5246<br>±0.0532 | 0.6803<br>±0.0298 | 0.7639<br>±0.0248 | 0.4156<br>±0.0776 |
|                   | <b>NSCLC</b> | 0.8320<br>±0.0135 | 0.9152<br>±0.0373 | 0.8713<br>±0.0205 |                   |                   |                   |

Table S3: Logistic regression on CONCH embeddings: Patient-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6667            | 0.2500            | 0.3636            | 0.6012            | 0.7321            | 0.2970            |
|                   | NSCLC        | 0.7692            | 0.9524            | 0.8511            |                   |                   |                   |
| Fold 2            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.8333            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 3            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.7679            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 4            | MET          | 0.4286            | 0.3750            | 0.4000            | 0.5923            | 0.7679            | 0.1927            |
|                   | NSCLC        | 0.7727            | 0.8095            | 0.7907            |                   |                   |                   |
| Fold 5            | MET          | 0.6667            | 0.2500            | 0.3636            | 0.6012            | 0.7440            | 0.2970            |
|                   | NSCLC        | 0.7692            | 0.9524            | 0.8511            |                   |                   |                   |
| Fold 6            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.8274            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 7            | MET          | 0.6000            | 0.3750            | 0.4615            | 0.6399            | 0.7738            | 0.3310            |
|                   | NSCLC        | 0.7917            | 0.9048            | 0.8444            |                   |                   |                   |
| Fold 8            | MET          | 0.6667            | 0.5000            | 0.5714            | 0.7024            | 0.7798            | 0.4466            |
|                   | NSCLC        | 0.8261            | 0.9048            | 0.8636            |                   |                   |                   |
| Fold 9            | MET          | 0.5000            | 0.3750            | 0.4286            | 0.6161            | 0.7619            | 0.2561            |
|                   | NSCLC        | 0.7826            | 0.8571            | 0.8182            |                   |                   |                   |
| Fold 10           | MET          | 0.4286            | 0.3750            | 0.4000            | 0.5923            | 0.7857            | 0.1927            |
|                   | NSCLC        | 0.7727            | 0.8095            | 0.7907            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6207<br>±0.1271 | 0.3625<br>±0.0710 | 0.4489<br>±0.0689 | 0.6336<br>±0.0385 | 0.7774<br>±0.0321 | 0.3286<br>±0.0975 |
|                   | <b>NSCLC</b> | 0.7884<br>±0.0185 | 0.9048<br>±0.0594 | 0.8418<br>±0.0312 |                   |                   |                   |

Table S4: Logistic regression on CTransPath embeddings: Patch-level performance metrics NSCLC vs. MET.

| Fold                             | Class        | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------------------------|--------------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1                           | MET          | 0.6393                 | 0.3548                 | 0.4564                 | 0.6046                 | 0.7102                 | 0.2442                 |
|                                  | NSCLC        | 0.6456                 | 0.8545                 | 0.7355                 |                        |                        |                        |
| Fold 2                           | MET          | 0.6897                 | 0.4622                 | 0.5535                 | 0.6555                 | 0.7680                 | 0.3412                 |
|                                  | NSCLC        | 0.6846                 | 0.8488                 | 0.7579                 |                        |                        |                        |
| Fold 3                           | MET          | 0.6628                 | 0.4373                 | 0.5269                 | 0.6378                 | 0.7322                 | 0.3037                 |
|                                  | NSCLC        | 0.6720                 | 0.8382                 | 0.7460                 |                        |                        |                        |
| Fold 4                           | MET          | 0.6803                 | 0.4278                 | 0.5253                 | 0.6408                 | 0.7530                 | 0.3152                 |
|                                  | NSCLC        | 0.6724                 | 0.8538                 | 0.7523                 |                        |                        |                        |
| Fold 5                           | MET          | 0.6845                 | 0.4064                 | 0.5100                 | 0.6351                 | 0.7344                 | 0.3081                 |
|                                  | NSCLC        | 0.6668                 | 0.8638                 | 0.7527                 |                        |                        |                        |
| Fold 6                           | MET          | 0.6686                 | 0.4055                 | 0.5048                 | 0.6297                 | 0.7307                 | 0.2936                 |
|                                  | NSCLC        | 0.6639                 | 0.8538                 | 0.7470                 |                        |                        |                        |
| Fold 7                           | MET          | 0.6720                 | 0.3960                 | 0.4984                 | 0.6278                 | 0.7323                 | 0.2921                 |
|                                  | NSCLC        | 0.6619                 | 0.8595                 | 0.7478                 |                        |                        |                        |
| Fold 8                           | MET          | 0.6707                 | 0.3763                 | 0.4821                 | 0.6210                 | 0.7180                 | 0.2813                 |
|                                  | NSCLC        | 0.6562                 | 0.8657                 | 0.7466                 |                        |                        |                        |
| Fold 9                           | MET          | 0.6618                 | 0.4287                 | 0.5203                 | 0.6347                 | 0.7318                 | 0.2987                 |
|                                  | NSCLC        | 0.6693                 | 0.8407                 | 0.7453                 |                        |                        |                        |
| Fold 10                          | MET          | 0.6841                 | 0.4261                 | 0.5251                 | 0.6415                 | 0.7469                 | 0.3178                 |
|                                  | NSCLC        | 0.6725                 | 0.8570                 | 0.7536                 |                        |                        |                        |
| <b>Mean <math>\pm</math> std</b> | <b>MET</b>   | 0.6714<br>$\pm 0.0147$ | 0.4121<br>$\pm 0.0312$ | 0.5103<br>$\pm 0.0270$ | 0.6329<br>$\pm 0.0136$ | 0.7357<br>$\pm 0.0167$ | 0.2996<br>$\pm 0.0256$ |
|                                  | <b>NSCLC</b> | 0.6665<br>$\pm 0.0106$ | 0.8536<br>$\pm 0.0090$ | 0.7485<br>$\pm 0.0061$ |                        |                        |                        |

Table S5: Logistic regression on CTransPath embeddings: Slide-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.4000            | 0.3636            | 0.3810            | 0.5909            | 0.7603            | 0.1879            |
|                   | NSCLC        | 0.7941            | 0.8182            | 0.8060            |                   |                   |                   |
| Fold 2            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.8512            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 3            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8457            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 4            | MET          | 0.6667            | 0.5455            | 0.6000            | 0.7273            | 0.8540            | 0.4880            |
|                   | NSCLC        | 0.8571            | 0.9091            | 0.8824            |                   |                   |                   |
| Fold 5            | MET          | 0.5000            | 0.4545            | 0.4762            | 0.6515            | 0.7961            | 0.3131            |
|                   | NSCLC        | 0.8235            | 0.8485            | 0.8358            |                   |                   |                   |
| Fold 6            | MET          | 0.5000            | 0.3636            | 0.4211            | 0.6212            | 0.8595            | 0.2722            |
|                   | NSCLC        | 0.8056            | 0.8788            | 0.8406            |                   |                   |                   |
| Fold 7            | MET          | 1.0000            | 0.3636            | 0.5333            | 0.6818            | 0.8512            | 0.5477            |
|                   | NSCLC        | 0.8250            | 1.0000            | 0.9041            |                   |                   |                   |
| Fold 8            | MET          | 0.8000            | 0.3636            | 0.5000            | 0.6667            | 0.8347            | 0.4548            |
|                   | NSCLC        | 0.8205            | 0.9697            | 0.8889            |                   |                   |                   |
| Fold 9            | MET          | 0.6250            | 0.4545            | 0.5263            | 0.6818            | 0.8292            | 0.4082            |
|                   | NSCLC        | 0.8333            | 0.9091            | 0.8696            |                   |                   |                   |
| Fold 10           | MET          | 0.5556            | 0.4545            | 0.5000            | 0.6667            | 0.8320            | 0.3578            |
|                   | NSCLC        | 0.8286            | 0.8788            | 0.8529            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6428<br>±0.1720 | 0.4182<br>±0.0636 | 0.4964<br>±0.0638 | 0.6636<br>±0.0383 | 0.8314<br>±0.0309 | 0.3878<br>±0.1088 |
|                   | <b>NSCLC</b> | 0.8241<br>±0.0174 | 0.9091<br>±0.0553 | 0.8639<br>±0.0298 |                   |                   |                   |

Table S6: Logistic regression on CTransPath embeddings: Patient-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.4000            | 0.2500            | 0.3077            | 0.5536            | 0.7500            | 0.1268            |
|                   | NSCLC        | 0.7500            | 0.8571            | 0.8000            |                   |                   |                   |
| Fold 2            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.8988            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 3            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8750            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 4            | MET          | 0.8000            | 0.5000            | 0.6154            | 0.7262            | 0.8750            | 0.5353            |
|                   | NSCLC        | 0.8333            | 0.9524            | 0.8889            |                   |                   |                   |
| Fold 5            | MET          | 0.6000            | 0.3750            | 0.4615            | 0.6399            | 0.8214            | 0.3310            |
|                   | NSCLC        | 0.7917            | 0.9048            | 0.8444            |                   |                   |                   |
| Fold 6            | MET          | 0.5000            | 0.2500            | 0.3333            | 0.5774            | 0.8750            | 0.2006            |
|                   | NSCLC        | 0.7600            | 0.9048            | 0.8261            |                   |                   |                   |
| Fold 7            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8690            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 8            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8452            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 9            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8571            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 10           | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.8690            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.7800<br>±0.2239 | 0.3375<br>±0.0844 | 0.4609<br>±0.0991 | 0.6449<br>±0.0523 | 0.8536<br>±0.0418 | 0.4025<br>±0.1442 |
|                   | <b>NSCLC</b> | 0.7906<br>±0.0247 | 0.9524<br>±0.0502 | 0.8636<br>±0.0309 |                   |                   |                   |

Table S7: Logistic regression on H-optimus-0 embeddings: Patch-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6192            | 0.3436            | 0.4420            | 0.5950            | 0.6787            | 0.2217            |
|                   | NSCLC        | 0.6395            | 0.8463            | 0.7285            |                   |                   |                   |
| Fold 2            | MET          | 0.6303            | 0.3823            | 0.4759            | 0.6096            | 0.7036            | 0.2483            |
|                   | NSCLC        | 0.6508            | 0.8370            | 0.7322            |                   |                   |                   |
| Fold 3            | MET          | 0.6535            | 0.3402            | 0.4475            | 0.6045            | 0.6919            | 0.2495            |
|                   | NSCLC        | 0.6443            | 0.8688            | 0.7399            |                   |                   |                   |
| Fold 4            | MET          | 0.6658            | 0.4313            | 0.5235            | 0.6369            | 0.7219            | 0.3036            |
|                   | NSCLC        | 0.6708            | 0.8426            | 0.7470            |                   |                   |                   |
| Fold 5            | MET          | 0.6731            | 0.3574            | 0.4669            | 0.6156            | 0.6978            | 0.2740            |
|                   | NSCLC        | 0.6516            | 0.8738            | 0.7465            |                   |                   |                   |
| Fold 6            | MET          | 0.6683            | 0.3514            | 0.4606            | 0.6123            | 0.6910            | 0.2671            |
|                   | NSCLC        | 0.6493            | 0.8732            | 0.7448            |                   |                   |                   |
| Fold 7            | MET          | 0.6404            | 0.3488            | 0.4516            | 0.6032            | 0.6845            | 0.2424            |
|                   | NSCLC        | 0.6443            | 0.8576            | 0.7358            |                   |                   |                   |
| Fold 8            | MET          | 0.6838            | 0.3771            | 0.4862            | 0.6252            | 0.6964            | 0.2927            |
|                   | NSCLC        | 0.6585            | 0.8732            | 0.7508            |                   |                   |                   |
| Fold 9            | MET          | 0.6257            | 0.4021            | 0.4895            | 0.6136            | 0.6820            | 0.2525            |
|                   | NSCLC        | 0.6549            | 0.8251            | 0.7302            |                   |                   |                   |
| Fold 10           | MET          | 0.6520            | 0.3832            | 0.4827            | 0.6173            | 0.7052            | 0.2683            |
|                   | NSCLC        | 0.6550            | 0.8513            | 0.7404            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6512<br>±0.0218 | 0.3717<br>±0.0292 | 0.4726<br>±0.0244 | 0.6133<br>±0.0118 | 0.6953<br>±0.0128 | 0.2620<br>±0.0243 |
|                   | <b>NSCLC</b> | 0.6519<br>±0.0088 | 0.8549<br>±0.0172 | 0.7396<br>±0.0077 |                   |                   |                   |

Table S8: Logistic regression on H-optimus-0 embeddings: Slide-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.7245            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 2            | MET          | 0.4286            | 0.2727            | 0.3333            | 0.5758            | 0.7273            | 0.1794            |
|                   | NSCLC        | 0.7838            | 0.8788            | 0.8286            |                   |                   |                   |
| Fold 3            | MET          | 0.8000            | 0.3636            | 0.5000            | 0.6667            | 0.8072            | 0.4548            |
|                   | NSCLC        | 0.8205            | 0.9697            | 0.8889            |                   |                   |                   |
| Fold 4            | MET          | 0.8750            | 0.6364            | 0.7368            | 0.8030            | 0.7879            | 0.6804            |
|                   | NSCLC        | 0.8889            | 0.9697            | 0.9275            |                   |                   |                   |
| Fold 5            | MET          | 0.8333            | 0.4545            | 0.5882            | 0.7121            | 0.7769            | 0.5353            |
|                   | NSCLC        | 0.8421            | 0.9697            | 0.9014            |                   |                   |                   |
| Fold 6            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8292            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 7            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.7851            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 8            | MET          | 0.7500            | 0.5455            | 0.6316            | 0.7424            | 0.7631            | 0.5443            |
|                   | NSCLC        | 0.8611            | 0.9394            | 0.8986            |                   |                   |                   |
| Fold 9            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.7548            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 10           | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.7934            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.7115<br>±0.1234 | 0.4273<br>±0.1054 | 0.5313<br>±0.1095 | 0.6848<br>±0.0614 | 0.7749<br>±0.0333 | 0.4474<br>±0.1320 |
|                   | <b>NSCLC</b> | 0.8319<br>±0.0289 | 0.9424<br>±0.0265 | 0.8836<br>±0.0255 |                   |                   |                   |

Table S9: Logistic regression on H-optimus-0 embeddings: Patient-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6667            | 0.2500            | 0.3636            | 0.6012            | 0.7262            | 0.2970            |
|                   | NSCLC        | 0.7692            | 0.9524            | 0.8511            |                   |                   |                   |
| Fold 2            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.7917            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 3            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8155            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 4            | MET          | 1.0000            | 0.6250            | 0.7692            | 0.8125            | 0.8095            | 0.7395            |
|                   | NSCLC        | 0.8750            | 1.0000            | 0.9333            |                   |                   |                   |
| Fold 5            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.7798            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 6            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.8155            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 7            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.7619            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 8            | MET          | 1.0000            | 0.5000            | 0.6667            | 0.7500            | 0.7738            | 0.6481            |
|                   | NSCLC        | 0.8400            | 1.0000            | 0.9130            |                   |                   |                   |
| Fold 9            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.7679            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 10           | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8095            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.9417<br>±0.1245 | 0.3500<br>±0.1291 | 0.4990<br>±0.1346 | 0.6702<br>±0.0668 | 0.7851<br>±0.0290 | 0.4973<br>±0.1270 |
|                   | <b>NSCLC</b> | 0.8011<br>±0.0338 | 0.9905<br>±0.0201 | 0.8854<br>±0.0237 |                   |                   |                   |

Table S10: Logistic regression on H-optimus-1 embeddings: Patch-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6054            | 0.3282            | 0.4256            | 0.5863            | 0.6945            | 0.2031            |
|                   | NSCLC        | 0.6336            | 0.8445            | 0.7240            |                   |                   |                   |
| Fold 2            | MET          | 0.6334            | 0.3814            | 0.4761            | 0.6105            | 0.7223            | 0.2507            |
|                   | NSCLC        | 0.6512            | 0.8395            | 0.7334            |                   |                   |                   |
| Fold 3            | MET          | 0.5938            | 0.3780            | 0.4619            | 0.5950            | 0.6922            | 0.2118            |
|                   | NSCLC        | 0.6423            | 0.8120            | 0.7172            |                   |                   |                   |
| Fold 4            | MET          | 0.6327            | 0.3952            | 0.4865            | 0.6142            | 0.7250            | 0.2562            |
|                   | NSCLC        | 0.6546            | 0.8332            | 0.7332            |                   |                   |                   |
| Fold 5            | MET          | 0.6746            | 0.3634            | 0.4724            | 0.6180            | 0.7266            | 0.2782            |
|                   | NSCLC        | 0.6534            | 0.8726            | 0.7473            |                   |                   |                   |
| Fold 6            | MET          | 0.6205            | 0.3119            | 0.4151            | 0.5866            | 0.6944            | 0.2094            |
|                   | NSCLC        | 0.6326            | 0.8613            | 0.7294            |                   |                   |                   |
| Fold 7            | MET          | 0.6335            | 0.3505            | 0.4513            | 0.6016            | 0.7057            | 0.2372            |
|                   | NSCLC        | 0.6436            | 0.8526            | 0.7335            |                   |                   |                   |
| Fold 8            | MET          | 0.6098            | 0.3101            | 0.4112            | 0.5829            | 0.7011            | 0.1996            |
|                   | NSCLC        | 0.6305            | 0.8557            | 0.7260            |                   |                   |                   |
| Fold 9            | MET          | 0.6043            | 0.4107            | 0.4890            | 0.6076            | 0.7073            | 0.2350            |
|                   | NSCLC        | 0.6525            | 0.8045            | 0.7206            |                   |                   |                   |
| Fold 10           | MET          | 0.6397            | 0.3875            | 0.4826            | 0.6144            | 0.7254            | 0.2592            |
|                   | NSCLC        | 0.6539            | 0.8413            | 0.7359            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6248<br>±0.0234 | 0.3617<br>±0.0353 | 0.4572<br>±0.0299 | 0.6017<br>±0.0132 | 0.7094<br>±0.0141 | 0.2340<br>±0.0271 |
|                   | <b>NSCLC</b> | 0.6448<br>±0.0097 | 0.8417<br>±0.0211 | 0.7300<br>±0.0086 |                   |                   |                   |

Table S11: Logistic regression on H-optimus-1 embeddings: Slide-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.5000            | 0.3636            | 0.4211            | 0.6212            | 0.7080            | 0.2722            |
|                   | NSCLC        | 0.8056            | 0.8788            | 0.8406            |                   |                   |                   |
| Fold 2            | MET          | 0.6250            | 0.4545            | 0.5263            | 0.6818            | 0.8292            | 0.4082            |
|                   | NSCLC        | 0.8333            | 0.9091            | 0.8696            |                   |                   |                   |
| Fold 3            | MET          | 1.0000            | 0.4545            | 0.6250            | 0.7273            | 0.8044            | 0.6202            |
|                   | NSCLC        | 0.8462            | 1.0000            | 0.9167            |                   |                   |                   |
| Fold 4            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8209            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 5            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.8402            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 6            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8264            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 7            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8264            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 8            | MET          | 0.8333            | 0.4545            | 0.5882            | 0.7121            | 0.7741            | 0.5353            |
|                   | NSCLC        | 0.8421            | 0.9697            | 0.9014            |                   |                   |                   |
| Fold 9            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8237            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 10           | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8347            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.7196<br>±0.1298 | 0.4364<br>±0.0383 | 0.5409<br>±0.0576 | 0.6879<br>±0.0305 | 0.8088<br>±0.0401 | 0.4550<br>±0.0915 |
|                   | <b>NSCLC</b> | 0.8332<br>±0.0126 | 0.9394<br>±0.0319 | 0.8830<br>±0.0200 |                   |                   |                   |

Table S12: Logistic regression on H-optimus-1 embeddings: Patient-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6667            | 0.2500            | 0.3636            | 0.6012            | 0.7083            | 0.2970            |
|                   | NSCLC        | 0.7692            | 0.9524            | 0.8511            |                   |                   |                   |
| Fold 2            | MET          | 0.8000            | 0.5000            | 0.6154            | 0.7262            | 0.8571            | 0.5353            |
|                   | NSCLC        | 0.8333            | 0.9524            | 0.8889            |                   |                   |                   |
| Fold 3            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8095            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 4            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8571            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 5            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8631            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 6            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8274            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 7            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8274            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 8            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.7679            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 9            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8393            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 10           | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8571            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.9467<br>±0.1167 | 0.3500<br>±0.0791 | 0.5052<br>±0.0844 | 0.6702<br>±0.0391 | 0.8214<br>±0.0492 | 0.5016<br>±0.0847 |
|                   | <b>NSCLC</b> | 0.8004<br>±0.0194 | 0.9905<br>±0.0201 | 0.8852<br>±0.0142 |                   |                   |                   |

Table S13: Logistic regression on hibou-L embeddings: Patch-level performance metrics NSCLC vs. MET

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6631            | 0.3737            | 0.4780            | 0.6178            | 0.7252            | 0.2735            |
|                   | NSCLC        | 0.6543            | 0.8620            | 0.7439            |                   |                   |                   |
| Fold 2            | MET          | 0.7160            | 0.5026            | 0.5906            | 0.6788            | 0.7900            | 0.3870            |
|                   | NSCLC        | 0.7028            | 0.8551            | 0.7715            |                   |                   |                   |
| Fold 3            | MET          | 0.6844            | 0.4527            | 0.5450            | 0.6505            | 0.7442            | 0.3315            |
|                   | NSCLC        | 0.6807            | 0.8482            | 0.7553            |                   |                   |                   |
| Fold 4            | MET          | 0.7069            | 0.4682            | 0.5633            | 0.6635            | 0.7694            | 0.3601            |
|                   | NSCLC        | 0.6896            | 0.8588            | 0.7650            |                   |                   |                   |
| Fold 5            | MET          | 0.7430            | 0.4545            | 0.5640            | 0.6701            | 0.7808            | 0.3841            |
|                   | NSCLC        | 0.6907            | 0.8857            | 0.7761            |                   |                   |                   |
| Fold 6            | MET          | 0.7149            | 0.4330            | 0.5393            | 0.6537            | 0.7631            | 0.3483            |
|                   | NSCLC        | 0.6796            | 0.8745            | 0.7648            |                   |                   |                   |
| Fold 7            | MET          | 0.6831            | 0.3926            | 0.4986            | 0.6301            | 0.7570            | 0.3000            |
|                   | NSCLC        | 0.6627            | 0.8676            | 0.7514            |                   |                   |                   |
| Fold 8            | MET          | 0.6662            | 0.4201            | 0.5153            | 0.6335            | 0.7350            | 0.2986            |
|                   | NSCLC        | 0.6677            | 0.8470            | 0.7467            |                   |                   |                   |
| Fold 9            | MET          | 0.6709            | 0.4588            | 0.5449            | 0.6476            | 0.7515            | 0.3218            |
|                   | NSCLC        | 0.6800            | 0.8364            | 0.7501            |                   |                   |                   |
| Fold 10           | MET          | 0.7081            | 0.4751            | 0.5686            | 0.6663            | 0.7745            | 0.3648            |
|                   | NSCLC        | 0.6920            | 0.8576            | 0.7660            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6957<br>±0.0261 | 0.4431<br>±0.0389 | 0.5408<br>±0.0345 | 0.6512<br>±0.0194 | 0.7591<br>±0.0206 | 0.3370<br>±0.0384 |
|                   | <b>NSCLC</b> | 0.6800<br>±0.0148 | 0.8593<br>±0.0142 | 0.7591<br>±0.0110 |                   |                   |                   |

Table S14: Logistic regression on hibou-L embeddings: Slide-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.5556            | 0.4545            | 0.5000            | 0.6667            | 0.7466            | 0.3578            |
|                   | NSCLC        | 0.8286            | 0.8788            | 0.8529            |                   |                   |                   |
| Fold 2            | MET          | 0.6667            | 0.5455            | 0.6000            | 0.7273            | 0.8733            | 0.4880            |
|                   | NSCLC        | 0.8571            | 0.9091            | 0.8824            |                   |                   |                   |
| Fold 3            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8347            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 4            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8567            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 5            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8678            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 6            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8926            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 7            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.8347            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 8            | MET          | 0.6667            | 0.5455            | 0.6000            | 0.7273            | 0.8209            | 0.4880            |
|                   | NSCLC        | 0.8571            | 0.9091            | 0.8824            |                   |                   |                   |
| Fold 9            | MET          | 0.6250            | 0.4545            | 0.5263            | 0.6818            | 0.8264            | 0.4082            |
|                   | NSCLC        | 0.8333            | 0.9091            | 0.8696            |                   |                   |                   |
| Fold 10           | MET          | 0.6250            | 0.4545            | 0.5263            | 0.6818            | 0.8650            | 0.4082            |
|                   | NSCLC        | 0.8333            | 0.9091            | 0.8696            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6663<br>±0.0526 | 0.4636<br>±0.0516 | 0.5445<br>±0.0405 | 0.6924<br>±0.0237 | 0.8419<br>±0.0406 | 0.4398<br>±0.0465 |
|                   | <b>NSCLC</b> | 0.8377<br>±0.0123 | 0.9212<br>±0.0212 | 0.8773<br>±0.0109 |                   |                   |                   |

Table S15: Logistic regression on hibou-L embeddings: Patient-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.7321            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 2            | MET          | 1.0000            | 0.6250            | 0.7692            | 0.8125            | 0.9167            | 0.7395            |
|                   | NSCLC        | 0.8750            | 1.0000            | 0.9333            |                   |                   |                   |
| Fold 3            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8690            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 4            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8988            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 5            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.9167            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 6            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.9167            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 7            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8571            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 8            | MET          | 1.0000            | 0.5000            | 0.6667            | 0.7500            | 0.8274            | 0.6481            |
|                   | NSCLC        | 0.8400            | 1.0000            | 0.9130            |                   |                   |                   |
| Fold 9            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8512            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 10           | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8988            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.9750<br>±0.0791 | 0.4000<br>±0.0986 | 0.5609<br>±0.0975 | 0.6976<br>±0.0505 | 0.8685<br>±0.0573 | 0.5555<br>±0.0900 |
|                   | <b>NSCLC</b> | 0.8139<br>±0.0261 | 0.9952<br>±0.0151 | 0.8953<br>±0.0178 |                   |                   |                   |

Table S16: Logistic regression on Kaiko embeddings: Patch-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.5957            | 0.3582            | 0.4474            | 0.5907            | 0.6756            | 0.2061            |
|                   | NSCLC        | 0.6383            | 0.8232            | 0.7190            |                   |                   |                   |
| Fold 2            | MET          | 0.6137            | 0.4381            | 0.5113            | 0.6188            | 0.7131            | 0.2559            |
|                   | NSCLC        | 0.6618            | 0.7995            | 0.7242            |                   |                   |                   |
| Fold 3            | MET          | 0.6284            | 0.4184            | 0.5023            | 0.6192            | 0.6944            | 0.2622            |
|                   | NSCLC        | 0.6598            | 0.8201            | 0.7313            |                   |                   |                   |
| Fold 4            | MET          | 0.6097            | 0.4321            | 0.5058            | 0.6155            | 0.7074            | 0.2493            |
|                   | NSCLC        | 0.6593            | 0.7989            | 0.7224            |                   |                   |                   |
| Fold 5            | MET          | 0.6561            | 0.4278            | 0.5179            | 0.6324            | 0.7176            | 0.2930            |
|                   | NSCLC        | 0.6680            | 0.8370            | 0.7430            |                   |                   |                   |
| Fold 6            | MET          | 0.6142            | 0.3488            | 0.4449            | 0.5948            | 0.6603            | 0.2194            |
|                   | NSCLC        | 0.6397            | 0.8407            | 0.7266            |                   |                   |                   |
| Fold 7            | MET          | 0.6126            | 0.4021            | 0.4855            | 0.6086            | 0.7004            | 0.2398            |
|                   | NSCLC        | 0.6522            | 0.8151            | 0.7246            |                   |                   |                   |
| Fold 8            | MET          | 0.6461            | 0.3875            | 0.4844            | 0.6166            | 0.7018            | 0.2650            |
|                   | NSCLC        | 0.6551            | 0.8457            | 0.7383            |                   |                   |                   |
| Fold 9            | MET          | 0.5918            | 0.4210            | 0.4920            | 0.6049            | 0.6811            | 0.2262            |
|                   | NSCLC        | 0.6520            | 0.7889            | 0.7140            |                   |                   |                   |
| Fold 10           | MET          | 0.6027            | 0.4158            | 0.4921            | 0.6083            | 0.6992            | 0.2355            |
|                   | NSCLC        | 0.6534            | 0.8007            | 0.7196            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6171<br>±0.0208 | 0.4050<br>±0.0309 | 0.4884<br>±0.0247 | 0.6110<br>±0.0123 | 0.6951<br>±0.0178 | 0.2452<br>±0.0253 |
|                   | <b>NSCLC</b> | 0.6540<br>±0.0093 | 0.8170<br>±0.0198 | 0.7263<br>±0.0089 |                   |                   |                   |

Table S17: Logistic regression on Kaiko embeddings: Slide-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6250            | 0.4545            | 0.5263            | 0.6818            | 0.7052            | 0.4082            |
|                   | NSCLC        | 0.8333            | 0.9091            | 0.8696            |                   |                   |                   |
| Fold 2            | MET          | 0.6000            | 0.2727            | 0.3750            | 0.6061            | 0.7658            | 0.2894            |
|                   | NSCLC        | 0.7949            | 0.9394            | 0.8611            |                   |                   |                   |
| Fold 3            | MET          | 0.8571            | 0.5455            | 0.6667            | 0.7576            | 0.7961            | 0.6099            |
|                   | NSCLC        | 0.8649            | 0.9697            | 0.9143            |                   |                   |                   |
| Fold 4            | MET          | 0.6667            | 0.5455            | 0.6000            | 0.7273            | 0.8099            | 0.4880            |
|                   | NSCLC        | 0.8571            | 0.9091            | 0.8824            |                   |                   |                   |
| Fold 5            | MET          | 0.6667            | 0.5455            | 0.6000            | 0.7273            | 0.7989            | 0.4880            |
|                   | NSCLC        | 0.8571            | 0.9091            | 0.8824            |                   |                   |                   |
| Fold 6            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8099            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 7            | MET          | 0.7143            | 0.4545            | 0.5556            | 0.6970            | 0.8044            | 0.4664            |
|                   | NSCLC        | 0.8378            | 0.9394            | 0.8857            |                   |                   |                   |
| Fold 8            | MET          | 0.6667            | 0.5455            | 0.6000            | 0.7273            | 0.7989            | 0.4880            |
|                   | NSCLC        | 0.8571            | 0.9091            | 0.8824            |                   |                   |                   |
| Fold 9            | MET          | 0.6000            | 0.5455            | 0.5714            | 0.7121            | 0.7521            | 0.4384            |
|                   | NSCLC        | 0.8529            | 0.8788            | 0.8657            |                   |                   |                   |
| Fold 10           | MET          | 0.7500            | 0.5455            | 0.6316            | 0.7424            | 0.7851            | 0.5443            |
|                   | NSCLC        | 0.8611            | 0.9394            | 0.8986            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6861<br>±0.0779 | 0.4909<br>±0.0878 | 0.5682<br>±0.0790 | 0.7076<br>±0.0423 | 0.7826<br>±0.0331 | 0.4687<br>±0.0840 |
|                   | <b>NSCLC</b> | 0.8454<br>±0.0208 | 0.9242<br>±0.0258 | 0.8828<br>±0.0156 |                   |                   |                   |

Table S18: Logistic regression on Kaiko embeddings: Patient-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.5000            | 0.3750            | 0.4286            | 0.6161            | 0.6964            | 0.2561            |
|                   | NSCLC        | 0.7826            | 0.8571            | 0.8182            |                   |                   |                   |
| Fold 2            | MET          | 0.6667            | 0.2500            | 0.3636            | 0.6012            | 0.7619            | 0.2970            |
|                   | NSCLC        | 0.7692            | 0.9524            | 0.8511            |                   |                   |                   |
| Fold 3            | MET          | 1.0000            | 0.5000            | 0.6667            | 0.7500            | 0.8155            | 0.6481            |
|                   | NSCLC        | 0.8400            | 1.0000            | 0.9130            |                   |                   |                   |
| Fold 4            | MET          | 1.0000            | 0.5000            | 0.6667            | 0.7500            | 0.8214            | 0.6481            |
|                   | NSCLC        | 0.8400            | 1.0000            | 0.9130            |                   |                   |                   |
| Fold 5            | MET          | 0.8000            | 0.5000            | 0.6154            | 0.7262            | 0.8036            | 0.5353            |
|                   | NSCLC        | 0.8333            | 0.9524            | 0.8889            |                   |                   |                   |
| Fold 6            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8214            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 7            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.8214            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 8            | MET          | 1.0000            | 0.5000            | 0.6667            | 0.7500            | 0.7917            | 0.6481            |
|                   | NSCLC        | 0.8400            | 1.0000            | 0.9130            |                   |                   |                   |
| Fold 9            | MET          | 0.6667            | 0.5000            | 0.5714            | 0.7024            | 0.7619            | 0.4466            |
|                   | NSCLC        | 0.8261            | 0.9048            | 0.8636            |                   |                   |                   |
| Fold 10           | MET          | 0.8000            | 0.5000            | 0.6154            | 0.7262            | 0.7738            | 0.5353            |
|                   | NSCLC        | 0.8333            | 0.9524            | 0.8889            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.8183<br>±0.1779 | 0.4375<br>±0.0884 | 0.5640<br>±0.1053 | 0.6973<br>±0.0549 | 0.7869<br>±0.0399 | 0.4989<br>±0.1414 |
|                   | <b>NSCLC</b> | 0.8172<br>±0.0259 | 0.9571<br>±0.0474 | 0.8813<br>±0.0310 |                   |                   |                   |

Table S19: Logistic regression on Phikon embeddings: Patch-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6013            | 0.3162            | 0.4144            | 0.5819            | 0.6821            | 0.1947            |
|                   | NSCLC        | 0.6303            | 0.8476            | 0.7230            |                   |                   |                   |
| Fold 2            | MET          | 0.6264            | 0.3875            | 0.4788            | 0.6097            | 0.7085            | 0.2469            |
|                   | NSCLC        | 0.6513            | 0.8320            | 0.7307            |                   |                   |                   |
| Fold 3            | MET          | 0.6147            | 0.3591            | 0.4534            | 0.5977            | 0.6849            | 0.2241            |
|                   | NSCLC        | 0.6422            | 0.8364            | 0.7265            |                   |                   |                   |
| Fold 4            | MET          | 0.6277            | 0.3737            | 0.4685            | 0.6063            | 0.7185            | 0.2422            |
|                   | NSCLC        | 0.6482            | 0.8389            | 0.7313            |                   |                   |                   |
| Fold 5            | MET          | 0.6235            | 0.3557            | 0.4530            | 0.5998            | 0.6945            | 0.2306            |
|                   | NSCLC        | 0.6430            | 0.8438            | 0.7299            |                   |                   |                   |
| Fold 6            | MET          | 0.6270            | 0.3076            | 0.4127            | 0.5873            | 0.6754            | 0.2129            |
|                   | NSCLC        | 0.6326            | 0.8670            | 0.7315            |                   |                   |                   |
| Fold 7            | MET          | 0.6124            | 0.3393            | 0.4367            | 0.5916            | 0.6837            | 0.2139            |
|                   | NSCLC        | 0.6373            | 0.8438            | 0.7261            |                   |                   |                   |
| Fold 8            | MET          | 0.6300            | 0.3686            | 0.4650            | 0.6056            | 0.7022            | 0.2420            |
|                   | NSCLC        | 0.6473            | 0.8426            | 0.7322            |                   |                   |                   |
| Fold 9            | MET          | 0.5901            | 0.3771            | 0.4602            | 0.5933            | 0.6877            | 0.2078            |
|                   | NSCLC        | 0.6413            | 0.8095            | 0.7156            |                   |                   |                   |
| Fold 10           | MET          | 0.6238            | 0.3875            | 0.4780            | 0.6088            | 0.7113            | 0.2444            |
|                   | NSCLC        | 0.6508            | 0.8301            | 0.7296            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6177<br>±0.0131 | 0.3572<br>±0.0281 | 0.4521<br>±0.0238 | 0.5982<br>±0.0095 | 0.6949<br>±0.0145 | 0.2259<br>±0.0181 |
|                   | <b>NSCLC</b> | 0.6424<br>±0.0073 | 0.8392<br>±0.0146 | 0.7276<br>±0.0051 |                   |                   |                   |

Table S20: Logistic regression on Phikon embeddings: Slide-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.5000            | 0.3636            | 0.4211            | 0.6212            | 0.7521            | 0.2722            |
|                   | NSCLC        | 0.8056            | 0.8788            | 0.8406            |                   |                   |                   |
| Fold 2            | MET          | 0.5000            | 0.1818            | 0.2667            | 0.5606            | 0.7989            | 0.1826            |
|                   | NSCLC        | 0.7750            | 0.9394            | 0.8493            |                   |                   |                   |
| Fold 3            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.7851            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 4            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.8320            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 5            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.8237            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 6            | MET          | 0.8000            | 0.3636            | 0.5000            | 0.6667            | 0.8678            | 0.4548            |
|                   | NSCLC        | 0.8205            | 0.9697            | 0.8889            |                   |                   |                   |
| Fold 7            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.8127            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 8            | MET          | 0.7500            | 0.5455            | 0.6316            | 0.7424            | 0.7934            | 0.5443            |
|                   | NSCLC        | 0.8611            | 0.9394            | 0.8986            |                   |                   |                   |
| Fold 9            | MET          | 0.5714            | 0.3636            | 0.4444            | 0.6364            | 0.8072            | 0.3229            |
|                   | NSCLC        | 0.8108            | 0.9091            | 0.8571            |                   |                   |                   |
| Fold 10           | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.8292            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6455<br>±0.0971 | 0.3636<br>±0.0857 | 0.4617<br>±0.0886 | 0.6485<br>±0.0445 | 0.8102<br>±0.0312 | 0.3689<br>±0.0973 |
|                   | <b>NSCLC</b> | 0.8152<br>±0.0207 | 0.9333<br>±0.0239 | 0.8701<br>±0.0173 |                   |                   |                   |

Table S21: Logistic regression on Phikon embeddings: Patient-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.7500            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 2            | MET          | 0.5000            | 0.1250            | 0.2000            | 0.5387            | 0.8274            | 0.1365            |
|                   | NSCLC        | 0.7407            | 0.9524            | 0.8333            |                   |                   |                   |
| Fold 3            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8095            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 4            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8274            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 5            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8095            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 6            | MET          | 0.6667            | 0.2500            | 0.3636            | 0.6012            | 0.8869            | 0.2970            |
|                   | NSCLC        | 0.7692            | 0.9524            | 0.8511            |                   |                   |                   |
| Fold 7            | MET          | 0.6667            | 0.2500            | 0.3636            | 0.6012            | 0.7976            | 0.2970            |
|                   | NSCLC        | 0.7692            | 0.9524            | 0.8511            |                   |                   |                   |
| Fold 8            | MET          | 1.0000            | 0.5000            | 0.6667            | 0.7500            | 0.7798            | 0.6481            |
|                   | NSCLC        | 0.8400            | 1.0000            | 0.9130            |                   |                   |                   |
| Fold 9            | MET          | 0.6667            | 0.2500            | 0.3636            | 0.6012            | 0.8095            | 0.2970            |
|                   | NSCLC        | 0.7692            | 0.9524            | 0.8511            |                   |                   |                   |
| Fold 10           | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8333            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.8500<br>±0.1995 | 0.2625<br>±0.0922 | 0.3958<br>±0.1130 | 0.6217<br>±0.0524 | 0.8131<br>±0.0360 | 0.3880<br>±0.1373 |
|                   | <b>NSCLC</b> | 0.7777<br>±0.0246 | 0.9810<br>±0.0246 | 0.8675<br>±0.0219 |                   |                   |                   |

Table S22: Logistic regression on ProvGigaPath embeddings: Patch-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6394            | 0.2955            | 0.4042            | 0.5872            | 0.6835            | 0.2175            |
|                   | NSCLC        | 0.6318            | 0.8788            | 0.7351            |                   |                   |                   |
| Fold 2            | MET          | 0.6736            | 0.3600            | 0.4692            | 0.6166            | 0.7275            | 0.2757            |
|                   | NSCLC        | 0.6524            | 0.8732            | 0.7468            |                   |                   |                   |
| Fold 3            | MET          | 0.6588            | 0.3600            | 0.4656            | 0.6122            | 0.6975            | 0.2633            |
|                   | NSCLC        | 0.6501            | 0.8645            | 0.7421            |                   |                   |                   |
| Fold 4            | MET          | 0.6642            | 0.3840            | 0.4867            | 0.6214            | 0.7179            | 0.2794            |
|                   | NSCLC        | 0.6573            | 0.8588            | 0.7447            |                   |                   |                   |
| Fold 5            | MET          | 0.6992            | 0.3694            | 0.4834            | 0.6269            | 0.7392            | 0.3014            |
|                   | NSCLC        | 0.6586            | 0.8844            | 0.7550            |                   |                   |                   |
| Fold 6            | MET          | 0.6333            | 0.2878            | 0.3957            | 0.5833            | 0.6619            | 0.2091            |
|                   | NSCLC        | 0.6292            | 0.8788            | 0.7334            |                   |                   |                   |
| Fold 7            | MET          | 0.6820            | 0.3686            | 0.4785            | 0.6218            | 0.7257            | 0.2869            |
|                   | NSCLC        | 0.6559            | 0.8751            | 0.7498            |                   |                   |                   |
| Fold 8            | MET          | 0.6643            | 0.3162            | 0.4284            | 0.6000            | 0.6939            | 0.2467            |
|                   | NSCLC        | 0.6400            | 0.8838            | 0.7424            |                   |                   |                   |
| Fold 9            | MET          | 0.6473            | 0.3737            | 0.4739            | 0.6128            | 0.7041            | 0.2598            |
|                   | NSCLC        | 0.6517            | 0.8520            | 0.7385            |                   |                   |                   |
| Fold 10           | MET          | 0.6682            | 0.3720            | 0.4779            | 0.6189            | 0.7299            | 0.2770            |
|                   | NSCLC        | 0.6547            | 0.8657            | 0.7456            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6630<br>±0.0198 | 0.3487<br>±0.0351 | 0.4564<br>±0.0339 | 0.6101<br>±0.0150 | 0.7081<br>±0.0243 | 0.2617<br>±0.0296 |
|                   | <b>NSCLC</b> | 0.6482<br>±0.0107 | 0.8715<br>±0.0109 | 0.7433<br>±0.0066 |                   |                   |                   |

Table S23: Logistic regression on ProvGigaPath embeddings: Slide-level performance metrics NSCLC vs. MET.

| Fold           | Class | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------|-------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1         | MET   | 0.4000                 | 0.3636                 | 0.3810                 | 0.5909                 | 0.6777                 | 0.1879                 |
|                | NSCLC | 0.7941                 | 0.8182                 | 0.8060                 |                        |                        |                        |
| Fold 2         | MET   | 0.4000                 | 0.1818                 | 0.2500                 | 0.5455                 | 0.7273                 | 0.1240                 |
|                | NSCLC | 0.7692                 | 0.9091                 | 0.8333                 |                        |                        |                        |
| Fold 3         | MET   | 0.5714                 | 0.3636                 | 0.4444                 | 0.6364                 | 0.7658                 | 0.3229                 |
|                | NSCLC | 0.8108                 | 0.9091                 | 0.8571                 |                        |                        |                        |
| Fold 4         | MET   | 0.5714                 | 0.3636                 | 0.4444                 | 0.6364                 | 0.7631                 | 0.3229                 |
|                | NSCLC | 0.8108                 | 0.9091                 | 0.8571                 |                        |                        |                        |
| Fold 5         | MET   | 0.7143                 | 0.4545                 | 0.5556                 | 0.6970                 | 0.7713                 | 0.4664                 |
|                | NSCLC | 0.8378                 | 0.9394                 | 0.8857                 |                        |                        |                        |
| Fold 6         | MET   | 0.5714                 | 0.3636                 | 0.4444                 | 0.6364                 | 0.7824                 | 0.3229                 |
|                | NSCLC | 0.8108                 | 0.9091                 | 0.8571                 |                        |                        |                        |
| Fold 7         | MET   | 0.5714                 | 0.3636                 | 0.4444                 | 0.6364                 | 0.7603                 | 0.3229                 |
|                | NSCLC | 0.8108                 | 0.9091                 | 0.8571                 |                        |                        |                        |
| Fold 8         | MET   | 0.5714                 | 0.3636                 | 0.4444                 | 0.6364                 | 0.7576                 | 0.3229                 |
|                | NSCLC | 0.8108                 | 0.9091                 | 0.8571                 |                        |                        |                        |
| Fold 9         | MET   | 0.5714                 | 0.3636                 | 0.4444                 | 0.6364                 | 0.7355                 | 0.3229                 |
|                | NSCLC | 0.8108                 | 0.9091                 | 0.8571                 |                        |                        |                        |
| Fold 10        | MET   | 0.6667                 | 0.3636                 | 0.4706                 | 0.6515                 | 0.7741                 | 0.3824                 |
|                | NSCLC | 0.8158                 | 0.9394                 | 0.8732                 |                        |                        |                        |
| Mean $\pm$ std | MET   | 0.5610<br>$\pm 0.0984$ | 0.3545<br>$\pm 0.0671$ | 0.4324<br>$\pm 0.0770$ | 0.6303<br>$\pm 0.0393$ | 0.7515<br>$\pm 0.0309$ | 0.3098<br>$\pm 0.0944$ |
|                | NSCLC | 0.8082<br>$\pm 0.0173$ | 0.9061<br>$\pm 0.0333$ | 0.8541<br>$\pm 0.0215$ |                        |                        |                        |

Table S24: Logistic regression on ProvGigaPath embeddings: Patient-level performance metrics NSCLC vs. MET.

| Fold           | Class | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------|-------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1         | MET   | 0.5000                 | 0.2500                 | 0.3333                 | 0.5774                 | 0.6548                 | 0.2006                 |
|                | NSCLC | 0.7600                 | 0.9048                 | 0.8261                 |                        |                        |                        |
| Fold 2         | MET   | 0.5000                 | 0.1250                 | 0.2000                 | 0.5387                 | 0.7917                 | 0.1365                 |
|                | NSCLC | 0.7407                 | 0.9524                 | 0.8333                 |                        |                        |                        |
| Fold 3         | MET   | 0.6667                 | 0.2500                 | 0.3636                 | 0.6012                 | 0.8036                 | 0.2970                 |
|                | NSCLC | 0.7692                 | 0.9524                 | 0.8511                 |                        |                        |                        |
| Fold 4         | MET   | 0.6667                 | 0.2500                 | 0.3636                 | 0.6012                 | 0.7917                 | 0.2970                 |
|                | NSCLC | 0.7692                 | 0.9524                 | 0.8511                 |                        |                        |                        |
| Fold 5         | MET   | 0.7500                 | 0.3750                 | 0.5000                 | 0.6637                 | 0.7917                 | 0.4243                 |
|                | NSCLC | 0.8000                 | 0.9524                 | 0.8696                 |                        |                        |                        |
| Fold 6         | MET   | 0.5000                 | 0.2500                 | 0.3333                 | 0.5774                 | 0.7857                 | 0.2006                 |
|                | NSCLC | 0.7600                 | 0.9048                 | 0.8261                 |                        |                        |                        |
| Fold 7         | MET   | 0.6667                 | 0.2500                 | 0.3636                 | 0.6012                 | 0.8036                 | 0.2970                 |
|                | NSCLC | 0.7692                 | 0.9524                 | 0.8511                 |                        |                        |                        |
| Fold 8         | MET   | 0.6667                 | 0.2500                 | 0.3636                 | 0.6012                 | 0.7619                 | 0.2970                 |
|                | NSCLC | 0.7692                 | 0.9524                 | 0.8511                 |                        |                        |                        |
| Fold 9         | MET   | 0.5000                 | 0.2500                 | 0.3333                 | 0.5774                 | 0.7738                 | 0.2006                 |
|                | NSCLC | 0.7600                 | 0.9048                 | 0.8261                 |                        |                        |                        |
| Fold 10        | MET   | 0.6667                 | 0.2500                 | 0.3636                 | 0.6012                 | 0.7976                 | 0.2970                 |
|                | NSCLC | 0.7692                 | 0.9524                 | 0.8511                 |                        |                        |                        |
| Mean $\pm$ std | MET   | 0.6083<br>$\pm 0.0966$ | 0.2500<br>$\pm 0.0589$ | 0.3518<br>$\pm 0.0721$ | 0.5940<br>$\pm 0.0316$ | 0.7756<br>$\pm 0.0444$ | 0.2648<br>$\pm 0.0813$ |
|                | NSCLC | 0.7667<br>$\pm 0.0147$ | 0.9381<br>$\pm 0.0230$ | 0.8436<br>$\pm 0.0148$ |                        |                        |                        |

Table S25: Logistic regression on ResNet50 embeddings: Patch-level performance metrics NSCLC vs. MET.

| Fold                             | Class        | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------------------------|--------------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1                           | MET          | 0.6089                 | 0.3771                 | 0.4658                 | 0.6005                 | 0.6681                 | 0.2260                 |
|                                  | NSCLC        | 0.6453                 | 0.8239                 | 0.7237                 |                        |                        |                        |
| Fold 2                           | MET          | 0.5989                 | 0.3771                 | 0.4628                 | 0.5968                 | 0.6787                 | 0.2165                 |
|                                  | NSCLC        | 0.6432                 | 0.8164                 | 0.7195                 |                        |                        |                        |
| Fold 3                           | MET          | 0.5828                 | 0.3900                 | 0.4673                 | 0.5935                 | 0.6564                 | 0.2053                 |
|                                  | NSCLC        | 0.6425                 | 0.7970                 | 0.7115                 |                        |                        |                        |
| Fold 4                           | MET          | 0.5972                 | 0.4381                 | 0.5055                 | 0.6116                 | 0.6699                 | 0.2386                 |
|                                  | NSCLC        | 0.6578                 | 0.7851                 | 0.7158                 |                        |                        |                        |
| Fold 5                           | MET          | 0.5900                 | 0.3857                 | 0.4665                 | 0.5954                 | 0.6631                 | 0.2110                 |
|                                  | NSCLC        | 0.6432                 | 0.8051                 | 0.7151                 |                        |                        |                        |
| Fold 6                           | MET          | 0.6392                 | 0.4399                 | 0.5211                 | 0.6297                 | 0.6851                 | 0.2823                 |
|                                  | NSCLC        | 0.6680                 | 0.8195                 | 0.7360                 |                        |                        |                        |
| Fold 7                           | MET          | 0.6101                 | 0.3832                 | 0.4707                 | 0.6026                 | 0.6643                 | 0.2297                 |
|                                  | NSCLC        | 0.6470                 | 0.8220                 | 0.7241                 |                        |                        |                        |
| Fold 8                           | MET          | 0.5838                 | 0.3651                 | 0.4493                 | 0.5879                 | 0.6475                 | 0.1971                 |
|                                  | NSCLC        | 0.6372                 | 0.8107                 | 0.7136                 |                        |                        |                        |
| Fold 9                           | MET          | 0.6088                 | 0.4399                 | 0.5107                 | 0.6172                 | 0.6779                 | 0.2515                 |
|                                  | NSCLC        | 0.6611                 | 0.7945                 | 0.7217                 |                        |                        |                        |
| Fold 10                          | MET          | 0.6117                 | 0.4235                 | 0.5005                 | 0.6140                 | 0.6753                 | 0.2477                 |
|                                  | NSCLC        | 0.6575                 | 0.8045                 | 0.7236                 |                        |                        |                        |
| <b>Mean <math>\pm</math> std</b> | <b>MET</b>   | 0.6031<br>$\pm 0.0167$ | 0.4020<br>$\pm 0.0298$ | 0.4820<br>$\pm 0.0248$ | 0.6049<br>$\pm 0.0129$ | 0.6686<br>$\pm 0.0113$ | 0.2306<br>$\pm 0.0255$ |
|                                  | <b>NSCLC</b> | 0.6503<br>$\pm 0.0100$ | 0.8079<br>$\pm 0.0129$ | 0.7205<br>$\pm 0.0071$ |                        |                        |                        |

Table S26: Logistic regression on ResNet50 embeddings: Slide-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6250            | 0.4545            | 0.5263            | 0.6818            | 0.7713            | 0.4082            |
|                   | NSCLC        | 0.8333            | 0.9091            | 0.8696            |                   |                   |                   |
| Fold 2            | MET          | 0.5000            | 0.1818            | 0.2667            | 0.5606            | 0.7383            | 0.1826            |
|                   | NSCLC        | 0.7750            | 0.9394            | 0.8493            |                   |                   |                   |
| Fold 3            | MET          | 0.5714            | 0.3636            | 0.4444            | 0.6364            | 0.7548            | 0.3229            |
|                   | NSCLC        | 0.8108            | 0.9091            | 0.8571            |                   |                   |                   |
| Fold 4            | MET          | 0.6250            | 0.4545            | 0.5263            | 0.6818            | 0.7934            | 0.4082            |
|                   | NSCLC        | 0.8333            | 0.9091            | 0.8696            |                   |                   |                   |
| Fold 5            | MET          | 0.6250            | 0.4545            | 0.5263            | 0.6818            | 0.7493            | 0.4082            |
|                   | NSCLC        | 0.8333            | 0.9091            | 0.8696            |                   |                   |                   |
| Fold 6            | MET          | 0.5000            | 0.5455            | 0.5217            | 0.6818            | 0.8320            | 0.3536            |
|                   | NSCLC        | 0.8438            | 0.8182            | 0.8308            |                   |                   |                   |
| Fold 7            | MET          | 0.5714            | 0.3636            | 0.4444            | 0.6364            | 0.7851            | 0.3229            |
|                   | NSCLC        | 0.8108            | 0.9091            | 0.8571            |                   |                   |                   |
| Fold 8            | MET          | 0.8333            | 0.4545            | 0.5882            | 0.7121            | 0.8127            | 0.5353            |
|                   | NSCLC        | 0.8421            | 0.9697            | 0.9014            |                   |                   |                   |
| Fold 9            | MET          | 0.6250            | 0.4545            | 0.5263            | 0.6818            | 0.8127            | 0.4082            |
|                   | NSCLC        | 0.8333            | 0.9091            | 0.8696            |                   |                   |                   |
| Fold 10           | MET          | 0.5556            | 0.4545            | 0.5000            | 0.6667            | 0.7934            | 0.3578            |
|                   | NSCLC        | 0.8286            | 0.8788            | 0.8529            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6032<br>±0.0945 | 0.4182<br>±0.0977 | 0.4871<br>±0.0882 | 0.6621<br>±0.0423 | 0.7843<br>±0.0306 | 0.3708<br>±0.0902 |
|                   | <b>NSCLC</b> | 0.8244<br>±0.0206 | 0.9061<br>±0.0390 | 0.8627<br>±0.0184 |                   |                   |                   |

Table S27: Logistic regression on ResNet50 embeddings: Patient-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.8095            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 2            | MET          | 0.5000            | 0.1250            | 0.2000            | 0.5387            | 0.7857            | 0.1365            |
|                   | NSCLC        | 0.7407            | 0.9524            | 0.8333            |                   |                   |                   |
| Fold 3            | MET          | 0.6000            | 0.3750            | 0.4615            | 0.6399            | 0.7857            | 0.3310            |
|                   | NSCLC        | 0.7917            | 0.9048            | 0.8444            |                   |                   |                   |
| Fold 4            | MET          | 0.5000            | 0.3750            | 0.4286            | 0.6161            | 0.8155            | 0.2561            |
|                   | NSCLC        | 0.7826            | 0.8571            | 0.8182            |                   |                   |                   |
| Fold 5            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.7679            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 6            | MET          | 0.5000            | 0.3750            | 0.4286            | 0.6161            | 0.8690            | 0.2561            |
|                   | NSCLC        | 0.7826            | 0.8571            | 0.8182            |                   |                   |                   |
| Fold 7            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.8214            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 8            | MET          | 1.0000            | 0.3750            | 0.5455            | 0.6875            | 0.8333            | 0.5503            |
|                   | NSCLC        | 0.8077            | 1.0000            | 0.8936            |                   |                   |                   |
| Fold 9            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.8393            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 10           | MET          | 0.5000            | 0.3750            | 0.4286            | 0.6161            | 0.8333            | 0.2561            |
|                   | NSCLC        | 0.7826            | 0.8571            | 0.8182            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6600<br>±0.1680 | 0.3500<br>±0.0791 | 0.4493<br>±0.0961 | 0.6369<br>±0.0427 | 0.8161<br>±0.0301 | 0.3484<br>±0.1223 |
|                   | <b>NSCLC</b> | 0.7888<br>±0.0191 | 0.9238<br>±0.0512 | 0.8504<br>±0.0274 |                   |                   |                   |

Table S28: Logistic regression on TissueConcepts embeddings: Patch-level performance metrics NSCLC vs. MET.

| Fold           | Class | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------|-------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1         | MET   | 0.6211                 | 0.4648                 | 0.5317                 | 0.6293                 | 0.6997                 | 0.2749                 |
|                | NSCLC | 0.6711                 | 0.7939                 | 0.7273                 |                        |                        |                        |
| Fold 2         | MET   | 0.6207                 | 0.4905                 | 0.5480                 | 0.6363                 | 0.7066                 | 0.2856                 |
|                | NSCLC | 0.6786                 | 0.7820                 | 0.7266                 |                        |                        |                        |
| Fold 3         | MET   | 0.6093                 | 0.5172                 | 0.5595                 | 0.6380                 | 0.6911                 | 0.2844                 |
|                | NSCLC | 0.6837                 | 0.7589                 | 0.7194                 |                        |                        |                        |
| Fold 4         | MET   | 0.6155                 | 0.5447                 | 0.5779                 | 0.6487                 | 0.7117                 | 0.3036                 |
|                | NSCLC | 0.6945                 | 0.7527                 | 0.7224                 |                        |                        |                        |
| Fold 5         | MET   | 0.6132                 | 0.4725                 | 0.5337                 | 0.6279                 | 0.6931                 | 0.2697                 |
|                | NSCLC | 0.6713                 | 0.7833                 | 0.7230                 |                        |                        |                        |
| Fold 6         | MET   | 0.6655                 | 0.5026                 | 0.5727                 | 0.6595                 | 0.7077                 | 0.3382                 |
|                | NSCLC | 0.6930                 | 0.8164                 | 0.7496                 |                        |                        |                        |
| Fold 7         | MET   | 0.6256                 | 0.4708                 | 0.5373                 | 0.6330                 | 0.7036                 | 0.2822                 |
|                | NSCLC | 0.6739                 | 0.7951                 | 0.7295                 |                        |                        |                        |
| Fold 8         | MET   | 0.6168                 | 0.4605                 | 0.5273                 | 0.6262                 | 0.6904                 | 0.2685                 |
|                | NSCLC | 0.6688                 | 0.7920                 | 0.7252                 |                        |                        |                        |
| Fold 9         | MET   | 0.6176                 | 0.5258                 | 0.5680                 | 0.6445                 | 0.7029                 | 0.2976                 |
|                | NSCLC | 0.6888                 | 0.7633                 | 0.7241                 |                        |                        |                        |
| Fold 10        | MET   | 0.6231                 | 0.5198                 | 0.5667                 | 0.6456                 | 0.7138                 | 0.3011                 |
|                | NSCLC | 0.6884                 | 0.7714                 | 0.7275                 |                        |                        |                        |
| Mean $\pm$ std | MET   | 0.6228<br>$\pm 0.0157$ | 0.4969<br>$\pm 0.0294$ | 0.5523<br>$\pm 0.0189$ | 0.6389<br>$\pm 0.0106$ | 0.7021<br>$\pm 0.0084$ | 0.2906<br>$\pm 0.0208$ |
|                | NSCLC | 0.6812<br>$\pm 0.0097$ | 0.7809<br>$\pm 0.0196$ | 0.7275<br>$\pm 0.0083$ |                        |                        |                        |

Table S29: Logistic regression on TissueConcepts embeddings: Slide-level performance metrics NSCLC vs. MET.

| Fold           | Class | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------|-------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1         | MET   | 0.6250                 | 0.4545                 | 0.5263                 | 0.6818                 | 0.8072                 | 0.4082                 |
|                | NSCLC | 0.8333                 | 0.9091                 | 0.8696                 |                        |                        |                        |
| Fold 2         | MET   | 0.4000                 | 0.1818                 | 0.2500                 | 0.5455                 | 0.7025                 | 0.1240                 |
|                | NSCLC | 0.7692                 | 0.9091                 | 0.8333                 |                        |                        |                        |
| Fold 3         | MET   | 0.7500                 | 0.5455                 | 0.6316                 | 0.7424                 | 0.8237                 | 0.5443                 |
|                | NSCLC | 0.8611                 | 0.9394                 | 0.8986                 |                        |                        |                        |
| Fold 4         | MET   | 0.6364                 | 0.6364                 | 0.6364                 | 0.7576                 | 0.8540                 | 0.5152                 |
|                | NSCLC | 0.8788                 | 0.8788                 | 0.8788                 |                        |                        |                        |
| Fold 5         | MET   | 0.5556                 | 0.4545                 | 0.5000                 | 0.6667                 | 0.8099                 | 0.3578                 |
|                | NSCLC | 0.8286                 | 0.8788                 | 0.8529                 |                        |                        |                        |
| Fold 6         | MET   | 0.6364                 | 0.6364                 | 0.6364                 | 0.7576                 | 0.8898                 | 0.5152                 |
|                | NSCLC | 0.8788                 | 0.8788                 | 0.8788                 |                        |                        |                        |
| Fold 7         | MET   | 0.7143                 | 0.4545                 | 0.5556                 | 0.6970                 | 0.8733                 | 0.4664                 |
|                | NSCLC | 0.8378                 | 0.9394                 | 0.8857                 |                        |                        |                        |
| Fold 8         | MET   | 0.7143                 | 0.4545                 | 0.5556                 | 0.6970                 | 0.8650                 | 0.4664                 |
|                | NSCLC | 0.8378                 | 0.9394                 | 0.8857                 |                        |                        |                        |
| Fold 9         | MET   | 0.6000                 | 0.5455                 | 0.5714                 | 0.7121                 | 0.8678                 | 0.4384                 |
|                | NSCLC | 0.8529                 | 0.8788                 | 0.8657                 |                        |                        |                        |
| Fold 10        | MET   | 0.7778                 | 0.6364                 | 0.7000                 | 0.7879                 | 0.8705                 | 0.6181                 |
|                | NSCLC | 0.8857                 | 0.9394                 | 0.9118                 |                        |                        |                        |
| Mean $\pm$ std | MET   | 0.6410<br>$\pm 0.1099$ | 0.5000<br>$\pm 0.1372$ | 0.5563<br>$\pm 0.1235$ | 0.7045<br>$\pm 0.0679$ | 0.8364<br>$\pm 0.0549$ | 0.4454<br>$\pm 0.1344$ |
|                | NSCLC | 0.8464<br>$\pm 0.0341$ | 0.9091<br>$\pm 0.0286$ | 0.8761<br>$\pm 0.0223$ |                        |                        |                        |

*Table S30: Logistic regression on TissueConcepts embeddings: Patient-level performance metrics NSCLC vs. MET.*

| <b>Fold</b>       | <b>Class</b> | <b>PRE</b>        | <b>REC</b>        | <b>F1</b>         | <b>BA</b>         | <b>AUROC</b>      | <b>MCC</b>        |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6000            | 0.3750            | 0.4615            | 0.6399            | 0.8095            | 0.3310            |
|                   | NSCLC        | 0.7917            | 0.9048            | 0.8444            |                   |                   |                   |
| Fold 2            | MET          | 0.6667            | 0.2500            | 0.3636            | 0.6012            | 0.7560            | 0.2970            |
|                   | NSCLC        | 0.7692            | 0.9524            | 0.8511            |                   |                   |                   |
| Fold 3            | MET          | 0.8000            | 0.5000            | 0.6154            | 0.7262            | 0.8631            | 0.5353            |
|                   | NSCLC        | 0.8333            | 0.9524            | 0.8889            |                   |                   |                   |
| Fold 4            | MET          | 0.7143            | 0.6250            | 0.6667            | 0.7649            | 0.8750            | 0.5533            |
|                   | NSCLC        | 0.8636            | 0.9048            | 0.8837            |                   |                   |                   |
| Fold 5            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.8333            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 6            | MET          | 0.8000            | 0.5000            | 0.6154            | 0.7262            | 0.9048            | 0.5353            |
|                   | NSCLC        | 0.8333            | 0.9524            | 0.8889            |                   |                   |                   |
| Fold 7            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.8929            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 8            | MET          | 0.7500            | 0.3750            | 0.5000            | 0.6637            | 0.9048            | 0.4243            |
|                   | NSCLC        | 0.8000            | 0.9524            | 0.8696            |                   |                   |                   |
| Fold 9            | MET          | 0.6667            | 0.5000            | 0.5714            | 0.7024            | 0.8929            | 0.4466            |
|                   | NSCLC        | 0.8261            | 0.9048            | 0.8636            |                   |                   |                   |
| Fold 10           | MET          | 0.8333            | 0.6250            | 0.7143            | 0.7887            | 0.9048            | 0.6371            |
|                   | NSCLC        | 0.8696            | 0.9524            | 0.9091            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.7331<br>±0.0721 | 0.4500<br>±0.1208 | 0.5508<br>±0.1052 | 0.6940<br>±0.0581 | 0.8637<br>±0.0498 | 0.4609<br>±0.1047 |
|                   | <b>NSCLC</b> | 0.8187<br>±0.0322 | 0.9381<br>±0.0230 | 0.8738<br>±0.0192 |                   |                   |                   |

Table S31: Logistic regression on UNI2-h embeddings: Patch-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6083            | 0.2895            | 0.3923            | 0.5770            | 0.6807            | 0.1899            |
|                   | NSCLC        | 0.6260            | 0.8645            | 0.7261            |                   |                   |                   |
| Fold 2            | MET          | 0.6477            | 0.3428            | 0.4483            | 0.6036            | 0.7379            | 0.2459            |
|                   | NSCLC        | 0.6440            | 0.8645            | 0.7381            |                   |                   |                   |
| Fold 3            | MET          | 0.6403            | 0.3686            | 0.4678            | 0.6090            | 0.7183            | 0.2512            |
|                   | NSCLC        | 0.6492            | 0.8495            | 0.7359            |                   |                   |                   |
| Fold 4            | MET          | 0.6266            | 0.3677            | 0.4635            | 0.6042            | 0.7117            | 0.2386            |
|                   | NSCLC        | 0.6465            | 0.8407            | 0.7309            |                   |                   |                   |
| Fold 5            | MET          | 0.6164            | 0.3230            | 0.4239            | 0.5884            | 0.6946            | 0.2106            |
|                   | NSCLC        | 0.6343            | 0.8538            | 0.7279            |                   |                   |                   |
| Fold 6            | MET          | 0.6316            | 0.3093            | 0.4152            | 0.5891            | 0.6742            | 0.2174            |
|                   | NSCLC        | 0.6337            | 0.8688            | 0.7329            |                   |                   |                   |
| Fold 7            | MET          | 0.6276            | 0.3170            | 0.4212            | 0.5901            | 0.7038            | 0.2174            |
|                   | NSCLC        | 0.6348            | 0.8632            | 0.7316            |                   |                   |                   |
| Fold 8            | MET          | 0.6119            | 0.3170            | 0.4177            | 0.5854            | 0.6799            | 0.2043            |
|                   | NSCLC        | 0.6323            | 0.8538            | 0.7265            |                   |                   |                   |
| Fold 9            | MET          | 0.5962            | 0.3514            | 0.4422            | 0.5892            | 0.6820            | 0.2039            |
|                   | NSCLC        | 0.6368            | 0.8270            | 0.7196            |                   |                   |                   |
| Fold 10           | MET          | 0.6277            | 0.3505            | 0.4498            | 0.5997            | 0.7075            | 0.2321            |
|                   | NSCLC        | 0.6426            | 0.8488            | 0.7314            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6234<br>±0.0154 | 0.3337<br>±0.0264 | 0.4342<br>±0.0239 | 0.5936<br>±0.0101 | 0.6991<br>±0.0204 | 0.2211<br>±0.0201 |
|                   | <b>NSCLC</b> | 0.6380<br>±0.0073 | 0.8535<br>±0.0128 | 0.7301<br>±0.0053 |                   |                   |                   |

Table S32: Logistic regression on UNI2-h embeddings: Slide-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.8000            | 0.3636            | 0.5000            | 0.6667            | 0.7410            | 0.4548            |
|                   | NSCLC        | 0.8205            | 0.9697            | 0.8889            |                   |                   |                   |
| Fold 2            | MET          | 0.4000            | 0.1818            | 0.2500            | 0.5455            | 0.8430            | 0.1240            |
|                   | NSCLC        | 0.7692            | 0.9091            | 0.8333            |                   |                   |                   |
| Fold 3            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.8072            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 4            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.7879            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 5            | MET          | 0.8000            | 0.3636            | 0.5000            | 0.6667            | 0.7796            | 0.4548            |
|                   | NSCLC        | 0.8205            | 0.9697            | 0.8889            |                   |                   |                   |
| Fold 6            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.7686            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 7            | MET          | 0.6667            | 0.3636            | 0.4706            | 0.6515            | 0.8127            | 0.3824            |
|                   | NSCLC        | 0.8158            | 0.9394            | 0.8732            |                   |                   |                   |
| Fold 8            | MET          | 0.8000            | 0.3636            | 0.5000            | 0.6667            | 0.7631            | 0.4548            |
|                   | NSCLC        | 0.8205            | 0.9697            | 0.8889            |                   |                   |                   |
| Fold 9            | MET          | 0.5000            | 0.3636            | 0.4211            | 0.6212            | 0.7631            | 0.2722            |
|                   | NSCLC        | 0.8056            | 0.8788            | 0.8406            |                   |                   |                   |
| Fold 10           | MET          | 0.8000            | 0.3636            | 0.5000            | 0.6667            | 0.8099            | 0.4548            |
|                   | NSCLC        | 0.8205            | 0.9697            | 0.8889            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6767<br>±0.1370 | 0.3455<br>±0.0575 | 0.4553<br>±0.0762 | 0.6439<br>±0.0373 | 0.7876<br>±0.0305 | 0.3745<br>±0.1050 |
|                   | <b>NSCLC</b> | 0.8120<br>±0.0157 | 0.9424<br>±0.0301 | 0.8722<br>±0.0201 |                   |                   |                   |

Table S33: Logistic regression on UNI2-h embeddings: Patient-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.7143            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 2            | MET          | 0.0000            | 0.0000            | 0.0000            | 0.4762            | 0.8512            | -0.1166           |
|                   | NSCLC        | 0.7143            | 0.9524            | 0.8163            |                   |                   |                   |
| Fold 3            | MET          | 0.6667            | 0.2500            | 0.3636            | 0.6012            | 0.8214            | 0.2970            |
|                   | NSCLC        | 0.7692            | 0.9524            | 0.8511            |                   |                   |                   |
| Fold 4            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8036            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 5            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.7738            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 6            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.7619            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 7            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.7976            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 8            | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.7500            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| Fold 9            | MET          | 0.5000            | 0.2500            | 0.3333            | 0.5774            | 0.7560            | 0.2006            |
|                   | NSCLC        | 0.7600            | 0.9048            | 0.8261            |                   |                   |                   |
| Fold 10           | MET          | 1.0000            | 0.2500            | 0.4000            | 0.6250            | 0.8095            | 0.4410            |
|                   | NSCLC        | 0.7778            | 1.0000            | 0.8750            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.8167<br>±0.3375 | 0.2250<br>±0.0791 | 0.3497<br>±0.1249 | 0.6030<br>±0.0473 | 0.7839<br>±0.0402 | 0.3468<br>±0.1828 |
|                   | <b>NSCLC</b> | 0.7688<br>±0.0200 | 0.9810<br>±0.0333 | 0.8618<br>±0.0228 |                   |                   |                   |

Table S34: Logistic regression on Virchow2 embeddings: Patch-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.6253            | 0.3943            | 0.4837            | 0.6113            | 0.7140            | 0.2488            |
|                   | NSCLC        | 0.6529            | 0.8282            | 0.7302            |                   |                   |                   |
| Fold 2            | MET          | 0.6742            | 0.4373            | 0.5305            | 0.6418            | 0.7492            | 0.3143            |
|                   | NSCLC        | 0.6741            | 0.8463            | 0.7505            |                   |                   |                   |
| Fold 3            | MET          | 0.6604            | 0.4192            | 0.5129            | 0.6312            | 0.7182            | 0.2928            |
|                   | NSCLC        | 0.6663            | 0.8432            | 0.7444            |                   |                   |                   |
| Fold 4            | MET          | 0.6873            | 0.4493            | 0.5434            | 0.6503            | 0.7488            | 0.3324            |
|                   | NSCLC        | 0.6801            | 0.8513            | 0.7562            |                   |                   |                   |
| Fold 5            | MET          | 0.6616            | 0.4098            | 0.5061            | 0.6287            | 0.7305            | 0.2894            |
|                   | NSCLC        | 0.6639            | 0.8476            | 0.7446            |                   |                   |                   |
| Fold 6            | MET          | 0.7188            | 0.3754            | 0.4932            | 0.6343            | 0.7379            | 0.3202            |
|                   | NSCLC        | 0.6630            | 0.8932            | 0.7610            |                   |                   |                   |
| Fold 7            | MET          | 0.6631            | 0.4227            | 0.5163            | 0.6333            | 0.7277            | 0.2970            |
|                   | NSCLC        | 0.6678            | 0.8438            | 0.7456            |                   |                   |                   |
| Fold 8            | MET          | 0.6532            | 0.4158            | 0.5081            | 0.6276            | 0.7244            | 0.2846            |
|                   | NSCLC        | 0.6640            | 0.8395            | 0.7415            |                   |                   |                   |
| Fold 9            | MET          | 0.6316            | 0.4433            | 0.5209            | 0.6276            | 0.7226            | 0.2763            |
|                   | NSCLC        | 0.6674            | 0.8120            | 0.7326            |                   |                   |                   |
| Fold 10           | MET          | 0.6601            | 0.4304            | 0.5211            | 0.6346            | 0.7382            | 0.2979            |
|                   | NSCLC        | 0.6695            | 0.8389            | 0.7447            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.6635<br>±0.0265 | 0.4198<br>±0.0226 | 0.5136<br>±0.0173 | 0.6321<br>±0.0101 | 0.7311<br>±0.0121 | 0.2954<br>±0.0237 |
|                   | <b>NSCLC</b> | 0.6669<br>±0.0072 | 0.8444<br>±0.0206 | 0.7451<br>±0.0094 |                   |                   |                   |

Table S35: Logistic regression on Virchow2 embeddings: Slide-level performance metrics NSCLC vs. MET.

| Fold              | Class        | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | MET          | 0.7500            | 0.5455            | 0.6316            | 0.7424            | 0.7658            | 0.5443            |
|                   | NSCLC        | 0.8611            | 0.9394            | 0.8986            |                   |                   |                   |
| Fold 2            | MET          | 0.8000            | 0.3636            | 0.5000            | 0.6667            | 0.8760            | 0.4548            |
|                   | NSCLC        | 0.8205            | 0.9697            | 0.8889            |                   |                   |                   |
| Fold 3            | MET          | 1.0000            | 0.4545            | 0.6250            | 0.7273            | 0.8127            | 0.6202            |
|                   | NSCLC        | 0.8462            | 1.0000            | 0.9167            |                   |                   |                   |
| Fold 4            | MET          | 1.0000            | 0.6364            | 0.7778            | 0.8182            | 0.7961            | 0.7534            |
|                   | NSCLC        | 0.8919            | 1.0000            | 0.9429            |                   |                   |                   |
| Fold 5            | MET          | 0.8333            | 0.4545            | 0.5882            | 0.7121            | 0.8264            | 0.5353            |
|                   | NSCLC        | 0.8421            | 0.9697            | 0.9014            |                   |                   |                   |
| Fold 6            | MET          | 1.0000            | 0.4545            | 0.6250            | 0.7273            | 0.8512            | 0.6202            |
|                   | NSCLC        | 0.8462            | 1.0000            | 0.9167            |                   |                   |                   |
| Fold 7            | MET          | 1.0000            | 0.5455            | 0.7059            | 0.7727            | 0.8320            | 0.6882            |
|                   | NSCLC        | 0.8684            | 1.0000            | 0.9296            |                   |                   |                   |
| Fold 8            | MET          | 1.0000            | 0.5455            | 0.7059            | 0.7727            | 0.8402            | 0.6882            |
|                   | NSCLC        | 0.8684            | 1.0000            | 0.9296            |                   |                   |                   |
| Fold 9            | MET          | 1.0000            | 0.5455            | 0.7059            | 0.7727            | 0.8209            | 0.6882            |
|                   | NSCLC        | 0.8684            | 1.0000            | 0.9296            |                   |                   |                   |
| Fold 10           | MET          | 1.0000            | 0.5455            | 0.7059            | 0.7727            | 0.8237            | 0.6882            |
|                   | NSCLC        | 0.8684            | 1.0000            | 0.9296            |                   |                   |                   |
| <b>Mean ± std</b> | <b>MET</b>   | 0.9383<br>±0.1012 | 0.5091<br>±0.0767 | 0.6571<br>±0.0790 | 0.7485<br>±0.0424 | 0.8245<br>±0.0300 | 0.6281<br>±0.0919 |
|                   | <b>NSCLC</b> | 0.8582<br>±0.0198 | 0.9879<br>±0.0212 | 0.9183<br>±0.0172 |                   |                   |                   |

Table S36: Logistic regression on Virchow2 embeddings: Patient-level performance metrics NSCLC vs. MET.

| Fold           | Class | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------|-------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1         | MET   | 0.8000                 | 0.5000                 | 0.6154                 | 0.7262                 | 0.7857                 | 0.5353                 |
|                | NSCLC | 0.8333                 | 0.9524                 | 0.8889                 |                        |                        |                        |
| Fold 2         | MET   | 1.0000                 | 0.3750                 | 0.5455                 | 0.6875                 | 0.9167                 | 0.5503                 |
|                | NSCLC | 0.8077                 | 1.0000                 | 0.8936                 |                        |                        |                        |
| Fold 3         | MET   | 1.0000                 | 0.3750                 | 0.5455                 | 0.6875                 | 0.8393                 | 0.5503                 |
|                | NSCLC | 0.8077                 | 1.0000                 | 0.8936                 |                        |                        |                        |
| Fold 4         | MET   | 1.0000                 | 0.6250                 | 0.7692                 | 0.8125                 | 0.8333                 | 0.7395                 |
|                | NSCLC | 0.8750                 | 1.0000                 | 0.9333                 |                        |                        |                        |
| Fold 5         | MET   | 1.0000                 | 0.3750                 | 0.5455                 | 0.6875                 | 0.8571                 | 0.5503                 |
|                | NSCLC | 0.8077                 | 1.0000                 | 0.8936                 |                        |                        |                        |
| Fold 6         | MET   | 1.0000                 | 0.3750                 | 0.5455                 | 0.6875                 | 0.8869                 | 0.5503                 |
|                | NSCLC | 0.8077                 | 1.0000                 | 0.8936                 |                        |                        |                        |
| Fold 7         | MET   | 1.0000                 | 0.5000                 | 0.6667                 | 0.7500                 | 0.8452                 | 0.6481                 |
|                | NSCLC | 0.8400                 | 1.0000                 | 0.9130                 |                        |                        |                        |
| Fold 8         | MET   | 1.0000                 | 0.5000                 | 0.6667                 | 0.7500                 | 0.8512                 | 0.6481                 |
|                | NSCLC | 0.8400                 | 1.0000                 | 0.9130                 |                        |                        |                        |
| Fold 9         | MET   | 1.0000                 | 0.5000                 | 0.6667                 | 0.7500                 | 0.8274                 | 0.6481                 |
|                | NSCLC | 0.8400                 | 1.0000                 | 0.9130                 |                        |                        |                        |
| Fold 10        | MET   | 1.0000                 | 0.5000                 | 0.6667                 | 0.7500                 | 0.8512                 | 0.6481                 |
|                | NSCLC | 0.8400                 | 1.0000                 | 0.9130                 |                        |                        |                        |
| Mean $\pm$ std | MET   | 0.9800<br>$\pm 0.0632$ | 0.4625<br>$\pm 0.0844$ | 0.6233<br>$\pm 0.0768$ | 0.7289<br>$\pm 0.0417$ | 0.8494<br>$\pm 0.0348$ | 0.6068<br>$\pm 0.0685$ |
|                | NSCLC | 0.8299<br>$\pm 0.0222$ | 0.9952<br>$\pm 0.0151$ | 0.9049<br>$\pm 0.0143$ |                        |                        |                        |

Table S37: MLP: Performance metrics NSCLC vs. MET.

| Architecture   | Level   | Class | PRE    | REC    | F1     | BA (95% CI)     | AUROC (95% CI)  | MCC (95% CI)     |
|----------------|---------|-------|--------|--------|--------|-----------------|-----------------|------------------|
| ResNet50       | Patch   | MET   | 0.6369 | 0.5395 | 0.5842 | 0.6580          | 0.7206          | 0.3256           |
|                |         | NSCLC | 0.6987 | 0.7764 | 0.7355 | (0.6403-0.6761) | (0.7028-0.7394) | (0.2888-0.3630)  |
|                | Slide   | MET   | 0.5714 | 0.7273 | 0.6400 | 0.7727          | 0.8127          | 0.5071           |
|                |         | NSCLC | 0.9000 | 0.8182 | 0.8571 | (0.6041-0.9103) | (0.6323-0.9474) | (0.1992-0.7531)  |
|                | Patient | MET   | 0.5556 | 0.6250 | 0.5882 | 0.7173          | 0.8155          | 0.4198           |
|                |         | NSCLC | 0.8500 | 0.8095 | 0.8293 | (0.4975-0.9091) | (0.6250-0.9638) | (-0.0052-0.7533) |
| CONCH          | Patch   | MET   | 0.6201 | 0.4081 | 0.4922 | 0.6132          | 0.6824          | 0.2497           |
|                |         | NSCLC | 0.6553 | 0.8182 | 0.7278 | (0.5967-0.6299) | (0.6632-0.7016) | (0.2131-0.2847)  |
|                | Slide   | MET   | 0.5556 | 0.4545 | 0.5000 | 0.6667          | 0.7493          | 0.3578           |
|                |         | NSCLC | 0.8286 | 0.8788 | 0.8529 | (0.5024-0.8334) | (0.5651-0.9092) | (0.0053-0.6616)  |
|                | Patient | MET   | 0.5000 | 0.3750 | 0.4286 | 0.6161          | 0.7440          | 0.2561           |
|                |         | NSCLC | 0.7826 | 0.8571 | 0.8182 | (0.4259-0.8150) | (0.5315-0.9400) | (-0.1600-0.6282) |
| CTransPath     | Patch   | MET   | 0.7409 | 0.3660 | 0.4899 | 0.6365          | 0.7554          | 0.3320           |
|                |         | NSCLC | 0.6630 | 0.9069 | 0.7660 | (0.6205-0.6536) | (0.7364-0.7738) | (0.2966-0.3689)  |
|                | Slide   | MET   | 0.7143 | 0.4545 | 0.5556 | 0.6970          | 0.8072          | 0.4664           |
|                |         | NSCLC | 0.8378 | 0.9394 | 0.8857 | (0.5508-0.8572) | (0.6525-0.9410) | (0.1269-0.7534)  |
|                | Patient | MET   | 0.7500 | 0.3750 | 0.5000 | 0.6637          | 0.8274          | 0.4243           |
|                |         | NSCLC | 0.8000 | 0.9524 | 0.8696 | (0.4808-0.8732) | (0.6521-0.9744) | (-0.0534-0.7583) |
| H-optimus-0    | Patch   | MET   | 0.6989 | 0.2672 | 0.3866 | 0.5917          | 0.6859          | 0.2465           |
|                |         | NSCLC | 0.6323 | 0.9163 | 0.7483 | (0.5781-0.6066) | (0.6657-0.7058) | (0.2111-0.2838)  |
|                | Slide   | MET   | 0.5714 | 0.3636 | 0.4444 | 0.6364          | 0.6942          | 0.3229           |
|                |         | NSCLC | 0.8108 | 0.9091 | 0.8571 | (0.4780-0.7912) | (0.4768-0.9035) | (-0.0443-0.6367) |
|                | Patient | MET   | 0.6667 | 0.2500 | 0.3636 | 0.6012          | 0.6845          | 0.2970           |
|                |         | NSCLC | 0.7692 | 0.9524 | 0.8511 | (0.4583-0.7793) | (0.4156-0.9334) | (-0.1359-0.6683) |
| H-optimus-1    | Patch   | MET   | 0.7089 | 0.4708 | 0.5658 | 0.6651          | 0.7566          | 0.3633           |
|                |         | NSCLC | 0.6908 | 0.8595 | 0.7659 | (0.6495-0.6817) | (0.7391-0.7749) | (0.3304-0.3983)  |
|                | Slide   | MET   | 0.5556 | 0.4545 | 0.5000 | 0.6667          | 0.8209          | 0.3578           |
|                |         | NSCLC | 0.8286 | 0.8788 | 0.8529 | (0.5111-0.8206) | (0.6690-0.9559) | (0.0222-0.6616)  |
|                | Patient | MET   | 0.7500 | 0.3750 | 0.5000 | 0.6637          | 0.8452          | 0.4243           |
|                |         | NSCLC | 0.8000 | 0.9524 | 0.8696 | (0.4792-0.8737) | (0.6520-1.0000) | (-0.0777-0.7832) |
| hibou-L        | Patch   | MET   | 0.7022 | 0.3849 | 0.4972 | 0.6331          | 0.7423          | 0.3120           |
|                |         | NSCLC | 0.6634 | 0.8813 | 0.7570 | (0.6170-0.6488) | (0.7231-0.7606) | (0.2762-0.3485)  |
|                | Slide   | MET   | 0.8333 | 0.4545 | 0.5882 | 0.7121          | 0.8264          | 0.5353           |
|                |         | NSCLC | 0.8421 | 0.9697 | 0.9014 | (0.5677-0.8746) | (0.6588-0.9531) | (0.2057-0.8142)  |
|                | Patient | MET   | 0.7500 | 0.3750 | 0.5000 | 0.6637          | 0.8274          | 0.4243           |
|                |         | NSCLC | 0.8000 | 0.9524 | 0.8696 | (0.4805-0.8641) | (0.6377-0.9805) | (-0.0643-0.7832) |
| Kaiko          | Patch   | MET   | 0.6957 | 0.4596 | 0.5535 | 0.6567          | 0.7582          | 0.3454           |
|                |         | NSCLC | 0.6849 | 0.8538 | 0.7601 | (0.6397-0.6726) | (0.7393-0.7744) | (0.3078-0.3807)  |
|                | Slide   | MET   | 0.5000 | 0.5455 | 0.5217 | 0.6818          | 0.7466          | 0.3536           |
|                |         | NSCLC | 0.8438 | 0.8182 | 0.8308 | (0.5126-0.8475) | (0.5521-0.9118) | (0.0256-0.6423)  |
|                | Patient | MET   | 0.5714 | 0.5000 | 0.5333 | 0.6786          | 0.7679          | 0.3730           |
|                |         | NSCLC | 0.8182 | 0.8571 | 0.8372 | (0.4750-0.8814) | (0.5416-0.9501) | (-0.0517-0.7336) |
| Phikon         | Patch   | MET   | 0.7120 | 0.3780 | 0.4938 | 0.6334          | 0.7432          | 0.3162           |
|                |         | NSCLC | 0.6628 | 0.8888 | 0.7593 | (0.6173-0.6485) | (0.7247-0.7601) | (0.2786-0.3505)  |
|                | Slide   | MET   | 0.6667 | 0.3636 | 0.4706 | 0.6515          | 0.8154          | 0.3824           |
|                |         | NSCLC | 0.8158 | 0.9394 | 0.8732 | (0.4999-0.8031) | (0.6437-0.9460) | (-0.0002-0.6806) |
|                | Patient | MET   | 0.6667 | 0.2500 | 0.3636 | 0.6012          | 0.8571          | 0.2970           |
|                |         | NSCLC | 0.7692 | 0.9524 | 0.8511 | (0.4583-0.7793) | (0.6616-0.9935) | (-0.1359-0.6683) |
| ProvGigaPath   | Patch   | MET   | 0.6922 | 0.3265 | 0.4437 | 0.6105          | 0.7213          | 0.2734           |
|                |         | NSCLC | 0.6462 | 0.8944 | 0.7503 | (0.5951-0.6257) | (0.7024-0.7401) | (0.2377-0.3087)  |
|                | Slide   | MET   | 0.4444 | 0.3636 | 0.4000 | 0.6061          | 0.7576          | 0.2277           |
|                |         | NSCLC | 0.8000 | 0.8485 | 0.8235 | (0.4510-0.7618) | (0.5857-0.9082) | (-0.1047-0.5636) |
|                | Patient | MET   | 0.6667 | 0.2500 | 0.3636 | 0.6012          | 0.7917          | 0.2970           |
|                |         | NSCLC | 0.7692 | 0.9524 | 0.8511 | (0.4583-0.7793) | (0.5844-0.9465) | (-0.1359-0.6683) |
| TissueConcepts | Patch   | MET   | 0.6671 | 0.4734 | 0.5538 | 0.6508          | 0.7102          | 0.3253           |
|                |         | NSCLC | 0.6839 | 0.8282 | 0.7492 | (0.6345-0.6682) | (0.6895-0.7301) | (0.2900-0.3610)  |
|                | Slide   | MET   | 0.8333 | 0.4545 | 0.5882 | 0.7121          | 0.8815          | 0.5353           |
|                |         | NSCLC | 0.8421 | 0.9697 | 0.9014 | (0.5706-0.8636) | (0.7429-0.9846) | (0.2293-0.8020)  |
|                | Patient | MET   | 0.7500 | 0.3750 | 0.5000 | 0.6637          | 0.9286          | 0.4243           |
|                |         | NSCLC | 0.8000 | 0.9524 | 0.8696 | (0.4792-0.8732) | (0.7986-1.0000) | (-0.0757-0.7901) |
| UNI2-h         | Patch   | MET   | 0.7524 | 0.3419 | 0.4702 | 0.6301          | 0.7522          | 0.3265           |
|                |         | NSCLC | 0.6574 | 0.9182 | 0.7662 | (0.6149-0.6445) | (0.7343-0.7695) | (0.2911-0.3595)  |
|                | Slide   | MET   | 0.6667 | 0.3636 | 0.4706 | 0.6515          | 0.7989          | 0.3824           |
|                |         | NSCLC | 0.8158 | 0.9394 | 0.8732 | (0.5059-0.8030) | (0.6382-0.9421) | (0.0170-0.6719)  |
|                | Patient | MET   | 0.6667 | 0.2500 | 0.3636 | 0.6012          | 0.8571          | 0.2970           |
|                |         | NSCLC | 0.7692 | 0.9524 | 0.8511 | (0.4565-0.7857) | (0.6736-0.9872) | (-0.1390-0.6651) |
| Virchow2       | Patch   | MET   | 0.6736 | 0.4450 | 0.5360 | 0.6441          | 0.7432          | 0.3176           |
|                |         | NSCLC | 0.6764 | 0.8432 | 0.7506 | (0.6258-0.6620) | (0.7247-0.7613) | (0.2767-0.3538)  |
|                | Slide   | MET   | 0.8571 | 0.5455 | 0.6667 | 0.7576          | 0.7824          | 0.6099           |
|                |         | NSCLC | 0.8649 | 0.9697 | 0.9143 | (0.6095-0.9167) | (0.5999-0.9429) | (0.3185-0.8605)  |
|                | Patient | MET   | 1.0000 | 0.5000 | 0.6667 | 0.7500          | 0.7976          | 0.6481           |
|                |         | NSCLC | 0.8400 | 1.0000 | 0.9130 | (0.5712-0.9444) | (0.5667-0.9855) | (0.3343-0.9201)  |

#### 4. Performance metrics tables AC vs. SCC

Table S38: Logistic regression on CONCH embeddings: Patch-level performance metrics AC vs. SCC.

| Fold           | Class | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------|-------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1         | AC    | 0.4516                 | 0.3526                 | 0.3960                 | 0.5330                 | 0.5673                 | 0.0697                 |
|                | SCC   | 0.6221                 | 0.7133                 | 0.6646                 |                        |                        |                        |
| Fold 2         | AC    | 0.4403                 | 0.3526                 | 0.3916                 | 0.5262                 | 0.5813                 | 0.0551                 |
|                | SCC   | 0.6176                 | 0.6998                 | 0.6561                 |                        |                        |                        |
| Fold 3         | AC    | 0.4162                 | 0.3501                 | 0.3803                 | 0.5106                 | 0.5382                 | 0.0221                 |
|                | SCC   | 0.6067                 | 0.6712                 | 0.6373                 |                        |                        |                        |
| Fold 4         | AC    | 0.4406                 | 0.3552                 | 0.3933                 | 0.5267                 | 0.5460                 | 0.0559                 |
|                | SCC   | 0.6179                 | 0.6981                 | 0.6556                 |                        |                        |                        |
| Fold 5         | AC    | 0.4361                 | 0.3955                 | 0.4148                 | 0.5266                 | 0.5503                 | 0.0541                 |
|                | SCC   | 0.6190                 | 0.6577                 | 0.6378                 |                        |                        |                        |
| Fold 6         | AC    | 0.4695                 | 0.3879                 | 0.4248                 | 0.5472                 | 0.5749                 | 0.0984                 |
|                | SCC   | 0.6329                 | 0.7066                 | 0.6677                 |                        |                        |                        |
| Fold 7         | AC    | 0.4702                 | 0.3980                 | 0.4311                 | 0.5489                 | 0.5869                 | 0.1012                 |
|                | SCC   | 0.6346                 | 0.6998                 | 0.6656                 |                        |                        |                        |
| Fold 8         | AC    | 0.4433                 | 0.4232                 | 0.4330                 | 0.5337                 | 0.5626                 | 0.0679                 |
|                | SCC   | 0.6252                 | 0.6442                 | 0.6346                 |                        |                        |                        |
| Fold 9         | AC    | 0.4380                 | 0.4181                 | 0.4278                 | 0.5295                 | 0.5644                 | 0.0594                 |
|                | SCC   | 0.6219                 | 0.6408                 | 0.6312                 |                        |                        |                        |
| Fold 10        | AC    | 0.3853                 | 0.3174                 | 0.3481                 | 0.4892                 | 0.5138                 | -0.0225                |
|                | SCC   | 0.5913                 | 0.6610                 | 0.6242                 |                        |                        |                        |
| Mean $\pm$ std | AC    | 0.4391<br>$\pm 0.0247$ | 0.3751<br>$\pm 0.0344$ | 0.4041<br>$\pm 0.0273$ | 0.5272<br>$\pm 0.0172$ | 0.5586<br>$\pm 0.0220$ | 0.0561<br>$\pm 0.0357$ |
|                | SCC   | 0.6189<br>$\pm 0.0125$ | 0.6793<br>$\pm 0.0272$ | 0.6475<br>$\pm 0.0161$ |                        |                        |                        |

Table S39: Logistic regression on CONCH embeddings: Slide-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5833            | 0.6481            | 0.1667            |
|                   | SCC        | 0.6667            | 0.6667            | 0.6667            |                   |                   |                   |
| Fold 2            | AC         | 0.4545            | 0.4167            | 0.4348            | 0.5417            | 0.6528            | 0.0847            |
|                   | SCC        | 0.6316            | 0.6667            | 0.6486            |                   |                   |                   |
| Fold 3            | AC         | 0.4545            | 0.4167            | 0.4348            | 0.5417            | 0.6111            | 0.0847            |
|                   | SCC        | 0.6316            | 0.6667            | 0.6486            |                   |                   |                   |
| Fold 4            | AC         | 0.4545            | 0.4167            | 0.4348            | 0.5417            | 0.5787            | 0.0847            |
|                   | SCC        | 0.6316            | 0.6667            | 0.6486            |                   |                   |                   |
| Fold 5            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.6343            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 6            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.5880            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 7            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5833            | 0.6435            | 0.1667            |
|                   | SCC        | 0.6667            | 0.6667            | 0.6667            |                   |                   |                   |
| Fold 8            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.6528            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 9            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5833            | 0.6574            | 0.1667            |
|                   | SCC        | 0.6667            | 0.6667            | 0.6667            |                   |                   |                   |
| Fold 10           | AC         | 0.4545            | 0.4167            | 0.4348            | 0.5417            | 0.6019            | 0.0847            |
|                   | SCC        | 0.6316            | 0.6667            | 0.6486            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4934<br>±0.0369 | 0.4917<br>±0.0730 | 0.4919<br>±0.0549 | 0.5792<br>±0.0365 | 0.6269<br>±0.0294 | 0.1580<br>±0.0711 |
|                   | <b>SCC</b> | 0.6644<br>±0.0325 | 0.6667<br>±0.0000 | 0.6652<br>±0.0162 |                   |                   |                   |

Table S40: Logistic regression on CONCH embeddings: Patient-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.6705            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| Fold 2            | AC         | 0.4286            | 0.3750            | 0.4000            | 0.5057            | 0.6932            | 0.0116            |
|                   | SCC        | 0.5833            | 0.6364            | 0.6087            |                   |                   |                   |
| Fold 3            | AC         | 0.4286            | 0.3750            | 0.4000            | 0.5057            | 0.6364            | 0.0116            |
|                   | SCC        | 0.5833            | 0.6364            | 0.6087            |                   |                   |                   |
| Fold 4            | AC         | 0.4286            | 0.3750            | 0.4000            | 0.5057            | 0.6250            | 0.0116            |
|                   | SCC        | 0.5833            | 0.6364            | 0.6087            |                   |                   |                   |
| Fold 5            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.6818            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 6            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.6250            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 7            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.6932            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| Fold 8            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.6705            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 9            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.6477            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| Fold 10           | AC         | 0.4286            | 0.3750            | 0.4000            | 0.5057            | 0.6023            | 0.0116            |
|                   | SCC        | 0.5833            | 0.6364            | 0.6087            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4881<br>±0.0560 | 0.4875<br>±0.1094 | 0.4865<br>±0.0827 | 0.5619<br>±0.0547 | 0.6545<br>±0.0318 | 0.1231<br>±0.1081 |
|                   | <b>SCC</b> | 0.6342<br>±0.0509 | 0.6364<br>±0.0000 | 0.6344<br>±0.0253 |                   |                   |                   |

Table S41: Logistic regression on CTransPath embeddings: Patch-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5078            | 0.4081            | 0.4525            | 0.5717            | 0.5977            | 0.1503            |
|                   | SCC        | 0.6498            | 0.7352            | 0.6899            |                   |                   |                   |
| Fold 2            | AC         | 0.4897            | 0.4207            | 0.4526            | 0.5636            | 0.6118            | 0.1312            |
|                   | SCC        | 0.6456            | 0.7066            | 0.6747            |                   |                   |                   |
| Fold 3            | AC         | 0.4573            | 0.3778            | 0.4138            | 0.5388            | 0.5751            | 0.0809            |
|                   | SCC        | 0.6269            | 0.6998            | 0.6614            |                   |                   |                   |
| Fold 4            | AC         | 0.4717            | 0.3778            | 0.4196            | 0.5473            | 0.5718            | 0.0992            |
|                   | SCC        | 0.6324            | 0.7167            | 0.6719            |                   |                   |                   |
| Fold 5            | AC         | 0.4727            | 0.4584            | 0.4655            | 0.5581            | 0.5879            | 0.1167            |
|                   | SCC        | 0.6446            | 0.6577            | 0.6511            |                   |                   |                   |
| Fold 6            | AC         | 0.4896            | 0.4156            | 0.4496            | 0.5628            | 0.5716            | 0.1299            |
|                   | SCC        | 0.6447            | 0.7099            | 0.6758            |                   |                   |                   |
| Fold 7            | AC         | 0.4972            | 0.4484            | 0.4715            | 0.5724            | 0.6029            | 0.1477            |
|                   | SCC        | 0.6535            | 0.6965            | 0.6743            |                   |                   |                   |
| Fold 8            | AC         | 0.4948            | 0.4811            | 0.4879            | 0.5761            | 0.5975            | 0.1530            |
|                   | SCC        | 0.6589            | 0.6712            | 0.6650            |                   |                   |                   |
| Fold 9            | AC         | 0.4882            | 0.4685            | 0.4781            | 0.5698            | 0.6278            | 0.1407            |
|                   | SCC        | 0.6535            | 0.6712            | 0.6622            |                   |                   |                   |
| Fold 10           | AC         | 0.4638            | 0.4358            | 0.4494            | 0.5493            | 0.5759            | 0.0996            |
|                   | SCC        | 0.6370            | 0.6627            | 0.6496            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4833<br>±0.0161 | 0.4292<br>±0.0357 | 0.4540<br>±0.0236 | 0.5610<br>±0.0124 | 0.5920<br>±0.0190 | 0.1249<br>±0.0249 |
|                   | <b>SCC</b> | 0.6447<br>±0.0101 | 0.6927<br>±0.0258 | 0.6676<br>±0.0122 |                   |                   |                   |

Table S42: Logistic regression on CTransPath embeddings: Slide-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5000            | 0.5833            | 0.5385            | 0.5972            | 0.5880            | 0.1909            |
|                   | SCC        | 0.6875            | 0.6111            | 0.6471            |                   |                   |                   |
| Fold 2            | AC         | 0.5000            | 0.6667            | 0.5714            | 0.6111            | 0.5926            | 0.2182            |
|                   | SCC        | 0.7143            | 0.5556            | 0.6250            |                   |                   |                   |
| Fold 3            | AC         | 0.4000            | 0.5000            | 0.4444            | 0.5000            | 0.5694            | 0.0000            |
|                   | SCC        | 0.6000            | 0.5000            | 0.5455            |                   |                   |                   |
| Fold 4            | AC         | 0.4286            | 0.5000            | 0.4615            | 0.5278            | 0.5139            | 0.0546            |
|                   | SCC        | 0.6250            | 0.5556            | 0.5882            |                   |                   |                   |
| Fold 5            | AC         | 0.4118            | 0.5833            | 0.4828            | 0.5139            | 0.5787            | 0.0275            |
|                   | SCC        | 0.6154            | 0.4444            | 0.5161            |                   |                   |                   |
| Fold 6            | AC         | 0.4667            | 0.5833            | 0.5185            | 0.5694            | 0.5370            | 0.1361            |
|                   | SCC        | 0.6667            | 0.5556            | 0.6061            |                   |                   |                   |
| Fold 7            | AC         | 0.4118            | 0.5833            | 0.4828            | 0.5139            | 0.5972            | 0.0275            |
|                   | SCC        | 0.6154            | 0.4444            | 0.5161            |                   |                   |                   |
| Fold 8            | AC         | 0.4706            | 0.6667            | 0.5517            | 0.5833            | 0.5833            | 0.1648            |
|                   | SCC        | 0.6923            | 0.5000            | 0.5806            |                   |                   |                   |
| Fold 9            | AC         | 0.4375            | 0.5833            | 0.5000            | 0.5417            | 0.5972            | 0.0818            |
|                   | SCC        | 0.6429            | 0.5000            | 0.5625            |                   |                   |                   |
| Fold 10           | AC         | 0.3750            | 0.5000            | 0.4286            | 0.4722            | 0.5370            | -0.0546           |
|                   | SCC        | 0.5714            | 0.4444            | 0.5000            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4402<br>±0.0427 | 0.5750<br>±0.0615 | 0.4980<br>±0.0469 | 0.5431<br>±0.0456 | 0.5694<br>±0.0296 | 0.0847<br>±0.0896 |
|                   | <b>SCC</b> | 0.6431<br>±0.0458 | 0.5111<br>±0.0574 | 0.5687<br>±0.0495 |                   |                   |                   |

Table S43: Logistic regression on CTransPath embeddings: Patient-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.6705            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 2            | AC         | 0.6000            | 0.7500            | 0.6667            | 0.6932            | 0.6818            | 0.3820            |
|                   | SCC        | 0.7778            | 0.6364            | 0.7000            |                   |                   |                   |
| Fold 3            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.6250            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| Fold 4            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.5682            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| Fold 5            | AC         | 0.5000            | 0.6250            | 0.5556            | 0.5852            | 0.6023            | 0.1685            |
|                   | SCC        | 0.6667            | 0.5455            | 0.6000            |                   |                   |                   |
| Fold 6            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.5909            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 7            | AC         | 0.5000            | 0.6250            | 0.5556            | 0.5852            | 0.6818            | 0.1685            |
|                   | SCC        | 0.6667            | 0.5455            | 0.6000            |                   |                   |                   |
| Fold 8            | AC         | 0.5455            | 0.7500            | 0.6316            | 0.6477            | 0.6818            | 0.2955            |
|                   | SCC        | 0.7500            | 0.5455            | 0.6316            |                   |                   |                   |
| Fold 9            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.6477            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 10           | AC         | 0.4000            | 0.5000            | 0.4444            | 0.4773            | 0.6023            | -0.0449           |
|                   | SCC        | 0.5556            | 0.4545            | 0.5000            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5212<br>±0.0546 | 0.6125<br>±0.0922 | 0.5619<br>±0.0662 | 0.6017<br>±0.0590 | 0.6352<br>±0.0430 | 0.2018<br>±0.1167 |
|                   | <b>SCC</b> | 0.6789<br>±0.0626 | 0.5909<br>±0.0643 | 0.6304<br>±0.0555 |                   |                   |                   |

Table S44: Logistic regression on H-optimus-0 embeddings: Patch-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5503            | 0.4131            | 0.4719            | 0.5936            | 0.6802            | 0.1999            |
|                   | SCC        | 0.6633            | 0.7740            | 0.7144            |                   |                   |                   |
| Fold 2            | AC         | 0.5813            | 0.4232            | 0.4898            | 0.6096            | 0.6918            | 0.2362            |
|                   | SCC        | 0.6733            | 0.7960            | 0.7295            |                   |                   |                   |
| Fold 3            | AC         | 0.5259            | 0.3577            | 0.4258            | 0.5709            | 0.6401            | 0.1561            |
|                   | SCC        | 0.6458            | 0.7841            | 0.7083            |                   |                   |                   |
| Fold 4            | AC         | 0.5382            | 0.3552            | 0.4279            | 0.5756            | 0.6354            | 0.1679            |
|                   | SCC        | 0.6484            | 0.7960            | 0.7146            |                   |                   |                   |
| Fold 5            | AC         | 0.5499            | 0.4861            | 0.5160            | 0.6099            | 0.6776            | 0.2251            |
|                   | SCC        | 0.6808            | 0.7336            | 0.7062            |                   |                   |                   |
| Fold 6            | AC         | 0.5479            | 0.4181            | 0.4743            | 0.5936            | 0.6461            | 0.1990            |
|                   | SCC        | 0.6638            | 0.7690            | 0.7125            |                   |                   |                   |
| Fold 7            | AC         | 0.5494            | 0.4484            | 0.4938            | 0.6011            | 0.6702            | 0.2112            |
|                   | SCC        | 0.6712            | 0.7538            | 0.7101            |                   |                   |                   |
| Fold 8            | AC         | 0.5167            | 0.3904            | 0.4448            | 0.5730            | 0.6496            | 0.1556            |
|                   | SCC        | 0.6493            | 0.7555            | 0.6984            |                   |                   |                   |
| Fold 9            | AC         | 0.5402            | 0.4736            | 0.5047            | 0.6019            | 0.6644            | 0.2091            |
|                   | SCC        | 0.6745            | 0.7302            | 0.7012            |                   |                   |                   |
| Fold 10           | AC         | 0.5130            | 0.3980            | 0.4482            | 0.5725            | 0.6317            | 0.1535            |
|                   | SCC        | 0.6496            | 0.7470            | 0.6949            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5413<br>±0.0198 | 0.4164<br>±0.0440 | 0.4697<br>±0.0319 | 0.5901<br>±0.0158 | 0.6587<br>±0.0209 | 0.1914<br>±0.0307 |
|                   | <b>SCC</b> | 0.6620<br>±0.0129 | 0.7639<br>±0.0238 | 0.7090<br>±0.0099 |                   |                   |                   |

Table S45: Logistic regression on H-optimus-0 embeddings: Slide-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5833            | 0.5833            | 0.5833            | 0.6528            | 0.7083            | 0.3056            |
|                   | SCC        | 0.7222            | 0.7222            | 0.7222            |                   |                   |                   |
| Fold 2            | AC         | 0.6667            | 0.6667            | 0.6667            | 0.7222            | 0.7315            | 0.4444            |
|                   | SCC        | 0.7778            | 0.7778            | 0.7778            |                   |                   |                   |
| Fold 3            | AC         | 0.6000            | 0.5000            | 0.5455            | 0.6389            | 0.6574            | 0.2887            |
|                   | SCC        | 0.7000            | 0.7778            | 0.7368            |                   |                   |                   |
| Fold 4            | AC         | 0.5455            | 0.5000            | 0.5217            | 0.6111            | 0.6481            | 0.2259            |
|                   | SCC        | 0.6842            | 0.7222            | 0.7027            |                   |                   |                   |
| Fold 5            | AC         | 0.6154            | 0.6667            | 0.6400            | 0.6944            | 0.7269            | 0.3845            |
|                   | SCC        | 0.7647            | 0.7222            | 0.7429            |                   |                   |                   |
| Fold 6            | AC         | 0.5455            | 0.5000            | 0.5217            | 0.6111            | 0.6389            | 0.2259            |
|                   | SCC        | 0.6842            | 0.7222            | 0.7027            |                   |                   |                   |
| Fold 7            | AC         | 0.6364            | 0.5833            | 0.6087            | 0.6806            | 0.6620            | 0.3671            |
|                   | SCC        | 0.7368            | 0.7778            | 0.7568            |                   |                   |                   |
| Fold 8            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.6389            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 9            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.7037            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 10           | AC         | 0.5455            | 0.5000            | 0.5217            | 0.6111            | 0.6944            | 0.2259            |
|                   | SCC        | 0.6842            | 0.7222            | 0.7027            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5815<br>±0.0464 | 0.5667<br>±0.0657 | 0.5729<br>±0.0512 | 0.6472<br>±0.0394 | 0.6810<br>±0.0360 | 0.2962<br>±0.0779 |
|                   | <b>SCC</b> | 0.7166<br>±0.0336 | 0.7278<br>±0.0410 | 0.7216<br>±0.0311 |                   |                   |                   |

Table S46: Logistic regression on H-optimus-0 embeddings: Patient-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.6250            | 0.6250            | 0.6250            | 0.6761            | 0.7500            | 0.3523            |
|                   | SCC        | 0.7273            | 0.7273            | 0.7273            |                   |                   |                   |
| Fold 2            | AC         | 0.7500            | 0.7500            | 0.7500            | 0.7841            | 0.7955            | 0.5682            |
|                   | SCC        | 0.8182            | 0.8182            | 0.8182            |                   |                   |                   |
| Fold 3            | AC         | 0.7143            | 0.6250            | 0.6667            | 0.7216            | 0.7273            | 0.4536            |
|                   | SCC        | 0.7500            | 0.8182            | 0.7826            |                   |                   |                   |
| Fold 4            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.6818            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 5            | AC         | 0.6667            | 0.7500            | 0.7059            | 0.7386            | 0.7614            | 0.4719            |
|                   | SCC        | 0.8000            | 0.7273            | 0.7619            |                   |                   |                   |
| Fold 6            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.6932            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 7            | AC         | 0.7500            | 0.7500            | 0.7500            | 0.7841            | 0.7614            | 0.5682            |
|                   | SCC        | 0.8182            | 0.8182            | 0.8182            |                   |                   |                   |
| Fold 8            | AC         | 0.6250            | 0.6250            | 0.6250            | 0.6761            | 0.7045            | 0.3523            |
|                   | SCC        | 0.7273            | 0.7273            | 0.7273            |                   |                   |                   |
| Fold 9            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.7500            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 10           | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.7159            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.6401<br>±0.0761 | 0.6250<br>±0.1021 | 0.6311<br>±0.0855 | 0.6852<br>±0.0685 | 0.7341<br>±0.0356 | 0.3723<br>±0.1356 |
|                   | <b>SCC</b> | 0.7341<br>±0.0611 | 0.7455<br>±0.0575 | 0.7389<br>±0.0539 |                   |                   |                   |

Table S47: Logistic regression on H-optimus-1 embeddings: Patch-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5665            | 0.4509            | 0.5021            | 0.6099            | 0.6889            | 0.2311            |
|                   | SCC        | 0.6766            | 0.7690            | 0.7198            |                   |                   |                   |
| Fold 2            | AC         | 0.5733            | 0.4433            | 0.5000            | 0.6112            | 0.6848            | 0.2357            |
|                   | SCC        | 0.6764            | 0.7791            | 0.7241            |                   |                   |                   |
| Fold 3            | AC         | 0.5220            | 0.4181            | 0.4643            | 0.5809            | 0.6334            | 0.1698            |
|                   | SCC        | 0.6562            | 0.7437            | 0.6972            |                   |                   |                   |
| Fold 4            | AC         | 0.5402            | 0.3552            | 0.4286            | 0.5764            | 0.6393            | 0.1700            |
|                   | SCC        | 0.6488            | 0.7976            | 0.7156            |                   |                   |                   |
| Fold 5            | AC         | 0.5259            | 0.5113            | 0.5185            | 0.6014            | 0.6548            | 0.2037            |
|                   | SCC        | 0.6788            | 0.6914            | 0.6850            |                   |                   |                   |
| Fold 6            | AC         | 0.5813            | 0.4685            | 0.5188            | 0.6213            | 0.6753            | 0.2542            |
|                   | SCC        | 0.6851            | 0.7740            | 0.7268            |                   |                   |                   |
| Fold 7            | AC         | 0.5417            | 0.4912            | 0.5152            | 0.6065            | 0.6763            | 0.2169            |
|                   | SCC        | 0.6794            | 0.7218            | 0.6999            |                   |                   |                   |
| Fold 8            | AC         | 0.5428            | 0.4635            | 0.5000            | 0.6010            | 0.6622            | 0.2087            |
|                   | SCC        | 0.6728            | 0.7386            | 0.7042            |                   |                   |                   |
| Fold 9            | AC         | 0.5889            | 0.5592            | 0.5736            | 0.6489            | 0.6965            | 0.3006            |
|                   | SCC        | 0.7145            | 0.7386            | 0.7264            |                   |                   |                   |
| Fold 10           | AC         | 0.5077            | 0.4156            | 0.4571            | 0.5729            | 0.6371            | 0.1522            |
|                   | SCC        | 0.6511            | 0.7302            | 0.6884            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5490<br>±0.0272 | 0.4577<br>±0.0563 | 0.4978<br>±0.0402 | 0.6030<br>±0.0228 | 0.6649<br>±0.0229 | 0.2143<br>±0.0444 |
|                   | <b>SCC</b> | 0.6740<br>±0.0192 | 0.7484<br>±0.0315 | 0.7088<br>±0.0158 |                   |                   |                   |

Table S48: Logistic regression on H-optimus-1 embeddings: Slide-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5556            | 0.4167            | 0.4762            | 0.5972            | 0.6852            | 0.2079            |
|                   | SCC        | 0.6667            | 0.7778            | 0.7179            |                   |                   |                   |
| Fold 2            | AC         | 0.5000            | 0.4167            | 0.4545            | 0.5694            | 0.6991            | 0.1443            |
|                   | SCC        | 0.6500            | 0.7222            | 0.6842            |                   |                   |                   |
| Fold 3            | AC         | 0.4444            | 0.3333            | 0.3810            | 0.5278            | 0.6481            | 0.0594            |
|                   | SCC        | 0.6190            | 0.7222            | 0.6667            |                   |                   |                   |
| Fold 4            | AC         | 0.4000            | 0.3333            | 0.3636            | 0.5000            | 0.5972            | 0.0000            |
|                   | SCC        | 0.6000            | 0.6667            | 0.6316            |                   |                   |                   |
| Fold 5            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5833            | 0.6898            | 0.1667            |
|                   | SCC        | 0.6667            | 0.6667            | 0.6667            |                   |                   |                   |
| Fold 6            | AC         | 0.6364            | 0.5833            | 0.6087            | 0.6806            | 0.6713            | 0.3671            |
|                   | SCC        | 0.7368            | 0.7778            | 0.7568            |                   |                   |                   |
| Fold 7            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.7037            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 8            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.6759            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 9            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5833            | 0.7037            | 0.1667            |
|                   | SCC        | 0.6667            | 0.6667            | 0.6667            |                   |                   |                   |
| Fold 10           | AC         | 0.4444            | 0.3333            | 0.3810            | 0.5278            | 0.6713            | 0.0594            |
|                   | SCC        | 0.6190            | 0.7222            | 0.6667            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5058<br>±0.0671 | 0.4583<br>±0.1058 | 0.4785<br>±0.0843 | 0.5819<br>±0.0542 | 0.6745<br>±0.0322 | 0.1666<br>±0.1086 |
|                   | <b>SCC</b> | 0.6637<br>±0.0437 | 0.7056<br>±0.0457 | 0.6829<br>±0.0340 |                   |                   |                   |

Table S49: Logistic regression on H-optimus-1 embeddings: Patient-level performance metrics AC vs. SCC.

| Fold           | Class | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------|-------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1         | AC    | 0.6667                 | 0.5000                 | 0.5714                 | 0.6591                 | 0.7500                 | 0.3380                 |
|                | SCC   | 0.6923                 | 0.8182                 | 0.7500                 |                        |                        |                        |
| Fold 2         | AC    | 0.6667                 | 0.5000                 | 0.5714                 | 0.6591                 | 0.8068                 | 0.3380                 |
|                | SCC   | 0.6923                 | 0.8182                 | 0.7500                 |                        |                        |                        |
| Fold 3         | AC    | 0.6667                 | 0.5000                 | 0.5714                 | 0.6591                 | 0.7273                 | 0.3380                 |
|                | SCC   | 0.6923                 | 0.8182                 | 0.7500                 |                        |                        |                        |
| Fold 4         | AC    | 0.5000                 | 0.3750                 | 0.4286                 | 0.5511                 | 0.6818                 | 0.1086                 |
|                | SCC   | 0.6154                 | 0.7273                 | 0.6667                 |                        |                        |                        |
| Fold 5         | AC    | 0.5714                 | 0.5000                 | 0.5333                 | 0.6136                 | 0.7500                 | 0.2326                 |
|                | SCC   | 0.6667                 | 0.7273                 | 0.6957                 |                        |                        |                        |
| Fold 6         | AC    | 0.7143                 | 0.6250                 | 0.6667                 | 0.7216                 | 0.7500                 | 0.4536                 |
|                | SCC   | 0.7500                 | 0.8182                 | 0.7826                 |                        |                        |                        |
| Fold 7         | AC    | 0.7500                 | 0.7500                 | 0.7500                 | 0.7841                 | 0.8068                 | 0.5682                 |
|                | SCC   | 0.8182                 | 0.8182                 | 0.8182                 |                        |                        |                        |
| Fold 8         | AC    | 0.7143                 | 0.6250                 | 0.6667                 | 0.7216                 | 0.7386                 | 0.4536                 |
|                | SCC   | 0.7500                 | 0.8182                 | 0.7826                 |                        |                        |                        |
| Fold 9         | AC    | 0.6667                 | 0.5000                 | 0.5714                 | 0.6591                 | 0.7273                 | 0.3380                 |
|                | SCC   | 0.6923                 | 0.8182                 | 0.7500                 |                        |                        |                        |
| Fold 10        | AC    | 0.6000                 | 0.3750                 | 0.4615                 | 0.5966                 | 0.7386                 | 0.2166                 |
|                | SCC   | 0.6429                 | 0.8182                 | 0.7200                 |                        |                        |                        |
| Mean $\pm$ std | AC    | 0.6517<br>$\pm 0.0749$ | 0.5250<br>$\pm 0.1149$ | 0.5792<br>$\pm 0.0962$ | 0.6625<br>$\pm 0.0675$ | 0.7477<br>$\pm 0.0370$ | 0.3385<br>$\pm 0.1326$ |
|                | SCC   | 0.7012<br>$\pm 0.0584$ | 0.8000<br>$\pm 0.0383$ | 0.7466<br>$\pm 0.0440$ |                        |                        |                        |

Table S50: Logistic regression on hibou-L embeddings: Patch-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5050            | 0.3804            | 0.4339            | 0.5654            | 0.6219            | 0.1396            |
|                   | SCC        | 0.6440            | 0.7504            | 0.6931            |                   |                   |                   |
| Fold 2            | AC         | 0.5240            | 0.4131            | 0.4620            | 0.5809            | 0.6427            | 0.1706            |
|                   | SCC        | 0.6558            | 0.7487            | 0.6992            |                   |                   |                   |
| Fold 3            | AC         | 0.4373            | 0.3249            | 0.3728            | 0.5225            | 0.5638            | 0.0482            |
|                   | SCC        | 0.6144            | 0.7201            | 0.6630            |                   |                   |                   |
| Fold 4            | AC         | 0.4645            | 0.3300            | 0.3859            | 0.5377            | 0.5801            | 0.0818            |
|                   | SCC        | 0.6243            | 0.7454            | 0.6795            |                   |                   |                   |
| Fold 5            | AC         | 0.4767            | 0.4383            | 0.4567            | 0.5581            | 0.6127            | 0.1180            |
|                   | SCC        | 0.6432            | 0.6779            | 0.6601            |                   |                   |                   |
| Fold 6            | AC         | 0.5115            | 0.3929            | 0.4444            | 0.5708            | 0.5996            | 0.1504            |
|                   | SCC        | 0.6482            | 0.7487            | 0.6948            |                   |                   |                   |
| Fold 7            | AC         | 0.5015            | 0.4282            | 0.4620            | 0.5716            | 0.6054            | 0.1479            |
|                   | SCC        | 0.6513            | 0.7150            | 0.6817            |                   |                   |                   |
| Fold 8            | AC         | 0.4769            | 0.4156            | 0.4441            | 0.5552            | 0.6000            | 0.1135            |
|                   | SCC        | 0.6398            | 0.6948            | 0.6661            |                   |                   |                   |
| Fold 9            | AC         | 0.5054            | 0.4736            | 0.4889            | 0.5816            | 0.6316            | 0.1652            |
|                   | SCC        | 0.6618            | 0.6897            | 0.6755            |                   |                   |                   |
| Fold 10           | AC         | 0.4343            | 0.3577            | 0.3923            | 0.5229            | 0.5704            | 0.0476            |
|                   | SCC        | 0.6154            | 0.6880            | 0.6497            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4837<br>±0.0311 | 0.3955<br>±0.0479 | 0.4343<br>±0.0382 | 0.5567<br>±0.0221 | 0.6028<br>±0.0258 | 0.1183<br>±0.0454 |
|                   | <b>SCC</b> | 0.6398<br>±0.0165 | 0.7179<br>±0.0290 | 0.6763<br>±0.0165 |                   |                   |                   |

Table S51: Logistic regression on hibou-L embeddings: Slide-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.6667            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 2            | AC         | 0.6667            | 0.5000            | 0.5714            | 0.6667            | 0.7361            | 0.3563            |
|                   | SCC        | 0.7143            | 0.8333            | 0.7692            |                   |                   |                   |
| Fold 3            | AC         | 0.5000            | 0.4167            | 0.4545            | 0.5694            | 0.6111            | 0.1443            |
|                   | SCC        | 0.6500            | 0.7222            | 0.6842            |                   |                   |                   |
| Fold 4            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5833            | 0.6343            | 0.1667            |
|                   | SCC        | 0.6667            | 0.6667            | 0.6667            |                   |                   |                   |
| Fold 5            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5833            | 0.6574            | 0.1667            |
|                   | SCC        | 0.6667            | 0.6667            | 0.6667            |                   |                   |                   |
| Fold 6            | AC         | 0.5000            | 0.5833            | 0.5385            | 0.5972            | 0.5972            | 0.1909            |
|                   | SCC        | 0.6875            | 0.6111            | 0.6471            |                   |                   |                   |
| Fold 7            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.6435            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 8            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.6898            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 9            | AC         | 0.5455            | 0.5000            | 0.5217            | 0.6111            | 0.7037            | 0.2259            |
|                   | SCC        | 0.6842            | 0.7222            | 0.7027            |                   |                   |                   |
| Fold 10           | AC         | 0.4167            | 0.4167            | 0.4167            | 0.5139            | 0.6250            | 0.0278            |
|                   | SCC        | 0.6111            | 0.6111            | 0.6111            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5244<br>±0.0626 | 0.5167<br>±0.0657 | 0.5183<br>±0.0511 | 0.6000<br>±0.0413 | 0.6565<br>±0.0435 | 0.2020<br>±0.0862 |
|                   | <b>SCC</b> | 0.6798<br>±0.0321 | 0.6833<br>±0.0644 | 0.6805<br>±0.0405 |                   |                   |                   |

Table S52: Logistic regression on hibou-L embeddings: Patient-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.6250            | 0.6250            | 0.6250            | 0.6761            | 0.7386            | 0.3523            |
|                   | SCC        | 0.7273            | 0.7273            | 0.7273            |                   |                   |                   |
| Fold 2            | AC         | 0.6667            | 0.5000            | 0.5714            | 0.6591            | 0.7955            | 0.3380            |
|                   | SCC        | 0.6923            | 0.8182            | 0.7500            |                   |                   |                   |
| Fold 3            | AC         | 0.4286            | 0.3750            | 0.4000            | 0.5057            | 0.6591            | 0.0116            |
|                   | SCC        | 0.5833            | 0.6364            | 0.6087            |                   |                   |                   |
| Fold 4            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.6932            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 5            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.7159            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 6            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.6818            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 7            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.7159            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 8            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.6932            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 9            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.7386            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| Fold 10           | AC         | 0.4286            | 0.3750            | 0.4000            | 0.5057            | 0.6477            | 0.0116            |
|                   | SCC        | 0.5833            | 0.6364            | 0.6087            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5458<br>±0.0761 | 0.5250<br>±0.0986 | 0.5328<br>±0.0786 | 0.6034<br>±0.0589 | 0.7080<br>±0.0432 | 0.2090<br>±0.1196 |
|                   | <b>SCC</b> | 0.6656<br>±0.0500 | 0.6818<br>±0.0643 | 0.6722<br>±0.0467 |                   |                   |                   |

Table S53: Logistic regression on Kaiko embeddings: Patch-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.4824            | 0.3451            | 0.4023            | 0.5486            | 0.5736            | 0.1053            |
|                   | SCC        | 0.6317            | 0.7521            | 0.6867            |                   |                   |                   |
| Fold 2            | AC         | 0.4645            | 0.3627            | 0.4074            | 0.5414            | 0.5663            | 0.0875            |
|                   | SCC        | 0.6279            | 0.7201            | 0.6709            |                   |                   |                   |
| Fold 3            | AC         | 0.3986            | 0.2872            | 0.3338            | 0.4986            | 0.5090            | -0.0031           |
|                   | SCC        | 0.5980            | 0.7099            | 0.6492            |                   |                   |                   |
| Fold 4            | AC         | 0.4348            | 0.3023            | 0.3566            | 0.5196            | 0.5343            | 0.0428            |
|                   | SCC        | 0.6120            | 0.7369            | 0.6687            |                   |                   |                   |
| Fold 5            | AC         | 0.4348            | 0.4282            | 0.4315            | 0.5278            | 0.5404            | 0.0557            |
|                   | SCC        | 0.6210            | 0.6273            | 0.6242            |                   |                   |                   |
| Fold 6            | AC         | 0.4752            | 0.3627            | 0.4114            | 0.5473            | 0.5464            | 0.1006            |
|                   | SCC        | 0.6317            | 0.7319            | 0.6781            |                   |                   |                   |
| Fold 7            | AC         | 0.4938            | 0.3980            | 0.4407            | 0.5624            | 0.5805            | 0.1308            |
|                   | SCC        | 0.6433            | 0.7268            | 0.6825            |                   |                   |                   |
| Fold 8            | AC         | 0.4286            | 0.3854            | 0.4058            | 0.5207            | 0.5460            | 0.0422            |
|                   | SCC        | 0.6145            | 0.6560            | 0.6346            |                   |                   |                   |
| Fold 9            | AC         | 0.4798            | 0.4181            | 0.4468            | 0.5573            | 0.5943            | 0.1178            |
|                   | SCC        | 0.6413            | 0.6965            | 0.6677            |                   |                   |                   |
| Fold 10           | AC         | 0.4064            | 0.3501            | 0.3762            | 0.5039            | 0.5225            | 0.0080            |
|                   | SCC        | 0.6019            | 0.6577            | 0.6285            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4499<br>±0.0336 | 0.3640<br>±0.0459 | 0.4013<br>±0.0363 | 0.5327<br>±0.0220 | 0.5513<br>±0.0269 | 0.0688<br>±0.0464 |
|                   | <b>SCC</b> | 0.6223<br>±0.0156 | 0.7015<br>±0.0413 | 0.6591<br>±0.0232 |                   |                   |                   |

Table S54: Logistic regression on Kaiko embeddings: Slide-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.4545            | 0.4167            | 0.4348            | 0.5417            | 0.5972            | 0.0847            |
|                   | SCC        | 0.6316            | 0.6667            | 0.6486            |                   |                   |                   |
| Fold 2            | AC         | 0.4545            | 0.4167            | 0.4348            | 0.5417            | 0.6343            | 0.0847            |
|                   | SCC        | 0.6316            | 0.6667            | 0.6486            |                   |                   |                   |
| Fold 3            | AC         | 0.4000            | 0.3333            | 0.3636            | 0.5000            | 0.5417            | 0.0000            |
|                   | SCC        | 0.6000            | 0.6667            | 0.6316            |                   |                   |                   |
| Fold 4            | AC         | 0.4000            | 0.3333            | 0.3636            | 0.5000            | 0.5278            | 0.0000            |
|                   | SCC        | 0.6000            | 0.6667            | 0.6316            |                   |                   |                   |
| Fold 5            | AC         | 0.5714            | 0.6667            | 0.6154            | 0.6667            | 0.6343            | 0.3273            |
|                   | SCC        | 0.7500            | 0.6667            | 0.7059            |                   |                   |                   |
| Fold 6            | AC         | 0.5000            | 0.4167            | 0.4545            | 0.5694            | 0.5741            | 0.1443            |
|                   | SCC        | 0.6500            | 0.7222            | 0.6842            |                   |                   |                   |
| Fold 7            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.6019            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 8            | AC         | 0.4615            | 0.5000            | 0.4800            | 0.5556            | 0.6019            | 0.1098            |
|                   | SCC        | 0.6471            | 0.6111            | 0.6286            |                   |                   |                   |
| Fold 9            | AC         | 0.4444            | 0.3333            | 0.3810            | 0.5278            | 0.6574            | 0.0594            |
|                   | SCC        | 0.6190            | 0.7222            | 0.6667            |                   |                   |                   |
| Fold 10           | AC         | 0.4615            | 0.5000            | 0.4800            | 0.5556            | 0.5972            | 0.1098            |
|                   | SCC        | 0.6471            | 0.6111            | 0.6286            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4687<br>±0.0547 | 0.4500<br>±0.1125 | 0.4568<br>±0.0823 | 0.5583<br>±0.0523 | 0.5968<br>±0.0406 | 0.1167<br>±0.1026 |
|                   | <b>SCC</b> | 0.6482<br>±0.0468 | 0.6667<br>±0.0370 | 0.6560<br>±0.0281 |                   |                   |                   |

Table S55: Logistic regression on Kaiko embeddings: Patient-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.4286            | 0.3750            | 0.4000            | 0.5057            | 0.6364            | 0.0116            |
|                   | SCC        | 0.5833            | 0.6364            | 0.6087            |                   |                   |                   |
| Fold 2            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.6705            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 3            | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.6364            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| Fold 4            | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.5795            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| Fold 5            | AC         | 0.6000            | 0.7500            | 0.6667            | 0.6932            | 0.6818            | 0.3820            |
|                   | SCC        | 0.7778            | 0.6364            | 0.7000            |                   |                   |                   |
| Fold 6            | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.6591            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| Fold 7            | AC         | 0.6667            | 0.7500            | 0.7059            | 0.7386            | 0.6932            | 0.4719            |
|                   | SCC        | 0.8000            | 0.7273            | 0.7619            |                   |                   |                   |
| Fold 8            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.6250            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| Fold 9            | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.7045            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| Fold 10           | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.6250            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5267<br>±0.0674 | 0.4875<br>±0.1497 | 0.5020<br>±0.1063 | 0.5892<br>±0.0726 | 0.6511<br>±0.0379 | 0.1805<br>±0.1419 |
|                   | <b>SCC</b> | 0.6562<br>±0.0733 | 0.6909<br>±0.0469 | 0.6706<br>±0.0423 |                   |                   |                   |

Table S56: Logistic regression on Phikon embeddings: Patch-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5109            | 0.3552            | 0.4190            | 0.5638            | 0.6253            | 0.1394            |
|                   | SCC        | 0.6415            | 0.7723            | 0.7008            |                   |                   |                   |
| Fold 2            | AC         | 0.5123            | 0.3678            | 0.4282            | 0.5667            | 0.6183            | 0.1444            |
|                   | SCC        | 0.6440            | 0.7656            | 0.6995            |                   |                   |                   |
| Fold 3            | AC         | 0.4704            | 0.3401            | 0.3947            | 0.5419            | 0.5649            | 0.0904            |
|                   | SCC        | 0.6273            | 0.7437            | 0.6806            |                   |                   |                   |
| Fold 4            | AC         | 0.4905            | 0.3249            | 0.3909            | 0.5495            | 0.5786            | 0.1098            |
|                   | SCC        | 0.6314            | 0.7740            | 0.6955            |                   |                   |                   |
| Fold 5            | AC         | 0.4727            | 0.3929            | 0.4292            | 0.5498            | 0.5908            | 0.1035            |
|                   | SCC        | 0.6348            | 0.7066            | 0.6688            |                   |                   |                   |
| Fold 6            | AC         | 0.5051            | 0.3753            | 0.4306            | 0.5646            | 0.5769            | 0.1383            |
|                   | SCC        | 0.6432            | 0.7538            | 0.6941            |                   |                   |                   |
| Fold 7            | AC         | 0.5032            | 0.3929            | 0.4413            | 0.5666            | 0.6029            | 0.1408            |
|                   | SCC        | 0.6456            | 0.7403            | 0.6897            |                   |                   |                   |
| Fold 8            | AC         | 0.4841            | 0.3829            | 0.4276            | 0.5548            | 0.5890            | 0.1155            |
|                   | SCC        | 0.6376            | 0.7268            | 0.6793            |                   |                   |                   |
| Fold 9            | AC         | 0.5277            | 0.4559            | 0.4892            | 0.5914            | 0.6310            | 0.1882            |
|                   | SCC        | 0.6662            | 0.7268            | 0.6952            |                   |                   |                   |
| Fold 10           | AC         | 0.4220            | 0.2997            | 0.3505            | 0.5124            | 0.5234            | 0.0270            |
|                   | SCC        | 0.6073            | 0.7251            | 0.6610            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4899<br>±0.0300 | 0.3688<br>±0.0431 | 0.4201<br>±0.0363 | 0.5561<br>±0.0205 | 0.5901<br>±0.0321 | 0.1197<br>±0.0426 |
|                   | <b>SCC</b> | 0.6379<br>±0.0150 | 0.7435<br>±0.0227 | 0.6864<br>±0.0135 |                   |                   |                   |

Table S57: Logistic regression on Phikon embeddings: Slide-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5833            | 0.5833            | 0.5833            | 0.6528            | 0.6111            | 0.3056            |
|                   | SCC        | 0.7222            | 0.7222            | 0.7222            |                   |                   |                   |
| Fold 2            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.6435            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 3            | AC         | 0.4167            | 0.4167            | 0.4167            | 0.5139            | 0.6065            | 0.0278            |
|                   | SCC        | 0.6111            | 0.6111            | 0.6111            |                   |                   |                   |
| Fold 4            | AC         | 0.4545            | 0.4167            | 0.4348            | 0.5417            | 0.5417            | 0.0847            |
|                   | SCC        | 0.6316            | 0.6667            | 0.6486            |                   |                   |                   |
| Fold 5            | AC         | 0.5714            | 0.6667            | 0.6154            | 0.6667            | 0.6157            | 0.3273            |
|                   | SCC        | 0.7500            | 0.6667            | 0.7059            |                   |                   |                   |
| Fold 6            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5833            | 0.5926            | 0.1667            |
|                   | SCC        | 0.6667            | 0.6667            | 0.6667            |                   |                   |                   |
| Fold 7            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5833            | 0.6065            | 0.1667            |
|                   | SCC        | 0.6667            | 0.6667            | 0.6667            |                   |                   |                   |
| Fold 8            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.5926            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 9            | AC         | 0.5455            | 0.5000            | 0.5217            | 0.6111            | 0.6481            | 0.2259            |
|                   | SCC        | 0.6842            | 0.7222            | 0.7027            |                   |                   |                   |
| Fold 10           | AC         | 0.4615            | 0.5000            | 0.4800            | 0.5556            | 0.5185            | 0.1098            |
|                   | SCC        | 0.6471            | 0.6111            | 0.6286            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5110<br>±0.0541 | 0.5250<br>±0.0791 | 0.5172<br>±0.0637 | 0.5958<br>±0.0492 | 0.5977<br>±0.0405 | 0.1909<br>±0.0971 |
|                   | <b>SCC</b> | 0.6791<br>±0.0429 | 0.6667<br>±0.0370 | 0.6724<br>±0.0353 |                   |                   |                   |

Table S58: Logistic regression on Phikon embeddings: Patient-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.6250            | 0.6250            | 0.6250            | 0.6761            | 0.6705            | 0.3523            |
|                   | SCC        | 0.7273            | 0.7273            | 0.7273            |                   |                   |                   |
| Fold 2            | AC         | 0.6250            | 0.6250            | 0.6250            | 0.6761            | 0.7045            | 0.3523            |
|                   | SCC        | 0.7273            | 0.7273            | 0.7273            |                   |                   |                   |
| Fold 3            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.6705            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 4            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.6023            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 5            | AC         | 0.6667            | 0.7500            | 0.7059            | 0.7386            | 0.6932            | 0.4719            |
|                   | SCC        | 0.8000            | 0.7273            | 0.7619            |                   |                   |                   |
| Fold 6            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.6591            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| Fold 7            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.7159            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 8            | AC         | 0.6250            | 0.6250            | 0.6250            | 0.6761            | 0.6705            | 0.3523            |
|                   | SCC        | 0.7273            | 0.7273            | 0.7273            |                   |                   |                   |
| Fold 9            | AC         | 0.6250            | 0.6250            | 0.6250            | 0.6761            | 0.6818            | 0.3523            |
|                   | SCC        | 0.7273            | 0.7273            | 0.7273            |                   |                   |                   |
| Fold 10           | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.6136            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5865<br>±0.0565 | 0.5875<br>±0.0844 | 0.5861<br>±0.0673 | 0.6438<br>±0.0544 | 0.6682<br>±0.0363 | 0.2877<br>±0.1072 |
|                   | <b>SCC</b> | 0.7015<br>±0.0509 | 0.7000<br>±0.0439 | 0.7002<br>±0.0422 |                   |                   |                   |

Table S59: Logistic regression on ProvGigaPath embeddings: Patch-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.4922            | 0.3980            | 0.4401            | 0.5616            | 0.6466            | 0.1289            |
|                   | SCC        | 0.6428            | 0.7251            | 0.6815            |                   |                   |                   |
| Fold 2            | AC         | 0.5116            | 0.3879            | 0.4413            | 0.5700            | 0.6174            | 0.1492            |
|                   | SCC        | 0.6473            | 0.7521            | 0.6958            |                   |                   |                   |
| Fold 3            | AC         | 0.4491            | 0.3224            | 0.3754            | 0.5288            | 0.5670            | 0.0624            |
|                   | SCC        | 0.6184            | 0.7352            | 0.6718            |                   |                   |                   |
| Fold 4            | AC         | 0.4724            | 0.3451            | 0.3988            | 0.5435            | 0.5926            | 0.0938            |
|                   | SCC        | 0.6286            | 0.7420            | 0.6806            |                   |                   |                   |
| Fold 5            | AC         | 0.4558            | 0.4030            | 0.4278            | 0.5405            | 0.5796            | 0.0829            |
|                   | SCC        | 0.6291            | 0.6779            | 0.6526            |                   |                   |                   |
| Fold 6            | AC         | 0.5000            | 0.4106            | 0.4509            | 0.5679            | 0.5879            | 0.1415            |
|                   | SCC        | 0.6476            | 0.7251            | 0.6842            |                   |                   |                   |
| Fold 7            | AC         | 0.5215            | 0.4584            | 0.4879            | 0.5884            | 0.6060            | 0.1814            |
|                   | SCC        | 0.6646            | 0.7184            | 0.6904            |                   |                   |                   |
| Fold 8            | AC         | 0.4503            | 0.3879            | 0.4168            | 0.5354            | 0.5757            | 0.0731            |
|                   | SCC        | 0.6250            | 0.6830            | 0.6527            |                   |                   |                   |
| Fold 9            | AC         | 0.5180            | 0.5063            | 0.5121            | 0.5955            | 0.6332            | 0.1917            |
|                   | SCC        | 0.6744            | 0.6847            | 0.6795            |                   |                   |                   |
| Fold 10           | AC         | 0.4358            | 0.3249            | 0.3723            | 0.5217            | 0.5512            | 0.0464            |
|                   | SCC        | 0.6138            | 0.7184            | 0.6620            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4807<br>±0.0319 | 0.3945<br>±0.0572 | 0.4323<br>±0.0449 | 0.5553<br>±0.0252 | 0.5957<br>±0.0300 | 0.1151<br>±0.0506 |
|                   | <b>SCC</b> | 0.6392<br>±0.0198 | 0.7162<br>±0.0259 | 0.6751<br>±0.0150 |                   |                   |                   |

Table S60: Logistic regression on ProvGigaPath embeddings: Slide-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.6000            | 0.5000            | 0.5455            | 0.6389            | 0.7269            | 0.2887            |
|                   | SCC        | 0.7000            | 0.7778            | 0.7368            |                   |                   |                   |
| Fold 2            | AC         | 0.6000            | 0.5000            | 0.5455            | 0.6389            | 0.7037            | 0.2887            |
|                   | SCC        | 0.7000            | 0.7778            | 0.7368            |                   |                   |                   |
| Fold 3            | AC         | 0.5000            | 0.3333            | 0.4000            | 0.5556            | 0.6528            | 0.1231            |
|                   | SCC        | 0.6364            | 0.7778            | 0.7000            |                   |                   |                   |
| Fold 4            | AC         | 0.4545            | 0.4167            | 0.4348            | 0.5417            | 0.6574            | 0.0847            |
|                   | SCC        | 0.6316            | 0.6667            | 0.6486            |                   |                   |                   |
| Fold 5            | AC         | 0.5714            | 0.6667            | 0.6154            | 0.6667            | 0.7037            | 0.3273            |
|                   | SCC        | 0.7500            | 0.6667            | 0.7059            |                   |                   |                   |
| Fold 6            | AC         | 0.5833            | 0.5833            | 0.5833            | 0.6528            | 0.6481            | 0.3056            |
|                   | SCC        | 0.7222            | 0.7222            | 0.7222            |                   |                   |                   |
| Fold 7            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.6852            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 8            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.6713            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 9            | AC         | 0.5714            | 0.6667            | 0.6154            | 0.6667            | 0.7731            | 0.3273            |
|                   | SCC        | 0.7500            | 0.6667            | 0.7059            |                   |                   |                   |
| Fold 10           | AC         | 0.4545            | 0.4167            | 0.4348            | 0.5417            | 0.6389            | 0.0847            |
|                   | SCC        | 0.6316            | 0.6667            | 0.6486            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5412<br>±0.0550 | 0.5250<br>±0.1115 | 0.5295<br>±0.0780 | 0.6153<br>±0.0499 | 0.6861<br>±0.0417 | 0.2324<br>±0.0976 |
|                   | <b>SCC</b> | 0.6934<br>±0.0454 | 0.7056<br>±0.0527 | 0.6976<br>±0.0315 |                   |                   |                   |

Table S61: Logistic regression on ProvGigaPath embeddings: Patient-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.7500            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 2            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.7273            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 3            | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.6932            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| Fold 4            | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.6705            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| Fold 5            | AC         | 0.6000            | 0.7500            | 0.6667            | 0.6932            | 0.7273            | 0.3820            |
|                   | SCC        | 0.7778            | 0.6364            | 0.7000            |                   |                   |                   |
| Fold 6            | AC         | 0.6250            | 0.6250            | 0.6250            | 0.6761            | 0.6932            | 0.3523            |
|                   | SCC        | 0.7273            | 0.7273            | 0.7273            |                   |                   |                   |
| Fold 7            | AC         | 0.6250            | 0.6250            | 0.6250            | 0.6761            | 0.7273            | 0.3523            |
|                   | SCC        | 0.7273            | 0.7273            | 0.7273            |                   |                   |                   |
| Fold 8            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.6932            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 9            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.7727            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 10           | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.6818            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5604<br>±0.0485 | 0.5375<br>±0.1324 | 0.5446<br>±0.0896 | 0.6188<br>±0.0539 | 0.7136<br>±0.0325 | 0.2395<br>±0.1043 |
|                   | <b>SCC</b> | 0.6812<br>±0.0555 | 0.7000<br>±0.0439 | 0.6879<br>±0.0250 |                   |                   |                   |

Table S62: Logistic regression on ResNet50 embeddings: Patch-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.4375            | 0.4055            | 0.4209            | 0.5282            | 0.5513            | 0.0573            |
|                   | SCC        | 0.6206            | 0.6509            | 0.6354            |                   |                   |                   |
| Fold 2            | AC         | 0.4529            | 0.4484            | 0.4506            | 0.5429            | 0.5753            | 0.0859            |
|                   | SCC        | 0.6332            | 0.6374            | 0.6353            |                   |                   |                   |
| Fold 3            | AC         | 0.4015            | 0.4055            | 0.4035            | 0.5004            | 0.5263            | 0.0008            |
|                   | SCC        | 0.5993            | 0.5953            | 0.5973            |                   |                   |                   |
| Fold 4            | AC         | 0.4311            | 0.4332            | 0.4322            | 0.5252            | 0.5524            | 0.0504            |
|                   | SCC        | 0.6193            | 0.6172            | 0.6182            |                   |                   |                   |
| Fold 5            | AC         | 0.4282            | 0.4660            | 0.4463            | 0.5247            | 0.5509            | 0.0489            |
|                   | SCC        | 0.6201            | 0.5835            | 0.6012            |                   |                   |                   |
| Fold 6            | AC         | 0.4203            | 0.4181            | 0.4192            | 0.5160            | 0.5228            | 0.0320            |
|                   | SCC        | 0.6118            | 0.6138            | 0.6128            |                   |                   |                   |
| Fold 7            | AC         | 0.4400            | 0.4433            | 0.4417            | 0.5328            | 0.5459            | 0.0655            |
|                   | SCC        | 0.6254            | 0.6223            | 0.6238            |                   |                   |                   |
| Fold 8            | AC         | 0.4389            | 0.4887            | 0.4625            | 0.5352            | 0.5563            | 0.0695            |
|                   | SCC        | 0.6296            | 0.5818            | 0.6047            |                   |                   |                   |
| Fold 9            | AC         | 0.4463            | 0.4710            | 0.4583            | 0.5399            | 0.5649            | 0.0792            |
|                   | SCC        | 0.6322            | 0.6088            | 0.6203            |                   |                   |                   |
| Fold 10           | AC         | 0.4016            | 0.3904            | 0.3959            | 0.5004            | 0.5207            | 0.0009            |
|                   | SCC        | 0.5993            | 0.6105            | 0.6048            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4298<br>±0.0175 | 0.4370<br>±0.0322 | 0.4331<br>±0.0227 | 0.5246<br>±0.0149 | 0.5467<br>±0.0182 | 0.0490<br>±0.0297 |
|                   | <b>SCC</b> | 0.6191<br>±0.0123 | 0.6121<br>±0.0219 | 0.6154<br>±0.0136 |                   |                   |                   |

Table S63: Logistic regression on ResNet50 embeddings: Slide-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.3750            | 0.2500            | 0.3000            | 0.4861            | 0.4954            | -0.0308           |
|                   | SCC        | 0.5909            | 0.7222            | 0.6500            |                   |                   |                   |
| Fold 2            | AC         | 0.3636            | 0.3333            | 0.3478            | 0.4722            | 0.5139            | -0.0565           |
|                   | SCC        | 0.5789            | 0.6111            | 0.5946            |                   |                   |                   |
| Fold 3            | AC         | 0.2727            | 0.2500            | 0.2609            | 0.4028            | 0.4259            | -0.1977           |
|                   | SCC        | 0.5263            | 0.5556            | 0.5405            |                   |                   |                   |
| Fold 4            | AC         | 0.4167            | 0.4167            | 0.4167            | 0.5139            | 0.4861            | 0.0278            |
|                   | SCC        | 0.6111            | 0.6111            | 0.6111            |                   |                   |                   |
| Fold 5            | AC         | 0.4167            | 0.4167            | 0.4167            | 0.5139            | 0.5509            | 0.0278            |
|                   | SCC        | 0.6111            | 0.6111            | 0.6111            |                   |                   |                   |
| Fold 6            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5833            | 0.5185            | 0.1667            |
|                   | SCC        | 0.6667            | 0.6667            | 0.6667            |                   |                   |                   |
| Fold 7            | AC         | 0.4545            | 0.4167            | 0.4348            | 0.5417            | 0.5093            | 0.0847            |
|                   | SCC        | 0.6316            | 0.6667            | 0.6486            |                   |                   |                   |
| Fold 8            | AC         | 0.4545            | 0.4167            | 0.4348            | 0.5417            | 0.5926            | 0.0847            |
|                   | SCC        | 0.6316            | 0.6667            | 0.6486            |                   |                   |                   |
| Fold 9            | AC         | 0.4167            | 0.4167            | 0.4167            | 0.5139            | 0.5787            | 0.0278            |
|                   | SCC        | 0.6111            | 0.6111            | 0.6111            |                   |                   |                   |
| Fold 10           | AC         | 0.4000            | 0.3333            | 0.3636            | 0.5000            | 0.4861            | 0.0000            |
|                   | SCC        | 0.6000            | 0.6667            | 0.6316            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4070<br>±0.0619 | 0.3750<br>±0.0810 | 0.3892<br>±0.0711 | 0.5069<br>±0.0482 | 0.5157<br>±0.0488 | 0.0135<br>±0.0977 |
|                   | <b>SCC</b> | 0.6059<br>±0.0371 | 0.6389<br>±0.0472 | 0.6214<br>±0.0366 |                   |                   |                   |

Table S64: Logistic regression on ResNet50 embeddings: Patient-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.3333            | 0.2500            | 0.2857            | 0.4432            | 0.5455            | -0.1207           |
|                   | SCC        | 0.5385            | 0.6364            | 0.5833            |                   |                   |                   |
| Fold 2            | AC         | 0.5000            | 0.2500            | 0.3333            | 0.5341            | 0.5455            | 0.0826            |
|                   | SCC        | 0.6000            | 0.8182            | 0.6923            |                   |                   |                   |
| Fold 3            | AC         | 0.1667            | 0.1250            | 0.1429            | 0.3352            | 0.4091            | -0.3500           |
|                   | SCC        | 0.4615            | 0.5455            | 0.5000            |                   |                   |                   |
| Fold 4            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.5227            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| Fold 5            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.5682            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 6            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.5795            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| Fold 7            | AC         | 0.4286            | 0.3750            | 0.4000            | 0.5057            | 0.5909            | 0.0116            |
|                   | SCC        | 0.5833            | 0.6364            | 0.6087            |                   |                   |                   |
| Fold 8            | AC         | 0.4444            | 0.5000            | 0.4706            | 0.5227            | 0.5682            | 0.0449            |
|                   | SCC        | 0.6000            | 0.5455            | 0.5714            |                   |                   |                   |
| Fold 9            | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.6136            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| Fold 10           | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.5114            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4444<br>±0.1161 | 0.3750<br>±0.1318 | 0.4023<br>±0.1192 | 0.5193<br>±0.0787 | 0.5455<br>±0.0569 | 0.0391<br>±0.1652 |
|                   | <b>SCC</b> | 0.5953<br>±0.0583 | 0.6636<br>±0.0862 | 0.6257<br>±0.0612 |                   |                   |                   |

Table S65: Logistic regression on TissueConcepts embeddings: Patch-level performance metrics AC vs. SCC.

| Fold                             | Class      | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------------------------|------------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1                           | AC         | 0.4510                 | 0.3829                 | 0.4142                 | 0.5354                 | 0.5627                 | 0.0733                 |
|                                  | SCC        | 0.6248                 | 0.6880                 | 0.6549                 |                        |                        |                        |
| Fold 2                           | AC         | 0.4511                 | 0.4181                 | 0.4340                 | 0.5387                 | 0.5815                 | 0.0786                 |
|                                  | SCC        | 0.6286                 | 0.6594                 | 0.6436                 |                        |                        |                        |
| Fold 3                           | AC         | 0.4426                 | 0.3980                 | 0.4191                 | 0.5312                 | 0.5510                 | 0.0637                 |
|                                  | SCC        | 0.6224                 | 0.6644                 | 0.6427                 |                        |                        |                        |
| Fold 4                           | AC         | 0.4398                 | 0.3678                 | 0.4005                 | 0.5270                 | 0.5317                 | 0.0562                 |
|                                  | SCC        | 0.6185                 | 0.6863                 | 0.6507                 |                        |                        |                        |
| Fold 5                           | AC         | 0.4427                 | 0.4383                 | 0.4405                 | 0.5345                 | 0.5387                 | 0.0691                 |
|                                  | SCC        | 0.6265                 | 0.6307                 | 0.6286                 |                        |                        |                        |
| Fold 6                           | AC         | 0.4231                 | 0.3879                 | 0.4047                 | 0.5169                 | 0.5148                 | 0.0343                 |
|                                  | SCC        | 0.6118                 | 0.6459                 | 0.6284                 |                        |                        |                        |
| Fold 7                           | AC         | 0.4571                 | 0.4433                 | 0.4501                 | 0.5454                 | 0.5478                 | 0.0914                 |
|                                  | SCC        | 0.6347                 | 0.6476                 | 0.6411                 |                        |                        |                        |
| Fold 8                           | AC         | 0.4486                 | 0.4509                 | 0.4497                 | 0.5399                 | 0.5643                 | 0.0798                 |
|                                  | SCC        | 0.6311                 | 0.6290                 | 0.6301                 |                        |                        |                        |
| Fold 9                           | AC         | 0.4552                 | 0.4484                 | 0.4518                 | 0.5446                 | 0.5708                 | 0.0894                 |
|                                  | SCC        | 0.6344                 | 0.6408                 | 0.6376                 |                        |                        |                        |
| Fold 10                          | AC         | 0.4251                 | 0.4005                 | 0.4125                 | 0.5190                 | 0.5304                 | 0.0384                 |
|                                  | SCC        | 0.6136                 | 0.6374                 | 0.6253                 |                        |                        |                        |
| <b>Mean <math>\pm</math> std</b> | <b>AC</b>  | 0.4436<br>$\pm 0.0117$ | 0.4136<br>$\pm 0.0302$ | 0.4277<br>$\pm 0.0198$ | 0.5333<br>$\pm 0.0098$ | 0.5494<br>$\pm 0.0208$ | 0.0674<br>$\pm 0.0196$ |
|                                  | <b>SCC</b> | 0.6247<br>$\pm 0.0081$ | 0.6530<br>$\pm 0.0212$ | 0.6383<br>$\pm 0.0101$ |                        |                        |                        |

Table S66: Logistic regression on TissueConcepts embeddings: Slide-level performance metrics AC vs. SCC.

| Fold           | Class | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------|-------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1         | AC    | 0.5000                 | 0.5833                 | 0.5385                 | 0.5972                 | 0.5463                 | 0.1909                 |
|                | SCC   | 0.6875                 | 0.6111                 | 0.6471                 |                        |                        |                        |
| Fold 2         | AC    | 0.4667                 | 0.5833                 | 0.5185                 | 0.5694                 | 0.5370                 | 0.1361                 |
|                | SCC   | 0.6667                 | 0.5556                 | 0.6061                 |                        |                        |                        |
| Fold 3         | AC    | 0.4375                 | 0.5833                 | 0.5000                 | 0.5417                 | 0.5000                 | 0.0818                 |
|                | SCC   | 0.6429                 | 0.5000                 | 0.5625                 |                        |                        |                        |
| Fold 4         | AC    | 0.4375                 | 0.5833                 | 0.5000                 | 0.5417                 | 0.4583                 | 0.0818                 |
|                | SCC   | 0.6429                 | 0.5000                 | 0.5625                 |                        |                        |                        |
| Fold 5         | AC    | 0.4375                 | 0.5833                 | 0.5000                 | 0.5417                 | 0.5324                 | 0.0818                 |
|                | SCC   | 0.6429                 | 0.5000                 | 0.5625                 |                        |                        |                        |
| Fold 6         | AC    | 0.5000                 | 0.5833                 | 0.5385                 | 0.5972                 | 0.5000                 | 0.1909                 |
|                | SCC   | 0.6875                 | 0.6111                 | 0.6471                 |                        |                        |                        |
| Fold 7         | AC    | 0.5000                 | 0.5833                 | 0.5385                 | 0.5972                 | 0.5556                 | 0.1909                 |
|                | SCC   | 0.6875                 | 0.6111                 | 0.6471                 |                        |                        |                        |
| Fold 8         | AC    | 0.4667                 | 0.5833                 | 0.5185                 | 0.5694                 | 0.5417                 | 0.1361                 |
|                | SCC   | 0.6667                 | 0.5556                 | 0.6061                 |                        |                        |                        |
| Fold 9         | AC    | 0.4667                 | 0.5833                 | 0.5185                 | 0.5694                 | 0.5509                 | 0.1361                 |
|                | SCC   | 0.6667                 | 0.5556                 | 0.6061                 |                        |                        |                        |
| Fold 10        | AC    | 0.3571                 | 0.4167                 | 0.3846                 | 0.4583                 | 0.4954                 | -0.0818                |
|                | SCC   | 0.5625                 | 0.5000                 | 0.5294                 |                        |                        |                        |
| Mean $\pm$ std | AC    | 0.4570<br>$\pm 0.0434$ | 0.5667<br>$\pm 0.0527$ | 0.5056<br>$\pm 0.0453$ | 0.5583<br>$\pm 0.0418$ | 0.5218<br>$\pm 0.0316$ | 0.1145<br>$\pm 0.0821$ |
|                | SCC   | 0.6554<br>$\pm 0.0374$ | 0.5500<br>$\pm 0.0486$ | 0.5976<br>$\pm 0.0420$ |                        |                        |                        |

Table S67: Logistic regression on TissueConcepts embeddings: Patient-level performance metrics AC vs. SCC.

| Fold           | Class | PRE                    | REC                    | F1                     | BA                     | AUROC                  | MCC                    |
|----------------|-------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Fold 1         | AC    | 0.5556                 | 0.6250                 | 0.5882                 | 0.6307                 | 0.6250                 | 0.2584                 |
|                | SCC   | 0.7000                 | 0.6364                 | 0.6667                 |                        |                        |                        |
| Fold 2         | AC    | 0.5000                 | 0.6250                 | 0.5556                 | 0.5852                 | 0.6023                 | 0.1685                 |
|                | SCC   | 0.6667                 | 0.5455                 | 0.6000                 |                        |                        |                        |
| Fold 3         | AC    | 0.5000                 | 0.6250                 | 0.5556                 | 0.5852                 | 0.5568                 | 0.1685                 |
|                | SCC   | 0.6667                 | 0.5455                 | 0.6000                 |                        |                        |                        |
| Fold 4         | AC    | 0.5556                 | 0.6250                 | 0.5882                 | 0.6307                 | 0.5000                 | 0.2584                 |
|                | SCC   | 0.7000                 | 0.6364                 | 0.6667                 |                        |                        |                        |
| Fold 5         | AC    | 0.4545                 | 0.6250                 | 0.5263                 | 0.5398                 | 0.6023                 | 0.0795                 |
|                | SCC   | 0.6250                 | 0.4545                 | 0.5263                 |                        |                        |                        |
| Fold 6         | AC    | 0.5000                 | 0.6250                 | 0.5556                 | 0.5852                 | 0.5682                 | 0.1685                 |
|                | SCC   | 0.6667                 | 0.5455                 | 0.6000                 |                        |                        |                        |
| Fold 7         | AC    | 0.5556                 | 0.6250                 | 0.5882                 | 0.6307                 | 0.5909                 | 0.2584                 |
|                | SCC   | 0.7000                 | 0.6364                 | 0.6667                 |                        |                        |                        |
| Fold 8         | AC    | 0.5000                 | 0.6250                 | 0.5556                 | 0.5852                 | 0.6023                 | 0.1685                 |
|                | SCC   | 0.6667                 | 0.5455                 | 0.6000                 |                        |                        |                        |
| Fold 9         | AC    | 0.5556                 | 0.6250                 | 0.5882                 | 0.6307                 | 0.5795                 | 0.2584                 |
|                | SCC   | 0.7000                 | 0.6364                 | 0.6667                 |                        |                        |                        |
| Fold 10        | AC    | 0.4000                 | 0.5000                 | 0.4444                 | 0.4773                 | 0.5682                 | -0.0449                |
|                | SCC   | 0.5556                 | 0.4545                 | 0.5000                 |                        |                        |                        |
| Mean $\pm$ std | AC    | 0.5077<br>$\pm 0.0514$ | 0.6125<br>$\pm 0.0395$ | 0.5546<br>$\pm 0.0440$ | 0.5881<br>$\pm 0.0493$ | 0.5795<br>$\pm 0.0347$ | 0.1743<br>$\pm 0.0975$ |
|                | SCC   | 0.6647<br>$\pm 0.0453$ | 0.5636<br>$\pm 0.0717$ | 0.6093<br>$\pm 0.0599$ |                        |                        |                        |

Table S68: Logistic regression on UNI2-h embeddings: Patch-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5243            | 0.4081            | 0.4589            | 0.5801            | 0.6384            | 0.1694            |
|                   | SCC        | 0.6549            | 0.7521            | 0.7002            |                   |                   |                   |
| Fold 2            | AC         | 0.5292            | 0.4332            | 0.4765            | 0.5876            | 0.6411            | 0.1829            |
|                   | SCC        | 0.6617            | 0.7420            | 0.6995            |                   |                   |                   |
| Fold 3            | AC         | 0.5000            | 0.3904            | 0.4385            | 0.5645            | 0.6098            | 0.1364            |
|                   | SCC        | 0.6441            | 0.7386            | 0.6881            |                   |                   |                   |
| Fold 4            | AC         | 0.4817            | 0.3652            | 0.4155            | 0.5511            | 0.5817            | 0.1089            |
|                   | SCC        | 0.6343            | 0.7369            | 0.6817            |                   |                   |                   |
| Fold 5            | AC         | 0.5116            | 0.5013            | 0.5064            | 0.5904            | 0.6203            | 0.1815            |
|                   | SCC        | 0.6705            | 0.6796            | 0.6750            |                   |                   |                   |
| Fold 6            | AC         | 0.5284            | 0.4685            | 0.4967            | 0.5943            | 0.6050            | 0.1931            |
|                   | SCC        | 0.6693            | 0.7201            | 0.6937            |                   |                   |                   |
| Fold 7            | AC         | 0.5370            | 0.4937            | 0.5144            | 0.6044            | 0.6526            | 0.2120            |
|                   | SCC        | 0.6784            | 0.7150            | 0.6962            |                   |                   |                   |
| Fold 8            | AC         | 0.4890            | 0.4484            | 0.4678            | 0.5674            | 0.6092            | 0.1369            |
|                   | SCC        | 0.6502            | 0.6863            | 0.6678            |                   |                   |                   |
| Fold 9            | AC         | 0.5379            | 0.5189            | 0.5282            | 0.6102            | 0.6606            | 0.2218            |
|                   | SCC        | 0.6853            | 0.7015            | 0.6933            |                   |                   |                   |
| Fold 10           | AC         | 0.4735            | 0.4055            | 0.4369            | 0.5518            | 0.6004            | 0.1070            |
|                   | SCC        | 0.6369            | 0.6981            | 0.6661            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5113<br>±0.0237 | 0.4433<br>±0.0516 | 0.4740<br>±0.0372 | 0.5802<br>±0.0208 | 0.6219<br>±0.0253 | 0.1650<br>±0.0408 |
|                   | <b>SCC</b> | 0.6586<br>±0.0174 | 0.7170<br>±0.0251 | 0.6862<br>±0.0128 |                   |                   |                   |

Table S69: Logistic regression on UNI2-h embeddings: Slide-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.4167            | 0.4167            | 0.4167            | 0.5139            | 0.6435            | 0.0278            |
|                   | SCC        | 0.6111            | 0.6111            | 0.6111            |                   |                   |                   |
| Fold 2            | AC         | 0.5556            | 0.4167            | 0.4762            | 0.5972            | 0.7269            | 0.2079            |
|                   | SCC        | 0.6667            | 0.7778            | 0.7179            |                   |                   |                   |
| Fold 3            | AC         | 0.5556            | 0.4167            | 0.4762            | 0.5972            | 0.6991            | 0.2079            |
|                   | SCC        | 0.6667            | 0.7778            | 0.7179            |                   |                   |                   |
| Fold 4            | AC         | 0.5000            | 0.4167            | 0.4545            | 0.5694            | 0.6157            | 0.1443            |
|                   | SCC        | 0.6500            | 0.7222            | 0.6842            |                   |                   |                   |
| Fold 5            | AC         | 0.6250            | 0.8333            | 0.7143            | 0.7500            | 0.6806            | 0.4910            |
|                   | SCC        | 0.8571            | 0.6667            | 0.7500            |                   |                   |                   |
| Fold 6            | AC         | 0.5833            | 0.5833            | 0.5833            | 0.6528            | 0.6574            | 0.3056            |
|                   | SCC        | 0.7222            | 0.7222            | 0.7222            |                   |                   |                   |
| Fold 7            | AC         | 0.6154            | 0.6667            | 0.6400            | 0.6944            | 0.7176            | 0.3845            |
|                   | SCC        | 0.7647            | 0.7222            | 0.7429            |                   |                   |                   |
| Fold 8            | AC         | 0.5000            | 0.5833            | 0.5385            | 0.5972            | 0.6343            | 0.1909            |
|                   | SCC        | 0.6875            | 0.6111            | 0.6471            |                   |                   |                   |
| Fold 9            | AC         | 0.6154            | 0.6667            | 0.6400            | 0.6944            | 0.7083            | 0.3845            |
|                   | SCC        | 0.7647            | 0.7222            | 0.7429            |                   |                   |                   |
| Fold 10           | AC         | 0.4000            | 0.3333            | 0.3636            | 0.5000            | 0.6435            | 0.0000            |
|                   | SCC        | 0.6000            | 0.6667            | 0.6316            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5367<br>±0.0809 | 0.5333<br>±0.1581 | 0.5303<br>±0.1121 | 0.6167<br>±0.0808 | 0.6727<br>±0.0389 | 0.2344<br>±0.1581 |
|                   | <b>SCC</b> | 0.6991<br>±0.0791 | 0.7000<br>±0.0597 | 0.6968<br>±0.0504 |                   |                   |                   |

Table S70: Logistic regression on UNI2-h embeddings: Patient-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.7386            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| Fold 2            | AC         | 0.6667            | 0.5000            | 0.5714            | 0.6591            | 0.7841            | 0.3380            |
|                   | SCC        | 0.6923            | 0.8182            | 0.7500            |                   |                   |                   |
| Fold 3            | AC         | 0.6667            | 0.5000            | 0.5714            | 0.6591            | 0.7273            | 0.3380            |
|                   | SCC        | 0.6923            | 0.8182            | 0.7500            |                   |                   |                   |
| Fold 4            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.6591            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 5            | AC         | 0.7000            | 0.8750            | 0.7778            | 0.8011            | 0.7727            | 0.5955            |
|                   | SCC        | 0.8889            | 0.7273            | 0.8000            |                   |                   |                   |
| Fold 6            | AC         | 0.6250            | 0.6250            | 0.6250            | 0.6761            | 0.7159            | 0.3523            |
|                   | SCC        | 0.7273            | 0.7273            | 0.7273            |                   |                   |                   |
| Fold 7            | AC         | 0.7000            | 0.8750            | 0.7778            | 0.8011            | 0.7841            | 0.5955            |
|                   | SCC        | 0.8889            | 0.7273            | 0.8000            |                   |                   |                   |
| Fold 8            | AC         | 0.5556            | 0.6250            | 0.5882            | 0.6307            | 0.7045            | 0.2584            |
|                   | SCC        | 0.7000            | 0.6364            | 0.6667            |                   |                   |                   |
| Fold 9            | AC         | 0.6667            | 0.7500            | 0.7059            | 0.7386            | 0.7841            | 0.4719            |
|                   | SCC        | 0.8000            | 0.7273            | 0.7619            |                   |                   |                   |
| Fold 10           | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.7159            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.6152<br>±0.0778 | 0.6000<br>±0.1845 | 0.6008<br>±0.1247 | 0.6682<br>±0.0896 | 0.7386<br>±0.0422 | 0.3400<br>±0.1743 |
|                   | <b>SCC</b> | 0.7287<br>±0.0997 | 0.7364<br>±0.0516 | 0.7285<br>±0.0525 |                   |                   |                   |

Table S71: Logistic regression on Virchow2 embeddings: Patch-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.4551            | 0.3577            | 0.4006            | 0.5355            | 0.5844            | 0.0749            |
|                   | SCC        | 0.6239            | 0.7133            | 0.6656            |                   |                   |                   |
| Fold 2            | AC         | 0.5015            | 0.4131            | 0.4530            | 0.5691            | 0.6091            | 0.1440            |
|                   | SCC        | 0.6486            | 0.7251            | 0.6847            |                   |                   |                   |
| Fold 3            | AC         | 0.4281            | 0.3375            | 0.3775            | 0.5178            | 0.5428            | 0.0376            |
|                   | SCC        | 0.6115            | 0.6981            | 0.6520            |                   |                   |                   |
| Fold 4            | AC         | 0.4693            | 0.3275            | 0.3858            | 0.5398            | 0.5597            | 0.0869            |
|                   | SCC        | 0.6255            | 0.7521            | 0.6830            |                   |                   |                   |
| Fold 5            | AC         | 0.4338            | 0.4207            | 0.4271            | 0.5265            | 0.5501            | 0.0533            |
|                   | SCC        | 0.6198            | 0.6324            | 0.6260            |                   |                   |                   |
| Fold 6            | AC         | 0.4799            | 0.3904            | 0.4306            | 0.5536            | 0.5589            | 0.1120            |
|                   | SCC        | 0.6372            | 0.7167            | 0.6746            |                   |                   |                   |
| Fold 7            | AC         | 0.4797            | 0.4458            | 0.4621            | 0.5610            | 0.5913            | 0.1237            |
|                   | SCC        | 0.6457            | 0.6762            | 0.6606            |                   |                   |                   |
| Fold 8            | AC         | 0.4684            | 0.4106            | 0.4376            | 0.5493            | 0.5812            | 0.1012            |
|                   | SCC        | 0.6355            | 0.6880            | 0.6607            |                   |                   |                   |
| Fold 9            | AC         | 0.4621            | 0.4761            | 0.4690            | 0.5525            | 0.5939            | 0.1046            |
|                   | SCC        | 0.6420            | 0.6290            | 0.6354            |                   |                   |                   |
| Fold 10           | AC         | 0.4397            | 0.3854            | 0.4107            | 0.5283            | 0.5704            | 0.0581            |
|                   | SCC        | 0.6199            | 0.6712            | 0.6445            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4618<br>±0.0230 | 0.3965<br>±0.0468 | 0.4254<br>±0.0314 | 0.5433<br>±0.0165 | 0.5742<br>±0.0213 | 0.0896<br>±0.0337 |
|                   | <b>SCC</b> | 0.6310<br>±0.0125 | 0.6902<br>±0.0394 | 0.6587<br>±0.0195 |                   |                   |                   |

Table S72: Logistic regression on Virchow2 embeddings: Slide-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5000            | 0.4167            | 0.4545            | 0.5694            | 0.6250            | 0.1443            |
|                   | SCC        | 0.6500            | 0.7222            | 0.6842            |                   |                   |                   |
| Fold 2            | AC         | 0.5000            | 0.4167            | 0.4545            | 0.5694            | 0.6481            | 0.1443            |
|                   | SCC        | 0.6500            | 0.7222            | 0.6842            |                   |                   |                   |
| Fold 3            | AC         | 0.4444            | 0.3333            | 0.3810            | 0.5278            | 0.6157            | 0.0594            |
|                   | SCC        | 0.6190            | 0.7222            | 0.6667            |                   |                   |                   |
| Fold 4            | AC         | 0.4545            | 0.4167            | 0.4348            | 0.5417            | 0.5648            | 0.0847            |
|                   | SCC        | 0.6316            | 0.6667            | 0.6486            |                   |                   |                   |
| Fold 5            | AC         | 0.4615            | 0.5000            | 0.4800            | 0.5556            | 0.5926            | 0.1098            |
|                   | SCC        | 0.6471            | 0.6111            | 0.6286            |                   |                   |                   |
| Fold 6            | AC         | 0.5455            | 0.5000            | 0.5217            | 0.6111            | 0.5556            | 0.2259            |
|                   | SCC        | 0.6842            | 0.7222            | 0.7027            |                   |                   |                   |
| Fold 7            | AC         | 0.5455            | 0.5000            | 0.5217            | 0.6111            | 0.6204            | 0.2259            |
|                   | SCC        | 0.6842            | 0.7222            | 0.7027            |                   |                   |                   |
| Fold 8            | AC         | 0.5455            | 0.5000            | 0.5217            | 0.6111            | 0.6528            | 0.2259            |
|                   | SCC        | 0.6842            | 0.7222            | 0.7027            |                   |                   |                   |
| Fold 9            | AC         | 0.5385            | 0.5833            | 0.5600            | 0.6250            | 0.6759            | 0.2472            |
|                   | SCC        | 0.7059            | 0.6667            | 0.6857            |                   |                   |                   |
| Fold 10           | AC         | 0.4000            | 0.3333            | 0.3636            | 0.5000            | 0.6157            | 0.0000            |
|                   | SCC        | 0.6000            | 0.6667            | 0.6316            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.4935<br>±0.0515 | 0.4500<br>±0.0805 | 0.4694<br>±0.0643 | 0.5722<br>±0.0418 | 0.6167<br>±0.0379 | 0.1468<br>±0.0838 |
|                   | <b>SCC</b> | 0.6556<br>±0.0335 | 0.6944<br>±0.0393 | 0.6738<br>±0.0286 |                   |                   |                   |

Table S73: Logistic regression on Virchow2 embeddings: Patient-level performance metrics AC vs. SCC.

| Fold              | Class      | PRE               | REC               | F1                | BA                | AUROC             | MCC               |
|-------------------|------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Fold 1            | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.6591            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| Fold 2            | AC         | 0.6667            | 0.5000            | 0.5714            | 0.6591            | 0.6705            | 0.3380            |
|                   | SCC        | 0.6923            | 0.8182            | 0.7500            |                   |                   |                   |
| Fold 3            | AC         | 0.6000            | 0.3750            | 0.4615            | 0.5966            | 0.6364            | 0.2166            |
|                   | SCC        | 0.6429            | 0.8182            | 0.7200            |                   |                   |                   |
| Fold 4            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.5909            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 5            | AC         | 0.6250            | 0.6250            | 0.6250            | 0.6761            | 0.6477            | 0.3523            |
|                   | SCC        | 0.7273            | 0.7273            | 0.7273            |                   |                   |                   |
| Fold 6            | AC         | 0.5714            | 0.5000            | 0.5333            | 0.6136            | 0.6023            | 0.2326            |
|                   | SCC        | 0.6667            | 0.7273            | 0.6957            |                   |                   |                   |
| Fold 7            | AC         | 0.7143            | 0.6250            | 0.6667            | 0.7216            | 0.6818            | 0.4536            |
|                   | SCC        | 0.7500            | 0.8182            | 0.7826            |                   |                   |                   |
| Fold 8            | AC         | 0.6250            | 0.6250            | 0.6250            | 0.6761            | 0.6818            | 0.3523            |
|                   | SCC        | 0.7273            | 0.7273            | 0.7273            |                   |                   |                   |
| Fold 9            | AC         | 0.5000            | 0.5000            | 0.5000            | 0.5682            | 0.6705            | 0.1364            |
|                   | SCC        | 0.6364            | 0.6364            | 0.6364            |                   |                   |                   |
| Fold 10           | AC         | 0.5000            | 0.3750            | 0.4286            | 0.5511            | 0.6477            | 0.1086            |
|                   | SCC        | 0.6154            | 0.7273            | 0.6667            |                   |                   |                   |
| <b>Mean ± std</b> | <b>AC</b>  | 0.5874<br>±0.0736 | 0.5000<br>±0.1021 | 0.5373<br>±0.0844 | 0.6227<br>±0.0586 | 0.6489<br>±0.0314 | 0.2532<br>±0.1177 |
|                   | <b>SCC</b> | 0.6740<br>±0.0485 | 0.7455<br>±0.0575 | 0.7068<br>±0.0435 |                   |                   |                   |

Table S74: MLP: Performance metrics AC vs. SCC.

| Architecture   | Level   | Class | PRE    | REC    | F1     | BA (95% CI)     | AUROC (95% CI)  | MCC (95% CI)     |
|----------------|---------|-------|--------|--------|--------|-----------------|-----------------|------------------|
| ResNet50       | Patch   | AC    | 0.4561 | 0.4710 | 0.4634 | 0.5475          | 0.5749          | 0.0945           |
|                |         | SCC   | 0.6379 | 0.6239 | 0.6309 | (0.5169-0.5776) | (0.5401-0.6113) | (0.0337-0.1539)  |
|                | Slide   | AC    | 0.5455 | 0.5000 | 0.5217 | 0.6111          | 0.5880          | 0.2259           |
|                |         | SCC   | 0.6842 | 0.7222 | 0.7027 | (0.4389-0.7920) | (0.3600-0.8000) | (-0.1321-0.5769) |
|                | Patient | AC    | 0.5000 | 0.5000 | 0.5000 | 0.5682          | 0.6023          | 0.1364           |
|                |         | SCC   | 0.6364 | 0.6364 | 0.6364 | (0.3222-0.8000) | (0.3214-0.8571) | (-0.3307-0.5866) |
| CONCH          | Patch   | AC    | 0.4218 | 0.4005 | 0.4109 | 0.5164          | 0.5482          | 0.0332           |
|                |         | SCC   | 0.6117 | 0.6324 | 0.6219 | (0.4875-0.5476) | (0.5136-0.5826) | (-0.0255-0.0969) |
|                | Slide   | AC    | 0.3846 | 0.4167 | 0.4000 | 0.4861          | 0.5694          | -0.0275          |
|                |         | SCC   | 0.5882 | 0.5556 | 0.5714 | (0.3000-0.6866) | (0.3421-0.7822) | (-0.3889-0.3652) |
|                | Patient | AC    | 0.4444 | 0.5000 | 0.4706 | 0.5227          | 0.6364          | 0.0449           |
|                |         | SCC   | 0.6000 | 0.5455 | 0.5714 | (0.2786-0.7502) | (0.3690-0.8847) | (-0.4203-0.4781) |
| CTransPath     | Patch   | AC    | 0.5057 | 0.4433 | 0.4725 | 0.5766          | 0.6102          | 0.1573           |
|                |         | SCC   | 0.6558 | 0.7099 | 0.6818 | (0.5462-0.6054) | (0.5740-0.6450) | (0.0942-0.2173)  |
|                | Slide   | AC    | 0.4615 | 0.5000 | 0.4800 | 0.5556          | 0.5833          | 0.1098           |
|                |         | SCC   | 0.6471 | 0.6111 | 0.6286 | (0.3732-0.7500) | (0.3644-0.7991) | (-0.2467-0.4732) |
|                | Patient | AC    | 0.5714 | 0.5000 | 0.5333 | 0.6136          | 0.6477          | 0.2326           |
|                |         | SCC   | 0.6667 | 0.7273 | 0.6957 | (0.3555-0.8184) | (0.3778-0.9091) | (-0.2676-0.6445) |
| H-optimus-0    | Patch   | AC    | 0.5469 | 0.4408 | 0.4881 | 0.5981          | 0.6894          | 0.2057           |
|                |         | SCC   | 0.6687 | 0.7555 | 0.7094 | (0.5692-0.6289) | (0.6571-0.7236) | (0.1441-0.2716)  |
|                | Slide   | AC    | 0.6364 | 0.5833 | 0.6087 | 0.6806          | 0.7500          | 0.3671           |
|                |         | SCC   | 0.7368 | 0.7778 | 0.7568 | (0.4976-0.8501) | (0.5535-0.9095) | (-0.0049-0.6999) |
|                | Patient | AC    | 0.6250 | 0.6250 | 0.6250 | 0.6761          | 0.7500          | 0.3523           |
|                |         | SCC   | 0.7273 | 0.7273 | 0.7273 | (0.4499-0.8869) | (0.4889-0.9545) | (-0.0959-0.7738) |
| H-optimus-1    | Patch   | AC    | 0.5152 | 0.4685 | 0.4908 | 0.5867          | 0.6612          | 0.1766           |
|                |         | SCC   | 0.6645 | 0.7049 | 0.6841 | (0.5558-0.6175) | (0.6293-0.6948) | (0.1133-0.2391)  |
|                | Slide   | AC    | 0.5385 | 0.5833 | 0.5600 | 0.6250          | 0.7176          | 0.2472           |
|                |         | SCC   | 0.7059 | 0.6667 | 0.6857 | (0.4364-0.8230) | (0.5227-0.9034) | (-0.1321-0.6142) |
|                | Patient | AC    | 0.6250 | 0.6250 | 0.6250 | 0.6761          | 0.7841          | 0.3523           |
|                |         | SCC   | 0.7273 | 0.7273 | 0.7273 | (0.4277-0.8669) | (0.5427-0.9762) | (-0.1489-0.7246) |
| hibou-L        | Patch   | AC    | 0.5512 | 0.4610 | 0.5021 | 0.6048          | 0.6570          | 0.2177           |
|                |         | SCC   | 0.6748 | 0.7487 | 0.7098 | (0.5744-0.6351) | (0.6203-0.6913) | (0.1544-0.2787)  |
|                | Slide   | AC    | 0.6154 | 0.6667 | 0.6400 | 0.6944          | 0.7083          | 0.3845           |
|                |         | SCC   | 0.7647 | 0.7222 | 0.7429 | (0.5138-0.8661) | (0.5093-0.8978) | (0.0272-0.7321)  |
|                | Patient | AC    | 0.6667 | 0.7500 | 0.7059 | 0.7386          | 0.7727          | 0.4719           |
|                |         | SCC   | 0.8000 | 0.7273 | 0.7619 | (0.5104-0.9231) | (0.5235-0.9556) | (0.0163-0.8090)  |
| Kaiko          | Patch   | AC    | 0.4452 | 0.3476 | 0.3904 | 0.5288          | 0.5735          | 0.0608           |
|                |         | SCC   | 0.6191 | 0.7099 | 0.6614 | (0.4962-0.5562) | (0.5373-0.6095) | (-0.0082-0.1192) |
|                | Slide   | AC    | 0.5833 | 0.5833 | 0.5833 | 0.6528          | 0.6111          | 0.3056           |
|                |         | SCC   | 0.7222 | 0.7222 | 0.7222 | (0.4722-0.8230) | (0.3883-0.8215) | (-0.0565-0.6361) |
|                | Patient | AC    | 0.5556 | 0.6250 | 0.5882 | 0.6307          | 0.6591          | 0.2584           |
|                |         | SCC   | 0.7000 | 0.6364 | 0.6667 | (0.3929-0.8390) | (0.3809-0.9000) | (-0.2094-0.6746) |
| Phikon         | Patch   | AC    | 0.5114 | 0.4534 | 0.4806 | 0.5817          | 0.6292          | 0.1672           |
|                |         | SCC   | 0.6599 | 0.7099 | 0.6840 | (0.5481-0.6132) | (0.5923-0.6641) | (0.1002-0.2306)  |
|                | Slide   | AC    | 0.5833 | 0.5833 | 0.5833 | 0.6528          | 0.6204          | 0.3056           |
|                |         | SCC   | 0.7222 | 0.7222 | 0.7222 | (0.4603-0.8301) | (0.3900-0.8413) | (-0.0811-0.6591) |
|                | Patient | AC    | 0.6250 | 0.6250 | 0.6250 | 0.6761          | 0.6591          | 0.3523           |
|                |         | SCC   | 0.7273 | 0.7273 | 0.7273 | (0.4277-0.8669) | (0.3750-0.8974) | (-0.1489-0.7246) |
| ProvGigaPath   | Patch   | AC    | 0.4899 | 0.4282 | 0.4570 | 0.5649          | 0.6214          | 0.1333           |
|                |         | SCC   | 0.6470 | 0.7015 | 0.6731 | (0.5350-0.5958) | (0.5865-0.6574) | (0.0712-0.1979)  |
|                | Slide   | AC    | 0.5833 | 0.5833 | 0.5833 | 0.6528          | 0.6898          | 0.3056           |
|                |         | SCC   | 0.7222 | 0.7222 | 0.7222 | (0.4667-0.8349) | (0.4829-0.8704) | (-0.0667-0.6682) |
|                | Patient | AC    | 0.6250 | 0.6250 | 0.6250 | 0.6761          | 0.7159          | 0.3523           |
|                |         | SCC   | 0.7273 | 0.7273 | 0.7273 | (0.4277-0.8669) | (0.4522-0.9333) | (-0.1489-0.7246) |
| TissueConcepts | Patch   | AC    | 0.4454 | 0.3904 | 0.4161 | 0.5325          | 0.5585          | 0.0667           |
|                |         | SCC   | 0.6231 | 0.6745 | 0.6478 | (0.5028-0.5640) | (0.5243-0.5956) | (0.0058-0.1315)  |
|                | Slide   | AC    | 0.5000 | 0.5000 | 0.5000 | 0.5833          | 0.6065          | 0.1667           |
|                |         | SCC   | 0.6667 | 0.6667 | 0.6667 | (0.3995-0.7634) | (0.3750-0.8133) | (-0.2019-0.5233) |
|                | Patient | AC    | 0.6250 | 0.6250 | 0.6250 | 0.6761          | 0.6932          | 0.3523           |
|                |         | SCC   | 0.7273 | 0.7273 | 0.7273 | (0.4464-0.9000) | (0.3974-0.9333) | (-0.1207-0.7966) |
| UNI2-h         | Patch   | AC    | 0.5479 | 0.5038 | 0.5249 | 0.6128          | 0.6783          | 0.2291           |
|                |         | SCC   | 0.6848 | 0.7218 | 0.7028 | (0.5816-0.6447) | (0.6448-0.7115) | (0.1658-0.2940)  |
|                | Slide   | AC    | 0.5625 | 0.7500 | 0.6429 | 0.6806          | 0.7037          | 0.3546           |
|                |         | SCC   | 0.7857 | 0.6111 | 0.6875 | (0.5000-0.8421) | (0.4907-0.8889) | (0.0000-0.6804)  |
|                | Patient | AC    | 0.6000 | 0.7500 | 0.6667 | 0.6932          | 0.7273          | 0.3820           |
|                |         | SCC   | 0.7778 | 0.6364 | 0.7000 | (0.4667-0.8944) | (0.4545-0.9432) | (-0.0690-0.7889) |
| Virchow2       | Patch   | AC    | 0.5232 | 0.4257 | 0.4694 | 0.5830          | 0.6417          | 0.1735           |
|                |         | SCC   | 0.6582 | 0.7403 | 0.6968 | (0.5544-0.6131) | (0.6072-0.6761) | (0.1129-0.2349)  |
|                | Slide   | AC    | 0.5556 | 0.4167 | 0.4762 | 0.5972          | 0.6898          | 0.2079           |
|                |         | SCC   | 0.6667 | 0.7778 | 0.7179 | (0.4258-0.7656) | (0.4865-0.8731) | (-0.1545-0.5477) |
|                | Patient | AC    | 0.6667 | 0.5000 | 0.5714 | 0.6591          | 0.7045          | 0.3380           |
|                |         | SCC   | 0.6923 | 0.8182 | 0.7500 | (0.4261-0.8467) | (0.4318-0.9286) | (-0.1512-0.7246) |

## 5. p-values tables (patient-level)

Table S75: Patient-level p-values for ResNet50 compared to all foundation models for NSCLC vs. MET.

| Architecture   | Logreg |        |       |        |       |        | MLP   |        |       |        |       |        |
|----------------|--------|--------|-------|--------|-------|--------|-------|--------|-------|--------|-------|--------|
|                | BA     |        | AUROC |        | MCC   |        | BA    |        | AUROC |        | MCC   |        |
|                | p      | adj. p | p     | adj. p | p     | adj. p | p     | adj. p | p     | adj. p | p     | adj. p |
| CONCH          | 0.639  | 1.000  | 0.620 | 1.000  | 0.312 | 1.000  | 0.282 | 1.000  | 0.404 | 1.000  | 0.363 | 1.000  |
| CTransPath     | 0.217  | 1.000  | 0.694 | 1.000  | 0.158 | 1.000  | 0.559 | 1.000  | 0.874 | 1.000  | 0.988 | 1.000  |
| H-optimus-0    | 0.896  | 1.000  | 0.851 | 1.000  | 0.544 | 1.000  | 0.241 | 1.000  | 0.298 | 1.000  | 0.594 | 1.000  |
| H-optimus-1    | 0.639  | 1.000  | 0.865 | 1.000  | 0.312 | 1.000  | 0.557 | 1.000  | 0.726 | 1.000  | 0.985 | 1.000  |
| hibou-L        | 0.217  | 1.000  | 0.514 | 1.000  | 0.158 | 1.000  | 0.558 | 1.000  | 0.891 | 1.000  | 0.978 | 1.000  |
| Kaiko          | 0.217  | 1.000  | 0.686 | 1.000  | 0.158 | 1.000  | 0.776 | 1.000  | 0.580 | 1.000  | 0.854 | 1.000  |
| Phikon         | 0.896  | 1.000  | 1.000 | 1.000  | 0.544 | 1.000  | 0.241 | 1.000  | 0.591 | 1.000  | 0.594 | 1.000  |
| ProvGigaPath   | 0.650  | 1.000  | 0.740 | 1.000  | 0.915 | 1.000  | 0.241 | 1.000  | 0.815 | 1.000  | 0.594 | 1.000  |
| TissueConcepts | 0.698  | 1.000  | 0.315 | 1.000  | 0.666 | 1.000  | 0.610 | 1.000  | 0.140 | 1.000  | 0.986 | 1.000  |
| UNI2-h         | 0.896  | 1.000  | 0.848 | 1.000  | 0.544 | 1.000  | 0.254 | 1.000  | 0.592 | 1.000  | 0.565 | 1.000  |
| Virchow2       | 0.130  | 1.000  | 0.908 | 1.000  | 0.067 | 0.736  | 0.779 | 1.000  | 0.844 | 1.000  | 0.278 | 1.000  |

Table S76: Patient-level p-values for ResNet50 compared to all foundation models for AC vs. SCC.

| Architecture   | Logreg |        |       |        |       |        | MLP   |        |       |        |       |        |
|----------------|--------|--------|-------|--------|-------|--------|-------|--------|-------|--------|-------|--------|
|                | BA     |        | AUROC |        | MCC   |        | BA    |        | AUROC |        | MCC   |        |
|                | p      | adj. p | p     | adj. p | p     | adj. p | p     | adj. p | p     | adj. p | p     | adj. p |
| CONCH          | 0.683  | 1.000  | 0.083 | 0.414  | 0.653 | 1.000  | 0.761 | 1.000  | 0.661 | 1.000  | 0.729 | 1.000  |
| CTransPath     | 0.029  | 0.319  | 0.093 | 0.414  | 0.032 | 0.352  | 0.714 | 1.000  | 0.643 | 1.000  | 0.683 | 1.000  |
| H-optimus-0    | 0.206  | 1.000  | 0.028 | 0.313  | 0.212 | 1.000  | 0.389 | 1.000  | 0.117 | 1.000  | 0.353 | 1.000  |
| H-optimus-1    | 0.125  | 1.000  | 0.037 | 0.331  | 0.107 | 0.962  | 0.391 | 1.000  | 0.060 | 0.661  | 0.354 | 1.000  |
| hibou-L        | 1.000  | 1.000  | 0.046 | 0.357  | 1.000 | 1.000  | 0.079 | 0.868  | 0.066 | 0.661  | 0.061 | 0.670  |
| Kaiko          | 0.710  | 1.000  | 0.067 | 0.401  | 0.691 | 1.000  | 0.728 | 1.000  | 0.575 | 1.000  | 0.700 | 1.000  |
| Phikon         | 0.206  | 1.000  | 0.172 | 0.414  | 0.212 | 1.000  | 0.391 | 1.000  | 0.600 | 1.000  | 0.354 | 1.000  |
| ProvGigaPath   | 0.206  | 1.000  | 0.045 | 0.357  | 0.212 | 1.000  | 0.391 | 1.000  | 0.192 | 1.000  | 0.354 | 1.000  |
| TissueConcepts | 0.223  | 1.000  | 0.810 | 0.810  | 0.197 | 1.000  | 0.318 | 1.000  | 0.422 | 1.000  | 0.298 | 1.000  |
| UNI2-h         | 0.084  | 0.839  | 0.031 | 0.313  | 0.095 | 0.949  | 0.264 | 1.000  | 0.132 | 1.000  | 0.211 | 1.000  |
| Virchow2       | 0.239  | 1.000  | 0.097 | 0.414  | 0.198 | 1.000  | 0.423 | 1.000  | 0.266 | 1.000  | 0.362 | 1.000  |

## 6. Distribution of patch numbers

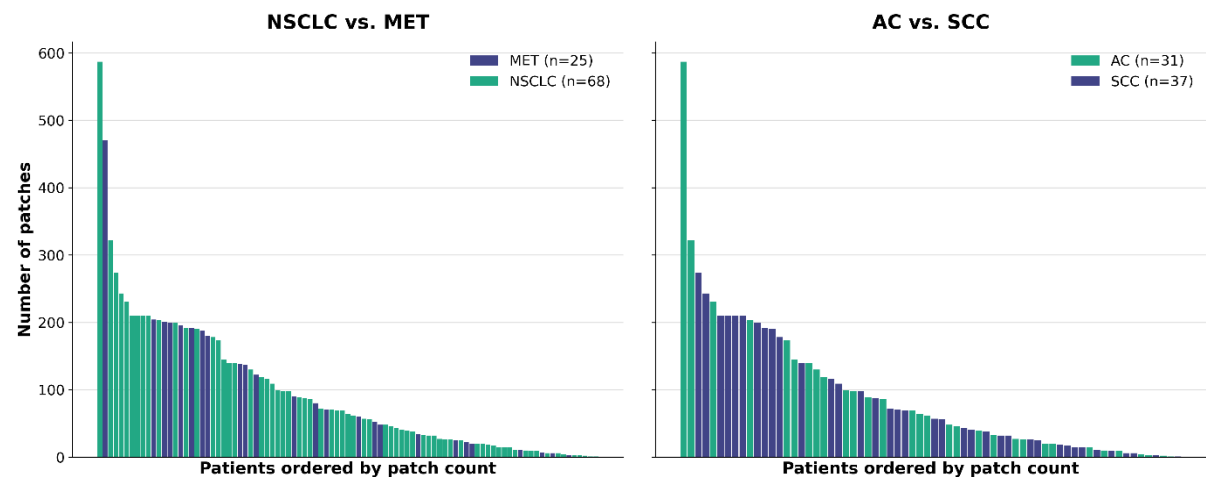


Figure S9: Distribution of number of patches per patient for NSCLC vs. MET and AC vs. SCC.