**Supplemental Material** 

## Supplementary Table 1. Performance comparison for brain tumor classification on different tasks.

|            | Task                  | ACC                   | AUC                   | F1                    | Sensitivity           | Specificity           |
|------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Validation | Seven-classification  | 93.29 <sub>1.17</sub> | 99.23 <sub>0.15</sub> | 93.19 <sub>1.17</sub> | 93.29 <sub>1.17</sub> | 98.88 <sub>0.20</sub> |
| Dataset    | Five- classification  | 94.64 <sub>1.09</sub> | 99.330.15             | 94.611.09             | 94.64 <sub>1.09</sub> | 98.660.27             |
| Test       | Seven- classification | 85.60 <sub>0.42</sub> | 97.33 <sub>0.43</sub> | 85.59 <sub>0.44</sub> | 85.60 <sub>0.42</sub> | $97.60_{0.07}$        |
| Dataset    | Five- classification  | 91.00 <sub>0.35</sub> | 98.38 <sub>0.14</sub> | 91.16 <sub>0.40</sub> | $91.00_{0.35}$        | 97.75 <sub>0.09</sub> |

## Supplementary Table 2. Performance comparison on the public dataset.

| Category    |        | Internal dataset      |                       |                       | External dataset      |                       |                       |  |
|-------------|--------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|--|
|             |        | ACC                   | AUC                   | F1                    | ACC                   | AUC                   | F1                    |  |
| ADMII       | 5×     | 89.251.15             | 97.460.66             | 87.551.38             | 86.67 <sub>1.64</sub> | 97.66 <sub>0.34</sub> | 84.851.64             |  |
| ABMIL       | 20×    | 94.11 <sub>1.25</sub> | 99.510.16             | 93.521.55             | 90.611.12             | 99.160.60             | 89.703.17             |  |
| CLAM CD     | 5×     | $90.96_{1.48}$        | 98.27 <sub>0.56</sub> | $89.80_{1.98}$        | $88.70_{1.02}$        | $98.31_{0.37}$        | 87.28 <sub>1.37</sub> |  |
| CLAM-SB     | 20×    | 95.613.19             | 99.70 <sub>0.35</sub> | 95.103.87             | 91.27 <sub>2.47</sub> | 98.49 <sub>0.67</sub> | 90.593.09             |  |
| CLAM MD     | 5×     | $90.70_{1.13}$        | 98.40 <sub>0.47</sub> | 90.151.09             | 88.442.47             | 98.330.39             | 87.593.31             |  |
| CLAM-MB     | 20×    | 96.812.89             | 99.810.27             | 96.403.59             | 91.99 <sub>1.25</sub> | 98.820.25             | 91.47 <sub>2.14</sub> |  |
| TID ANG MIL | 5×     | 88.202.01             | 95.10 <sub>1.41</sub> | 82.588.40             | 87.39 <sub>1.37</sub> | 95.99 <sub>0.50</sub> | 86.32 <sub>1.44</sub> |  |
| TRANS-MIL   | 20×    | 90.17 <sub>1.08</sub> | 96.911.11             | 89.471.30             | 90.281.40             | 99.021.50             | 89.452.15             |  |
| DEED        | 5×     | 90.301.22             | 98.280.26             | 88.721.35             | 88.310.77             | 98.24 <sub>0.27</sub> | 86.60 <sub>0.76</sub> |  |
| DTFD        | 20×    | 91.090.90             | 98.380.33             | 90.421.29             | 90.282.26             | 96.49 <sub>0.54</sub> | 89.413.06             |  |
| D.C.I       | 5×     | 93.87 <sub>1.54</sub> | 98.95 <sub>0.15</sub> | 93.54 <sub>1.50</sub> | $92.68_{0.86}$        | 99.03 <sub>0.48</sub> | 92.46 <sub>1.22</sub> |  |
| BCL         | 20×    | -                     | -                     | -                     | -                     | -                     | -                     |  |
| MS-ABMIL    | 5×+20× | 91.87 <sub>1.37</sub> | 98.75 <sub>0.25</sub> | 90.961.11             | 91.260.88             | 98.90 <sub>0.36</sub> | 90.36 <sub>1.24</sub> |  |
| номи        | 5×     | 95.84 <sub>0.62</sub> | 99.220.39             | 95.520.74             | 92.89 <sub>0.56</sub> | 99.16 <sub>0.33</sub> | 92.56 <sub>0.83</sub> |  |
| HOMIL       | 5×+20× | 97.380.53             | 99.57 <sub>0.16</sub> | 97.300.49             | 96.171.11             | 99.660.19             | 96.011.29             |  |

Supplementary Table 3. Performance comparison on the task of determining the origin of brain metastatic adenocarcinoma.

| Category     |        | Internal dataset |                       |                        | External dataset      |                       |                       |
|--------------|--------|------------------|-----------------------|------------------------|-----------------------|-----------------------|-----------------------|
|              |        | ACC              | AUC                   | F1                     | ACC                   | AUC                   | F1                    |
| ADMII        | 5×     | 68.993.15        | 70.063.36             | 67.723.91              | 65.721.25             | 68.601.74             | 65.631.40             |
| ABMIL        | 20×    | 75.966.81        | 81.275.81             | 75.876.57              | 72.432.60             | 76.280.99             | 73.002.11             |
| CI AM CD     | 5×     | $73.59_{6.18}$   | 79.27 <sub>4.94</sub> | $73.65_{6.13}$         | 69.83 <sub>2.35</sub> | 75.682.82             | $70.51_{2.25}$        |
| CLAM-SB      | 20×    | 78.715.12        | 81.796.81             | 78.615.07              | 72.57 <sub>2.43</sub> | 78.102.75             | 72.962.07             |
| CLAM MD      | 5×     | 71.125.75        | 72.816.61             | 71.355.73              | 67.276.38             | 74.685.41             | 68.216.041            |
| CLAM-MB      | 20×    | 79.326.60        | 82.815.42             | 79.456.52              | 68.452.76             | 76.302.29             | 69.50 <sub>2.51</sub> |
| TID AND MILE | 5×     | 72.637.96        | 80.686.54             | 69.20 <sub>10.45</sub> | $72.79_{2.88}$        | 78.27 <sub>3.91</sub> | 68.013.79             |
| TRANS-MIL    | 20×    | 78.396.03        | 84.845.41             | 77.945.93              | 73.04 <sub>2.86</sub> | 80.971.40             | 70.612.49             |
| DEED         | 5×     | 77.187.97        | 80.696.07             | 77.167.92              | 71.722.78             | 78.370.98             | 72.232.37             |
| DTFD         | 20×    | 81.455.72        | 86.204.02             | 81.265.95              | 74.802.33             | 81.951.03             | 75.19 <sub>1.93</sub> |
| D.C.I.       | 5×     | 81.825.67        | 83.915.68             | 81.295.96              | 63.414.28             | 66.271.72             | 63.582.93             |
| BCL          | 20×    | -                | -                     | -                      | -                     | -                     | -                     |
| MS-ABMIL     | 5×+20× | 80.534.52        | 82.905.46             | 80.584.40              | 73.94 <sub>0.92</sub> | 78.24 <sub>1.54</sub> | 74.331.05             |
| номи         | 5×     | 75.761.24        | 79.31 <sub>2.45</sub> | 75.14 <sub>1.78</sub>  | 71.070.55             | 72.24 <sub>1.54</sub> | 70.210.65             |
| HOMIL        | 5×+20× | 86.364.29        | 90.711.68             | 86.384.26              | 79.281.04             | 83.381.19             | 79.581.12             |

Supplementary Table 4. Performance comparison on the task of grading gliomas.

| Category  |        | Internal dataset      |                       |                       | External dataset      |                       |                       |  |
|-----------|--------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|--|
|           |        | ACC                   | AUC                   | F1                    | ACC                   | AUC                   | F1                    |  |
| ADMII     | 5×     | 84.27 <sub>2.92</sub> | 91.89 <sub>3.65</sub> | 84.162.99             | 93.01 <sub>2.28</sub> | 97.63 <sub>0.74</sub> | 92.95 <sub>2.37</sub> |  |
| ABMIL     | 20×    | 84.352.59             | 91.652.96             | 84.322.59             | 93.54 <sub>0.50</sub> | 97.430.38             | 93.530.50             |  |
| CLAM-SB   | 5×     | 85.603.17             | 92.51 <sub>2.83</sub> | 85.39 <sub>3.24</sub> | 95.093.62             | 98.071.19             | 94.44 <sub>4.17</sub> |  |
| CLAW-SD   | 20×    | 82.18 <sub>2.99</sub> | 91.682.91             | 82.062.97             | 91.80 <sub>2.59</sub> | 97.64 <sub>1.16</sub> | 91.62 <sub>2.77</sub> |  |
| CLAM MD   | 5×     | 84.27 <sub>3.80</sub> | 92.043.69             | 84.07 <sub>3.78</sub> | 92.27 <sub>2.28</sub> | $97.20_{0.77}$        | 91.32 <sub>2.51</sub> |  |
| CLAM-MB   | 20×    | 85.363.72             | 92.37 <sub>2.44</sub> | 85.323.71             | 93.54 <sub>2.24</sub> | 97.690.88             | 93.522.22             |  |
| TD AND MH | 5×     | 86.924.19             | 92.643.67             | 86.714.29             | 93.132.67             | 97.95 <sub>0.53</sub> | 92.203.13             |  |
| TRANS-MIL | 20×    | 84.67 <sub>3.69</sub> | 93.662.31             | 84.283.54             | 92.54 <sub>2.64</sub> | 98.27 <sub>0.54</sub> | 91.48 <sub>3.03</sub> |  |
| DTED      | 5×     | 85.33 <sub>4.27</sub> | $92.30_{3.92}$        | 84.93 <sub>4.87</sub> | 94.48 <sub>1.29</sub> | 98.37 <sub>0.70</sub> | 94.49 <sub>1.29</sub> |  |
| DTFD      | 20×    | 86.852.04             | 93.822.02             | 86.822.04             | 94.161.99             | 98.060.80             | 94.161.98             |  |
| D.C.I.    | 5×     | 88.743.33             | 94.512.47             | 88.723.31             | 95.091.64             | 98.471.19             | 95.031.68             |  |
| BCL       | 20×    | -                     | -                     | -                     | -                     | -                     | -                     |  |
| MS-ABMIL  | 5×+20× | 85.511.64             | 92.681.87             | 85.501.66             | 93.911.20             | 98.120.24             | 93.911.16             |  |
| номи      | 5×     | 89.402.25             | 95.861.89             | 89.372.20             | 95.091.86             | 98.44 <sub>0.94</sub> | 95.04 <sub>1.87</sub> |  |
| HOMIL     | 5×+20× | 91.212.07             | 96.091.62             | 91.192.09             | 96.93 <sub>1.86</sub> | 99.37 <sub>0.58</sub> | 96.921.87             |  |