Ivy GAP: An Anatomic Transcriptional Atlas of Glioblastoma

Nameeta Shah, Ph.D.
Ivy Glioblastoma Atlas Project (Ivy GAP)

THE BEN & CATHERINE IVY FOUNDATION
Funding Patient-Focused Research on Gliomas

SWEDISH

NEUROSCIENCE INSTITUTE

https://ivygap.swedish.org/

http://glioblastoma.alleninstitute.org/
Glioblastoma multiforme (GBM)

• Grade IV brain tumor

• Surgery, radiation + chemotherapy (TMZ)

• Median survival – 15 months, 2 year survival is 30%
Ivy Glioblastoma Atlas Project (Ivy GAP)

- GBM treatment challenges
  - Inter and intra tumor heterogeneity
  - GBM stem cells
Ivy Glioblastoma Atlas Project (Ivy GAP)

• Study Goals

  • Molecular characterization of
    1. GBM anatomic features
      • Glioblastoma, WHO grade IV — Glioblastomas are densely cellular, pleomorphic tumors with mitotic activity and either microvascular proliferation or necrosis, or both.
    2. GBM stem-like cells

• Community resource
Ivy Glioblastoma Atlas Project (Ivy GAP)
Tissue processing

Slide 1  Slide 2  Slide 3  Slide 4  Slide 5  Slide 45
1.1  5.1  1.2  5.2  1.3  5.3  1.4  5.4  1.5  5.5  1.45  5.45
2.1  6.1  2.2  6.2  2.3  6.3  2.4  6.4  2.5  6.5  2.45  6.45
3.1  7.1  3.2  7.2  3.3  7.3  3.4  7.4  3.5  7.5  3.45  7.45
4.1  8.1  4.2  8.2  4.3  8.3  4.4  8.4  4.5  8.5  4.45  8.45

D 9 x 7.5 x 9 mm
In situ hybridization (ISH)

• ISH is used to detect specific genes within a section of tissue.
  • non-radioactive, digoxigenin (DIG) based technique
  • Gene specific riboprobe (400-1000bp)

• Feulgen-HP yellow DNA counterstain is a nuclear stain
Anatomic features
Anatomic features

- LE
- Leading Edge
Anatomic features

• IT
  • Infiltrating Tumor
Anatomic features

- CT
  - Cellular Tumor
Anatomic features

- PAN
  - Pseudopalisading cells around necrosis
Anatomic features

• PNZ
  • Perinecrotic zone

- GBM - Glioblastoma
- LEregion - Leading Edge Region
- LE - Leading Edge
- LE-reference-histology
- LEh bv - Hyperplastic blood vessels in leading edge
- ITregion - Infiltrating Tumor Region
- IT - Infiltrating Tumor
- IT-reference-histology
- ITh bv - Hyperplastic blood vessels in infiltrating tumor
- CTRegion - Cellular Tumor Region
- CT - Cellular Tumor
  • CT-reference-histology
  • CT-reference-genes
  • CT-controls
- CTpnz - Perinecrotic zone
  • CTpnz-reference-genes
- CTpn - Pseudopalisading cells but no visible necrosis
- CTpan - Pseudopalisading cells around necrosis
  • CTpan-reference-histology
  • CTpan-reference-genes
- CTth b - Hyperplastic blood vessels in cellular tumor
  • CTth bv-reference-genes
- CTmvp - Microvascular proliferation
  • CTmvp-reference-histology
  • CTmvp-reference-genes
- CTne - Necrosis
Anatomic features

- MVP
- Microvascular proliferation
Anatomic features

- HBV
- Hyperplastic blood vessels
Anatomic features RNA-Seq

- Screen of 5 features identified by H&E staining
  - LE - 19 samples
  - IT - 24 samples
  - CT - 30 samples
  - MVP - 25 samples
  - PAN - 24 samples
- 10 tumors for a total of 122 RNA samples.
Anatomic features ISH for Enriched Genes

- Final screen of 29 tumors with 37 genes enriched in particular anatomic features as identified in Anatomic features RNA-Seq study.

<table>
<thead>
<tr>
<th>LE/IT</th>
<th>CT</th>
<th>PAN</th>
<th>MVP/PAN</th>
<th>MVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>MYL12B</td>
<td>BCAN</td>
<td>ARRDC3</td>
<td>ATF3</td>
<td>ELTD1</td>
</tr>
<tr>
<td>NREP</td>
<td>DDR1</td>
<td>BNIP3</td>
<td>BTG1</td>
<td>ENPEP</td>
</tr>
<tr>
<td>TAXBP3</td>
<td>HIST1HE</td>
<td>CA9</td>
<td>CLEC2B</td>
<td>ESM1</td>
</tr>
<tr>
<td>TNFAIP1</td>
<td>NOVA1</td>
<td>DOK5</td>
<td>ISG20</td>
<td>FAM62B</td>
</tr>
<tr>
<td>NUSAP1</td>
<td>NDRG1</td>
<td>KLF6</td>
<td>KLF6</td>
<td>ITGA1</td>
</tr>
<tr>
<td>PTPRZ1</td>
<td>PYGL</td>
<td>LGALS3</td>
<td>LGALS3</td>
<td>ITGA1</td>
</tr>
<tr>
<td>TPX2</td>
<td>TREM1</td>
<td>MYADM</td>
<td>MYADM</td>
<td>OR5E1</td>
</tr>
<tr>
<td>UHRF1</td>
<td></td>
<td>SOCS3</td>
<td>SOCS3</td>
<td>TES</td>
</tr>
<tr>
<td></td>
<td></td>
<td>STC1</td>
<td>STC1</td>
<td></td>
</tr>
</tbody>
</table>
Anatomic features ISH for Enriched Genes: LE

RNA-seq
SNAP25 p = 3.3e-18

ISH

Annotation

H&E
Anatomic features ISH for Enriched Genes: CT

$UHRF1\ p = 6.4e^{-19}$
Anatomic features ISH for Enriched Genes: PAN

TREM1 \( p = 4 \times 10^{-13} \)

RPKM

LE  IT  CT  PAN  MVP

795 microns
Anatomic features ISH for Enriched Genes: MVP

$ELTD1 \ p = 5.8e^{-17}$
Anatomic features ISH for Enriched Genes: MVP/PAN

KLF6 p = 2.7e-18
Cancer Stem Cells ISH Survey

• Initial screen of 16 tumors with 56 genes to putative cancer stem cell-enriched genes to identify a 20 probe reference set, which was then used in an extensive screen of 41 tumors.
Cancer Stem Cells ISH Survey

- 20 probe reference set, which was then used in an extensive screen of 41 tumors.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIRC5</td>
<td>MYC</td>
</tr>
<tr>
<td>CD44</td>
<td>NOS2</td>
</tr>
<tr>
<td>DANCR</td>
<td>OLIG2</td>
</tr>
<tr>
<td>EZH2</td>
<td>PDGFRA</td>
</tr>
<tr>
<td>HIF1A</td>
<td>PDPN</td>
</tr>
<tr>
<td>ID1</td>
<td>PI3</td>
</tr>
<tr>
<td>ID2</td>
<td>POSTN</td>
</tr>
<tr>
<td>IGFBP2</td>
<td>PROM1</td>
</tr>
<tr>
<td>ITGA6</td>
<td>TGFRB2</td>
</tr>
<tr>
<td>MECOM</td>
<td>TNFAIP3</td>
</tr>
<tr>
<td>MET</td>
<td></td>
</tr>
</tbody>
</table>
Cancer Stem Cells RNA-Seq

- Screen of 35 types of putative cancer stem cell clusters identified by ISH with 17 genes in 34 tumors for a total of 148 RNA samples.

<table>
<thead>
<tr>
<th>CT</th>
<th>PNZ</th>
<th>PAN</th>
<th>HBV</th>
<th>MVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD44</td>
<td>CD44</td>
<td>ID2</td>
<td>CD44</td>
<td>ITGA6</td>
</tr>
<tr>
<td>DANCR</td>
<td>DANCR</td>
<td>MYC</td>
<td>DANCR</td>
<td>TGFBR2</td>
</tr>
<tr>
<td>HIF1A</td>
<td>ID1</td>
<td>PDPN</td>
<td>HIF1A</td>
<td></td>
</tr>
<tr>
<td>ID1</td>
<td>IGFBP2</td>
<td>PI3</td>
<td>IGFBP2</td>
<td></td>
</tr>
<tr>
<td>IGFBP2</td>
<td>MYC</td>
<td>PROM1</td>
<td>MVP</td>
<td></td>
</tr>
<tr>
<td>MET</td>
<td>PDPN</td>
<td>TNFAIP3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NOS2</td>
<td>P13</td>
<td></td>
<td>POSTN</td>
<td></td>
</tr>
<tr>
<td>PDGFRA</td>
<td>PROM1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDPN</td>
<td>TNFAIP3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>POSTN</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cancer Stem Cells ISH for Enriched Genes

- Final screen of 37 tumors with 75 genes to genes enriched in putative cancer stem cell clusters as identified in Cancer Stem Cells RNA-Seq study.

<table>
<thead>
<tr>
<th>Gene 1</th>
<th>Gene 2</th>
<th>Gene 3</th>
<th>Gene 4</th>
<th>Gene 5</th>
<th>Gene 6</th>
<th>Gene 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADAM9</td>
<td>CTSH</td>
<td>FAS</td>
<td>FL30</td>
<td>OCIAD2</td>
<td>SERTAD1</td>
<td></td>
</tr>
<tr>
<td>ARL4C</td>
<td>CTSL1</td>
<td>FILP1</td>
<td>IL6</td>
<td>PPAP2A</td>
<td>SHC1</td>
<td></td>
</tr>
<tr>
<td>ASS1</td>
<td>CYR61</td>
<td>FN1</td>
<td>L3RA2</td>
<td>PPPR5A</td>
<td>SLC25A24</td>
<td></td>
</tr>
<tr>
<td>ATF3</td>
<td>DAB2</td>
<td>FNDC3B</td>
<td>LAPT4M</td>
<td>PPAP3B</td>
<td>SLC4A7</td>
<td></td>
</tr>
<tr>
<td>C2orf75</td>
<td>DCN</td>
<td>FZD7</td>
<td>LCP1</td>
<td>PRSS23</td>
<td>SQRDL</td>
<td></td>
</tr>
<tr>
<td>C5orf48</td>
<td>DIO2</td>
<td>GOS2</td>
<td>LIF</td>
<td>RAC2</td>
<td>SRPX</td>
<td></td>
</tr>
<tr>
<td>C8orf4</td>
<td>DKK1</td>
<td>GLPR1</td>
<td>LPAR6</td>
<td>RARRES2</td>
<td>TAGLN2</td>
<td></td>
</tr>
<tr>
<td>CAPG</td>
<td>EFEMP1</td>
<td>GLRX</td>
<td>LYVE1</td>
<td>RGS16</td>
<td>TGFB1</td>
<td></td>
</tr>
<tr>
<td>CCL2</td>
<td>EMP1</td>
<td>GNG12</td>
<td>MAP2K3</td>
<td>RNA2.7</td>
<td>THBS1</td>
<td></td>
</tr>
<tr>
<td>CD13</td>
<td>FABP7</td>
<td>GPC4</td>
<td>MECOM1</td>
<td>RUNX1</td>
<td>TNC</td>
<td></td>
</tr>
<tr>
<td>CDCP1</td>
<td>FAM129A</td>
<td>GPC6</td>
<td>NMRK1</td>
<td>SD10A4</td>
<td>WNT5A</td>
<td></td>
</tr>
<tr>
<td>CNR1</td>
<td>FAM46A</td>
<td>ICAM1</td>
<td>NRP2</td>
<td>SDC4</td>
<td>WWTR1</td>
<td></td>
</tr>
<tr>
<td>CSF3</td>
<td>FAP</td>
<td>IER3</td>
<td>NT5E</td>
<td>SEC24D</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Annotations

- Machine learning
  - Mill
  - Random forests

- **Training**
  - Manual annotation
  - 3-5 sections/sub block

- Apply
  - 5-33 sections/sub block
Annotations

- Machine learning
  - Mill
  - Random forests

- Training
  - Manual annotation
  - 3-5 sections/sub block

- Apply
  - 5-33 sections/sub block
Annotations

- Nuclei segmentation
- Definiens
- Watershed algorithm
## Annotations - Accuracy

<table>
<thead>
<tr>
<th></th>
<th>LE</th>
<th>CT</th>
<th>IT</th>
<th>NE</th>
<th>PAN</th>
<th>MVP</th>
<th>HBV</th>
<th>ED</th>
<th>ICE</th>
<th>FOLD</th>
<th>SPA</th>
<th>EN</th>
<th>Total</th>
<th>Recall</th>
</tr>
</thead>
<tbody>
<tr>
<td>LE</td>
<td>101336</td>
<td>40</td>
<td>797</td>
<td>158</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>0</td>
<td>9</td>
<td>13</td>
<td>2</td>
<td>65</td>
<td>102427</td>
<td>98.93%</td>
</tr>
<tr>
<td>CT</td>
<td>205</td>
<td>306309</td>
<td>1496</td>
<td>1419</td>
<td>2095</td>
<td>806</td>
<td>1815</td>
<td>0</td>
<td>27</td>
<td>47</td>
<td>2</td>
<td>1724</td>
<td>315945</td>
<td>96.95%</td>
</tr>
<tr>
<td>IT</td>
<td>1269</td>
<td>437</td>
<td>152562</td>
<td>148</td>
<td>18</td>
<td>3</td>
<td>55</td>
<td>0</td>
<td>36</td>
<td>17</td>
<td>0</td>
<td>263</td>
<td>154808</td>
<td>98.55%</td>
</tr>
<tr>
<td>NE</td>
<td>318</td>
<td>2589</td>
<td>557</td>
<td>215087</td>
<td>732</td>
<td>54</td>
<td>877</td>
<td>0</td>
<td>9</td>
<td>98</td>
<td>64</td>
<td>3312</td>
<td>223697</td>
<td>96.15%</td>
</tr>
<tr>
<td>PAN</td>
<td>2</td>
<td>1843</td>
<td>29</td>
<td>212</td>
<td>133975</td>
<td>229</td>
<td>725</td>
<td>0</td>
<td>16</td>
<td>57</td>
<td>0</td>
<td>240</td>
<td>137328</td>
<td>97.56%</td>
</tr>
<tr>
<td>MVP</td>
<td>2</td>
<td>754</td>
<td>10</td>
<td>23</td>
<td>223</td>
<td>56567</td>
<td>259</td>
<td>0</td>
<td>0</td>
<td>19</td>
<td>4</td>
<td>139</td>
<td>580000</td>
<td>97.53%</td>
</tr>
<tr>
<td>HBV</td>
<td>11</td>
<td>2080</td>
<td>64</td>
<td>193</td>
<td>701</td>
<td>203</td>
<td>136295</td>
<td>0</td>
<td>12</td>
<td>18</td>
<td>0</td>
<td>190</td>
<td>139767</td>
<td>97.52%</td>
</tr>
<tr>
<td>ED</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>750</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>750</td>
<td>100.00%</td>
</tr>
<tr>
<td>ICE</td>
<td>0</td>
<td>7</td>
<td>8</td>
<td>19</td>
<td>7</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>1455</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1500</td>
<td>97.00%</td>
</tr>
<tr>
<td>FOLD</td>
<td>7</td>
<td>87</td>
<td>9</td>
<td>46</td>
<td>31</td>
<td>6</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>1724</td>
<td>0</td>
<td>7</td>
<td>304631</td>
<td>99.93%</td>
</tr>
<tr>
<td>SPA</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>31</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>310443</td>
<td>99.98%</td>
</tr>
<tr>
<td>EN</td>
<td>168</td>
<td>1310</td>
<td>445</td>
<td>1776</td>
<td>300</td>
<td>87</td>
<td>195</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>26</td>
<td>178379</td>
<td>97.64%</td>
</tr>
</tbody>
</table>

**Total** 103320 315459 155977 219112 138082 57955 140247 750 1565 304697 310541 184333 1932038

**Precision** 98.08% 97.10% 97.81% 98.16% 97.03% 97.61% 97.18% 100.00% 92.97% 99.91% 99.97% 96.77%

**ACCURACY** 98.22%
Image registration

- A multi-resolution elastic registration algorithm was utilized.
Informatics Data Processing Pipeline
Ivy GAP Image and RNA-Seq Database

http://glioblastoma.alleninstitute.org/
Specimen Metadata and ISH Searches
VEGFA Expression in PAN

[Image of a histological section showing tissue samples with annotations and gene expression data from the IVY GAP database]
Anatomic Feature Boundaries
ISH and Anatomic Feature Masks
RNA-Seq Data Searches

IVY GAP
Ivy Glioblastoma Atlas Project

Browse By Differential Expression
- Leading Edge
- Cellular Tumor
- Pseudopalisading cells around necrosis
- Microvascular proliferation

Ivy Glioblastoma Atlas Project

About the Ivy Glioblastoma Atlas Project
The Ivy Glioblastoma Atlas Project is a foundational resource for exploring the anatomic and genetic basis of glioblastoma at the cellular and molecular levels. [more]

About the RNA-Seq Data
RNA sequencing data for anatomic structures and putative cancer stem cell clusters isolated by laser microdissection
- Anatomic Structures RNA-Seq
  Screen of 6 structures (Leading Edge, Infiltrating Tumor, Cellular Tumor, Microvascular Proliferation, and Pseudopalisading Cells Around Necrosis) identified by H&E staining. A total of 122 RNA samples were generated from 10 tumors.
- Cancer Stem Cells RNA-Seq
  Screen of 35 clusters of putative cancer stem cells identified by ISH with a 17
PAN-Enriched Gene Expression

<table>
<thead>
<tr>
<th>Tumor Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaplastic Tumors</td>
<td>Yes</td>
</tr>
<tr>
<td>Extent of Resection</td>
<td>Complete</td>
</tr>
<tr>
<td>MGMT Methylation</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gene Symbol</th>
<th>Fold Change</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL6</td>
<td>74.721</td>
<td>5.36e-13</td>
</tr>
<tr>
<td>VEGFA</td>
<td>53.597</td>
<td>4.62e-50</td>
</tr>
<tr>
<td>HIF1A</td>
<td>32.378</td>
<td>3.95e-35</td>
</tr>
<tr>
<td>ADAM</td>
<td>25.549</td>
<td>1.93e-29</td>
</tr>
<tr>
<td>C12orf16</td>
<td>20.295</td>
<td>2.09e-38</td>
</tr>
<tr>
<td>CAG</td>
<td>18.908</td>
<td>2.02e-18</td>
</tr>
<tr>
<td>LDG</td>
<td>16.796</td>
<td>3.51e-22</td>
</tr>
<tr>
<td>NDRG1</td>
<td>15.627</td>
<td>9.33e-21</td>
</tr>
<tr>
<td>MX1</td>
<td>13.304</td>
<td>1.40e-16</td>
</tr>
<tr>
<td>LOC100526105</td>
<td>13.237</td>
<td>6.45e-11</td>
</tr>
<tr>
<td>GI50248225</td>
<td>12.802</td>
<td>3.95e-12</td>
</tr>
<tr>
<td>TREM1</td>
<td>12.038</td>
<td>7.86e-11</td>
</tr>
<tr>
<td>ANXGPTL4</td>
<td>11.966</td>
<td>3.30e-15</td>
</tr>
<tr>
<td>2MIF55</td>
<td>11.087</td>
<td>5.54e-14</td>
</tr>
</tbody>
</table>
Ivy GAP Clinical and Genomic Database

About

The Ivy Glioblastoma Atlas Project Clinical and Genomic Database contains detailed clinical information including radiology and pathology images, genomic data, and prospectively collected outcomes data. This database is a companion database for the Ivy Glioblastoma Atlas Project.

Co-Principal Investigators

Swedish Neuroscience Institute
- Greg D. Polt, MD, Neurosurgeon
- Nameera Shah, PhD, Scientist

Allen Institute for Brain Science
- Ralph J. Pucihar, PhD, Research Alliance Manager

©2010-2015 IVY Glioblastoma Atlas Project, All Rights Reserved

https://ivygap.swedish.org/
Patient Treatment Timeline
Results

• Anatomic features RNA-Seq
  • 10 tumors for a total of 122 RNA samples.
    • LE - 19 samples
    • IT - 24 samples
    • CT - 30 samples
    • MVP - 25 samples
    • PAN - 24 samples
Molecular Subtype

840 genes are used to classify GBM in 4 molecular subtype

1. Neural
2. Proneural
3. Classical
4. Mesenchymal

An integrated genomic analysis identifies clinically relevant subtypes of glioblastoma characterized by abnormalities in PDGFRA, IDH1, EGFR and NF1.
Anatomic features and Molecular Subtype

Anatomic features and Molecular Subtype

Comparison of samples from the same tumor

Spearman’s $r$: 0.47, $p < 0.001$
Anatomic Features and Cell Types


- Molecular and genetic properties of tumors associated with local immune cytolytic activity, Rooney et. al., Cell, 2015.
Tumor Heterogeneity

First surgery - IDH1 mutation

Second surgery - IDH1 mutation

TP53 (Y234C)
ATRX (R2150S)
IDH1 (R123H)
IDH1 WT

TP53 (G244S)
PTPRZ1 → MET
EGFR amplification

MET (C541G)
IDH2 (A367S)

EGFR (V774M, P595L)
EGFR amplification

Tumor block
Histology
MSE
0
1
Conclusion

Histologically-distinct anatomic features exhibit highly conserved gene expression signatures across tumors despite intratumor and intertumor heterogeneity.

Fully-annotated anatomic transcriptional atlas

glioblastoma.alleninstitute.org

Allen Institute

Detailed clinical and genomic data

ivygap.org

Swedish Neuroscience Institute
Acknowledgements

Gene Selection and Advisors
Ken Aldape, MD, MD Anderson Cancer Center
Bruce Aronow, PhD, Cincinnati Children’s Hospital Medical Center
Brady Bernard, PhD, Institute for Systems Biology
Michael Berens, PhD, Translational Genomics Research Institute
Leroy Hood, MD, PhD, Institute for Systems Biology
Parvinder Hothi, PhD, Swedish Neuroscience Institute
Chris Hubert, PhD, Fred Hutchinson Cancer Research Center, Cleveland Clinic
Justin Lathia, PhD, Cleveland Clinic
Biaoyang Lin, PhD, Institute for Systems Biology
Jeremy Miller, PhD, Allen Institute
Jim Olson, MD PhD, Fred Hutchinson Cancer Research Center
Ralph B. Puchalski, PhD, Allen Institute
Robert Rostomily, MD, University of Washington
Nader Sanai, MD, Barrow Neurological Institute
Nameeta Shah, PhD, Swedish Neuroscience Institute
Ilya Shmulevich, PhD, Institute for Systems Biology
Qiang Tian, MD, PhD, Institute for Systems Biology
Ilya Ulasov, PhD, Swedish Neuroscience Institute

Tumor Accrual
Charles Cobbs, MD, Swedish Neuroscience Institute
Farrokh Farrokhi, MD, Virginia Mason Medical Center
Greg D. Foltz, MD, Swedish Neuroscience Institute

Neuropathology
Steve Rostad, MD, CellNetix

Radiology
Bart Keogh, MD, PhD, Swedish Neuroscience Institute and Radia, PS
Xu Feng, PhD, Radia, PS

Tissue and Clinical Data Collection, Data Analysis and Presentation
Swedish Neuroscience Institute team

Tissue Processing, Data Analysis and Presentation
Allen Institute teams

Semi-Automated Annotation
Steve White, PhD, White Marsh Forests, Inc.
Don Marsh, White Marsh Forests, Inc.
Steve Nomura, contractor and new medical school student
Questions?