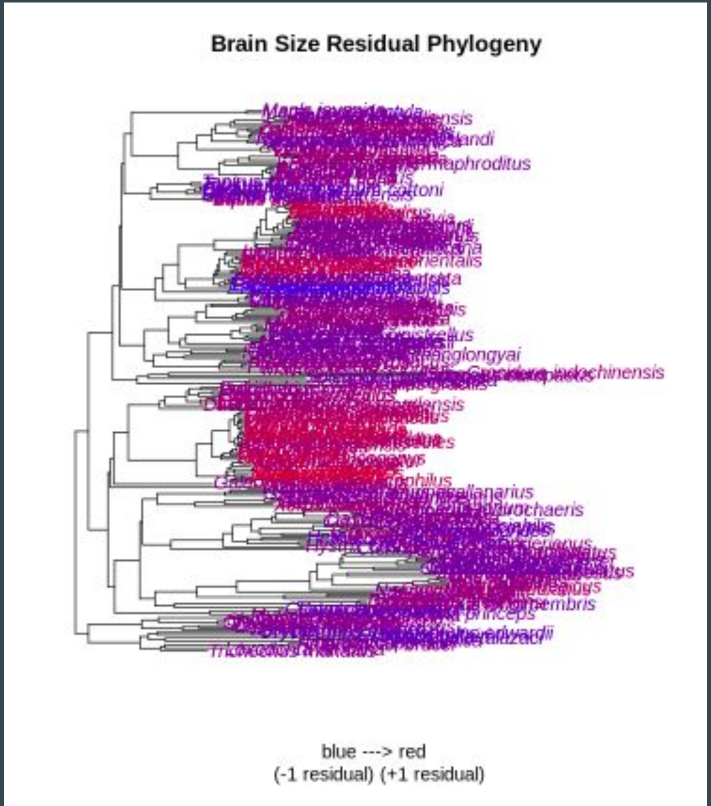
GEB - The Effect of Brain Size Residual on Striatal Cell Types

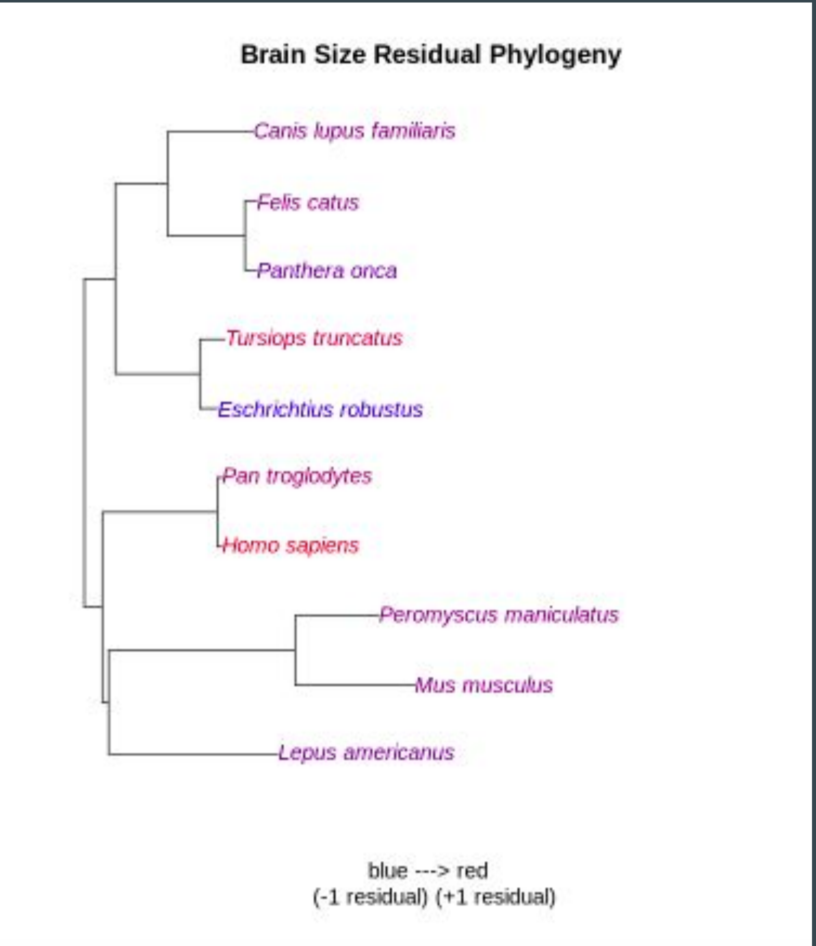
By Gabriel and Sumitra

Trait - Brain Size Residual



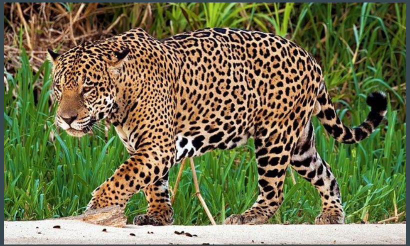
- Relation to cognition
- Possible limitations
- Brain size vs relative brain size
- Convergent evolution
- Cost of a larger brain size
- Advantages of larger brains
  - Foraging
  - Motor function
  - Social advantages

Species Of Interest



Canis lupus familiaris

Felis catus

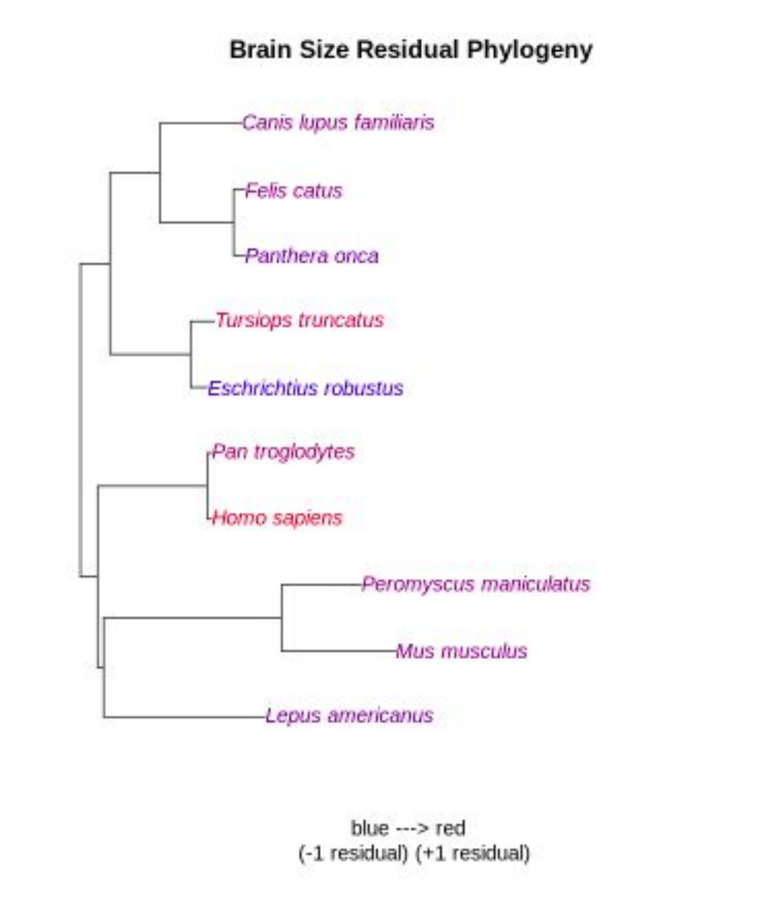


Panthera onca

Tursiops truncatus

Eschrichtius robustus

Species Of Interest



Pan troglodytes

Mus musculus

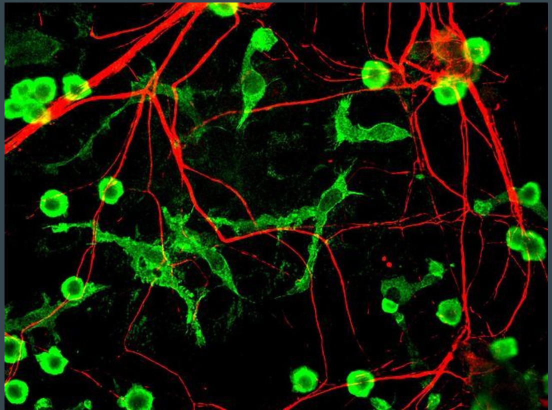
Peromyscus maniculatus

Lepus americanus

Cell types

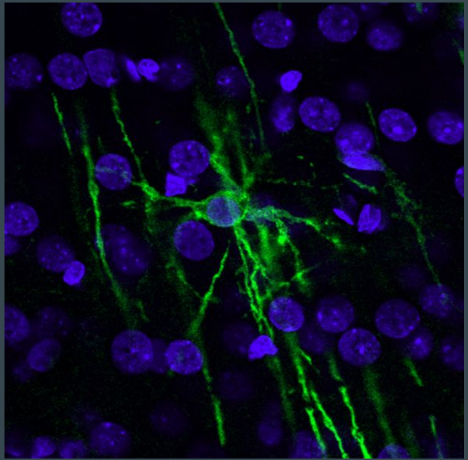
Microglia

- Immune system
- Relatively small
- Detects inflammation
- Synaptic pruning
- Neuron density



Oligodendrocyte Precursors

- Brain development
- Myelination in CNS
- Related to number of axons
- Multiple differentiation steps



Analysis

- Perform phylolm on every peak
- Correct p-values
- Visualize data
- Search UCSC genome browser for top peaks
- Carry out gene ontology analysis for each cell type
- Consult literature for relevance of results

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for (j in c(1:26408)){
```

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names of the data do not match with tip labels.
```

No results were found.

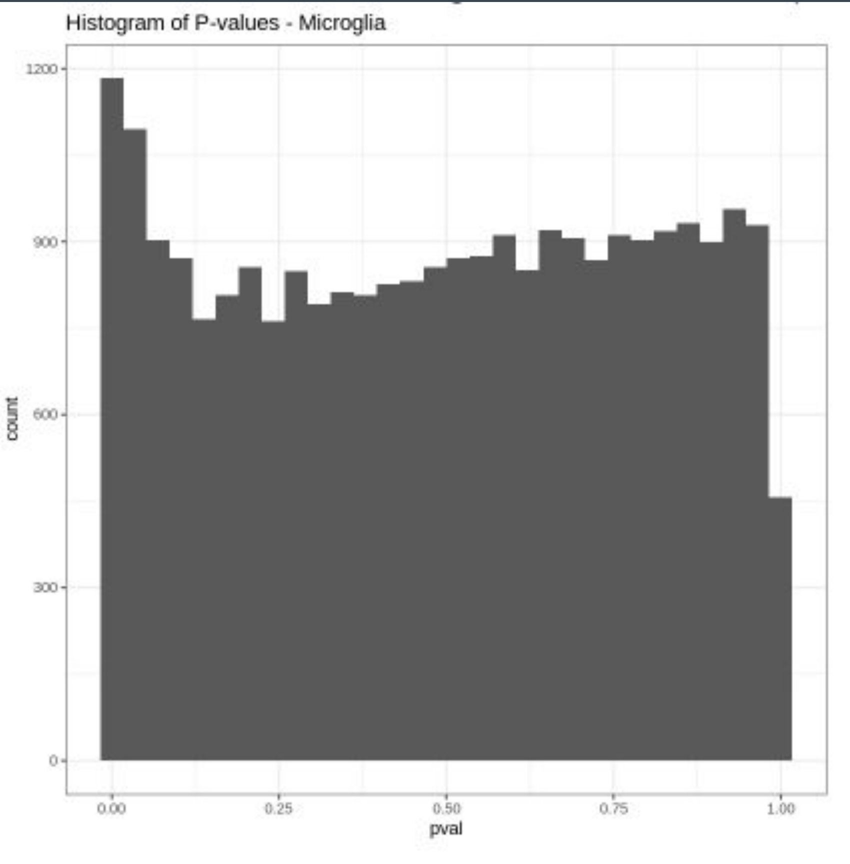
Your search was processed without automatic term mapping because it retrieved zero results.

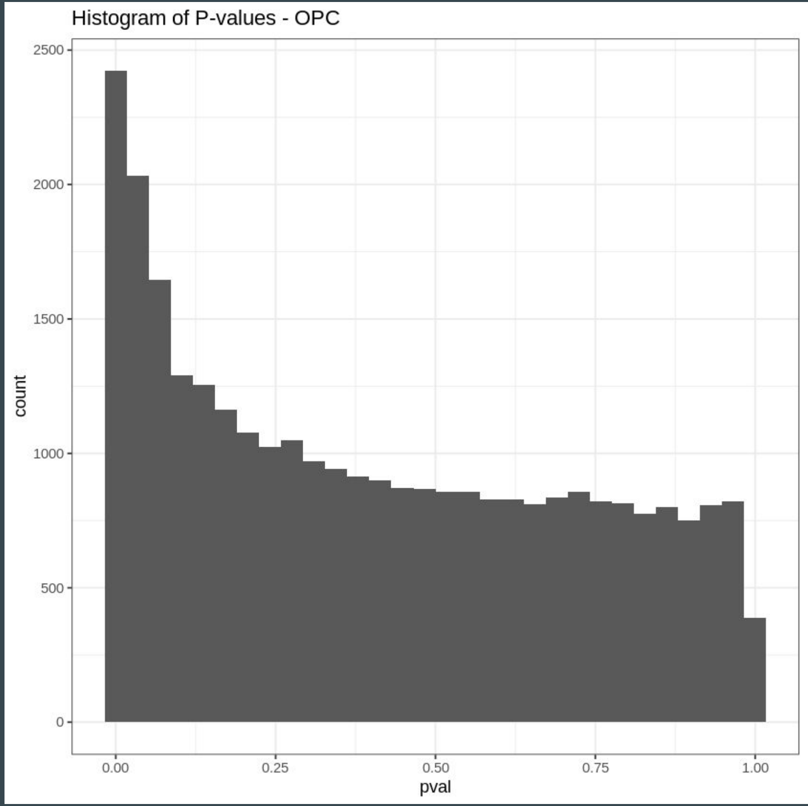
147536 rows × 2868 columns

Your session crashed after using all available RAM. If you are interested in access to high-RAM runtimes, you may want to check out Colab Pro.

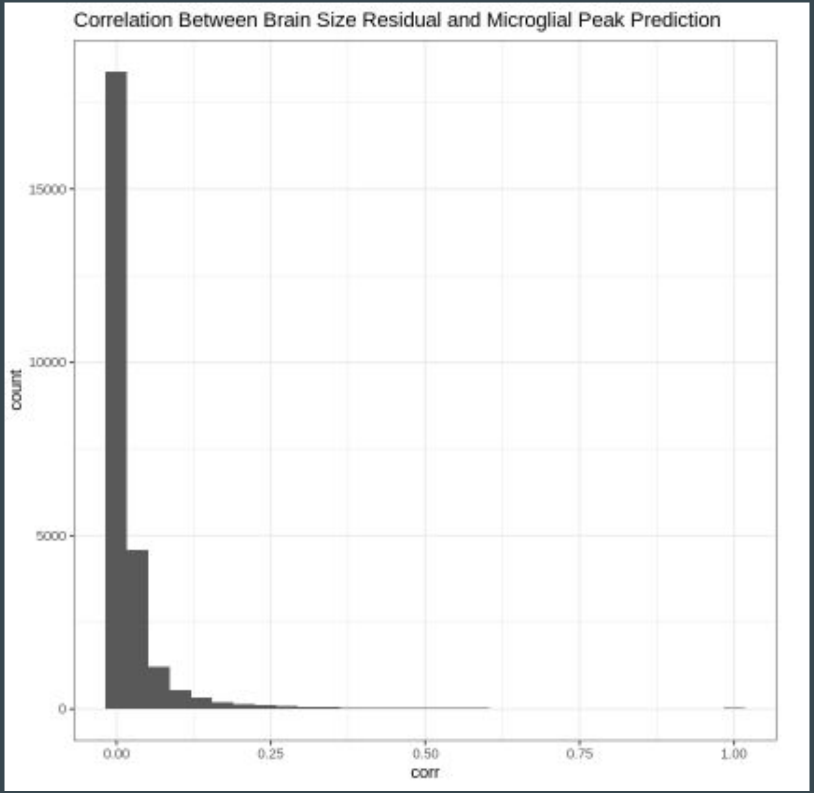
View runtime logs

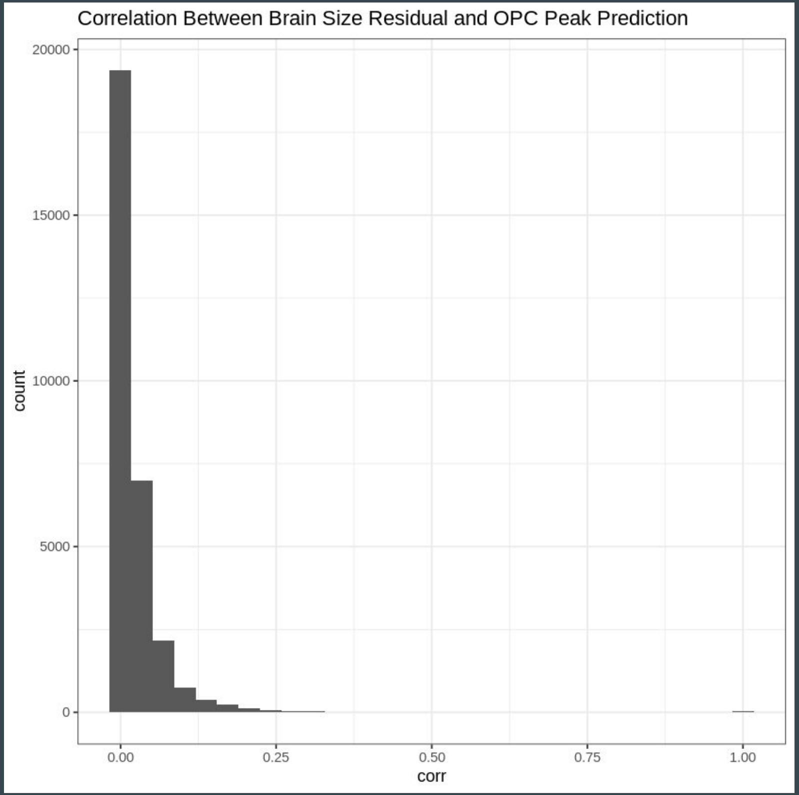
P-value histograms





Correlation histograms





Most significant peaks (microglia)

A data.frame: 54 × 6

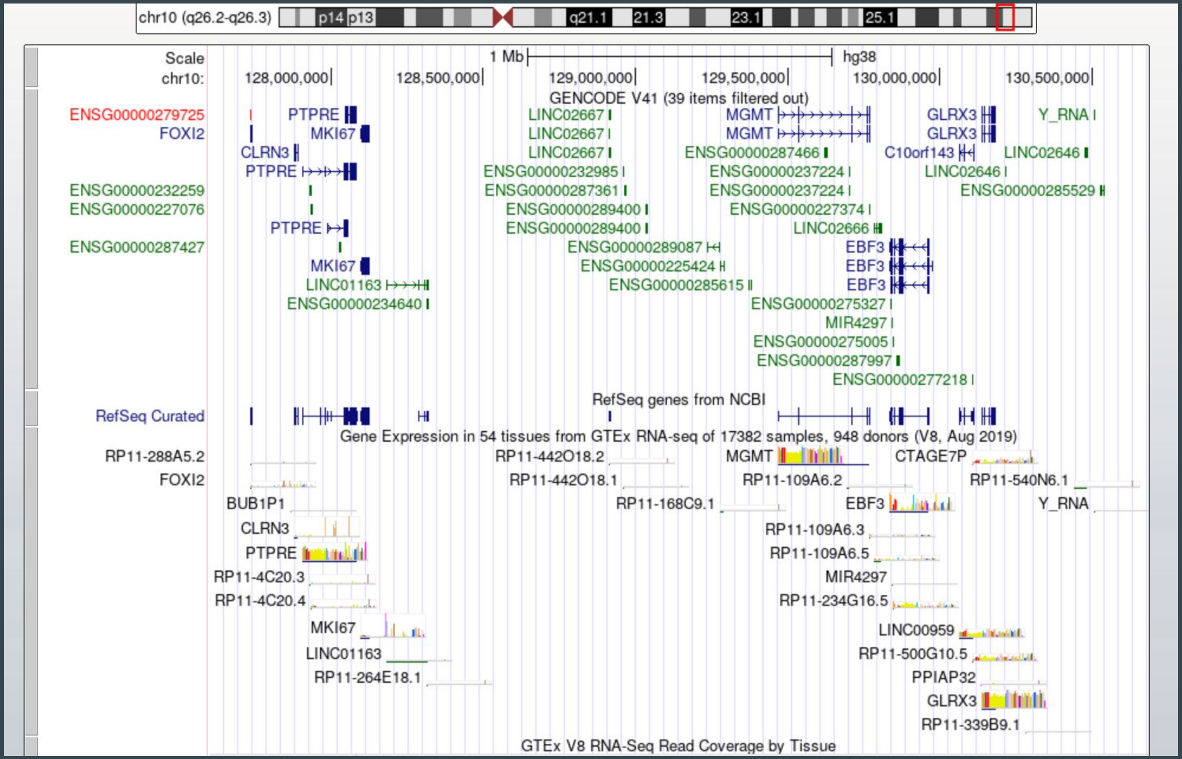
	X	id	pval	corr	adj_corr	padj
	<int>	<int>	<dbl>	<dbl>	<dbl>	<dbl>
22591	22591	22591	4.590132e-09	0.4278780	0.4186502	0.0001199034
10632	10632	10632	5.946320e-09	0.2638459	0.2572139	0.0001553238
15359	15359	15359	1.299916e-08	0.4413720	0.4313965	0.0003395380
16923	16923	16923	1.343928e-08	0.3755603	0.3665104	0.0003510205
24078	24078	24078	2.454625e-08	0.5356723	0.5243472	0.0006410991

Most significant peaks (OPCs)

A data.frame: 40 × 6

	X	id	pval	corr	adj_corr	padj
	<int>	<int>	<dbl>	<dbl>	<dbl>	<dbl>
247	247	247	1.035269e-10	0.2990387	0.2930983	3.135414e-06
24243	24243	24243	5.060544e-10	0.3166590	0.3099596	1.532586e-05
1588	1588	1588	2.789634e-09	0.2504935	0.2444000	8.448127e-05
15646	15646	15646	4.456784e-09	0.3025237	0.2952583	1.349648e-04
23536	23536	23536	4.911464e-09	0.2770063	0.2701856	1.487290e-04

Microglial Associated Genes



- MGMT
  - DNA damage repair
  - Cancer cell regulation
  - Link to autism
- EBF3
  - B-Cell transcription factor
  - ASD and brain development
  - Neurodevelopmental syndrome
- GLRX3
  - Cell cycle regulation
  - Apoptosis inhibition
  - Neurodegenerative disease

Microglia Gene Ontology

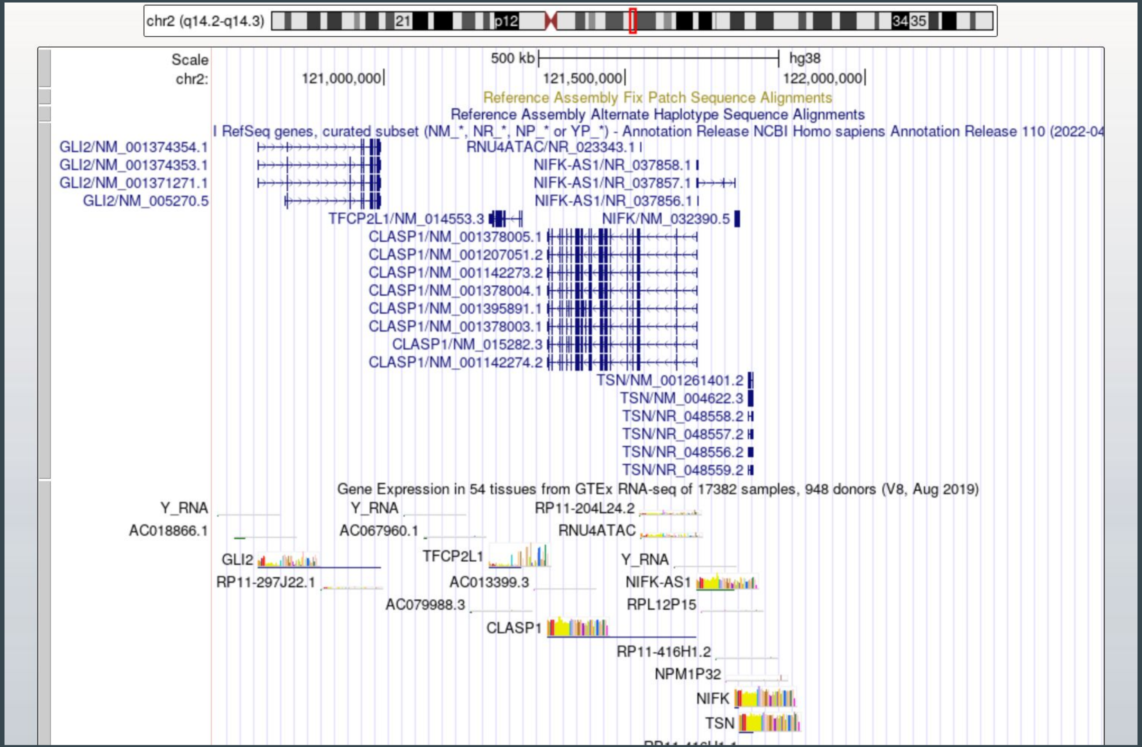
Term Name	Binom Rank	Binom Raw P-Value
hemopoiesis	2	1.1615e-6
hematopoietic or lymphoid organ development	4	3.2543e-6
immune system development	5	7.2083e-6
positive regulation of carbohydrate metabolic process	12	3.0820e-5
regulation of carbohydrate biosynthetic process	14	4.3490e-5

Positive

Term Name	Binom Rank	Binom Raw P-Value	*Binom FDR Q-Val*
positive regulation of GTPase activity	3	1.0939e-6	4.7981e-3
platelet activation	5	4.0224e-6	1.0586e-2
regulation of GTPase activity	11	6.1443e-6	7.3502e-3
positive regulation of hydrolase activity	13	6.5499e-6	6.6300e-3
small GTPase mediated signal transduction	20	1.3885e-5	9.1356e-3
hematopoietic or lymphoid organ development	29	2.4986e-5	1.1338e-2
hemopoiesis	31	2.8871e-5	1.2255e-2
regulation of lymphocyte activation	32	2.9903e-5	1.2297e-2
positive regulation of cell adhesion	36	4.0867e-5	1.4938e-2
immune system development	41	5.0888e-5	1.6332e-2
regulation of small GTPase mediated signal transduction	44	5.7862e-5	1.7305e-2
regulation of cell adhesion	45	6.1412e-5	1.7958e-2
regulation of leukocyte activation	49	7.1041e-5	1.9078e-2
lymphocyte differentiation	70	1.3507e-4	2.5392e-2
regulation of cell activation	80	1.9218e-4	3.1611e-2
leukocyte differentiation	86	2.4946e-4	3.8171e-2

Negative

OPC Associated Genes



- CLASP1
  - Microtubule assembly
  - CLASP2 specific to brain cells
  - Axon growth
  - Cell division
  - Basal cortex
  - Cell morphology in embryo
- TSN
  - Chromosome translocation
  - Expression and gene silencing

OPC Gene Ontology

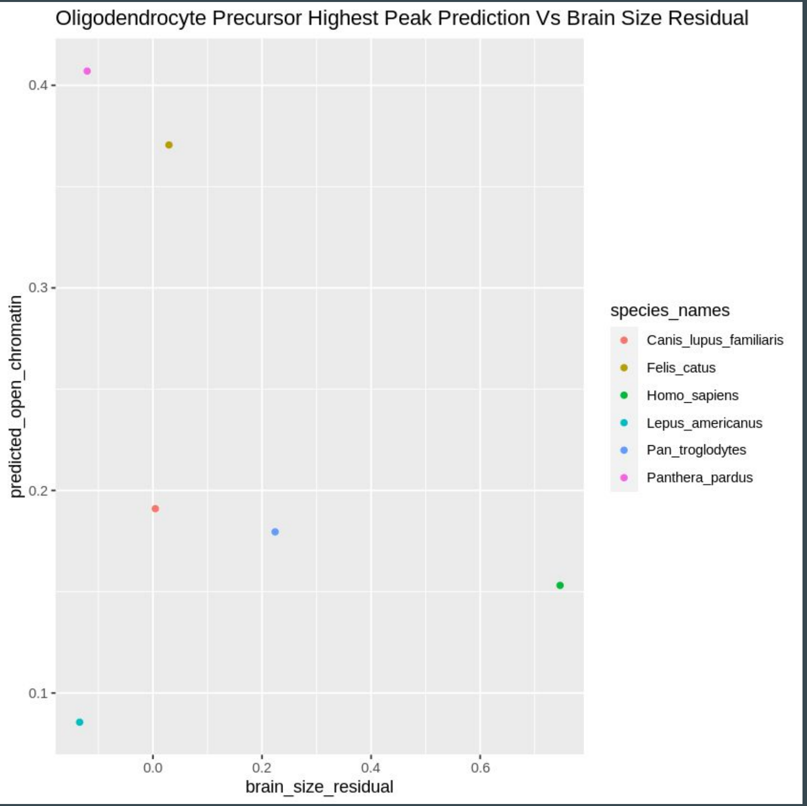
Term Name	Binom Rank	Binom Raw P-Value	*Binom FDR Q-Val*
3'-UTR-mediated mRNA destabilization	3	5.0916e-6	2.2333e-2

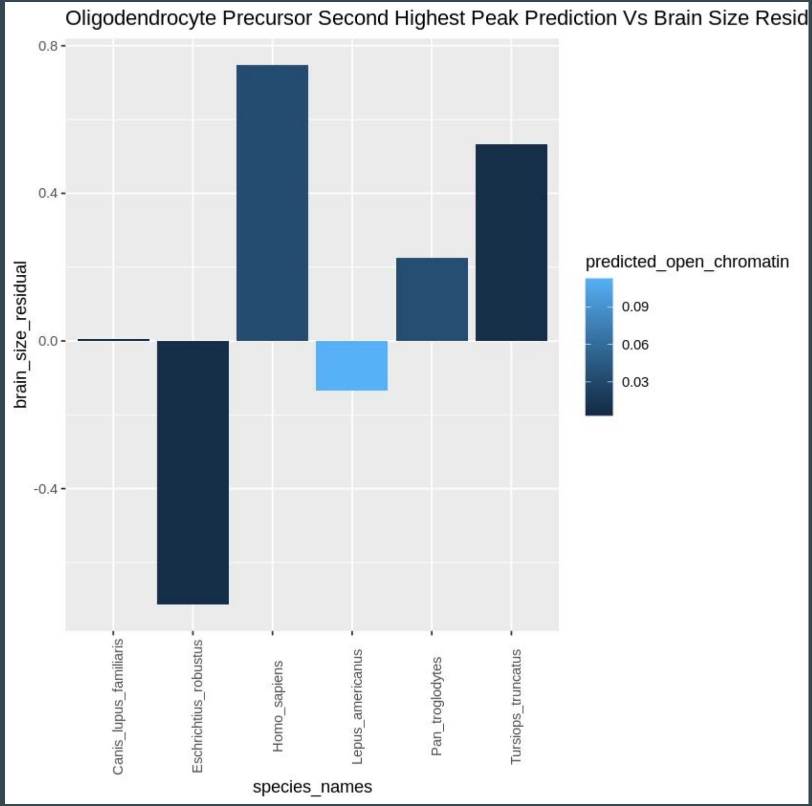
Positive

Term Name	Binom Rank	Binom Raw P-Value	*Binom FDR Q-Val*
respiratory distress	1	3.0456e-8	2.7888e-4
abnormal pectoral girdle bone morphology	2	2.1847e-7	1.0003e-3
abnormal appendicular skeleton morphology	3	3.0590e-7	9.3371e-4
abnormal breathing pattern	4	9.0387e-7	2.0692e-3
abnormal tarsal bone morphology	5	1.0303e-6	1.8868e-3
abnormal respiratory function	6	4.6178e-6	7.0476e-3
short limbs	7	5.5377e-6	7.2441e-3
abnormal thoracic cage morphology	10	1.3797e-5	1.2634e-2
small scapula	13	3.3635e-5	2.3692e-2
abnormal sternum morphology	14	3.4746e-5	2.2726e-2
small mandible	15	3.7774e-5	2.3060e-2
abnormal craniofacial bone morphology	16	4.6878e-5	2.6829e-2
neonatal lethality, complete penetrance	17	5.3627e-5	2.8886e-2
abnormal phalanx morphology	19	6.0274e-5	2.9049e-2
short mandible	21	6.6080e-5	2.8814e-2
abnormal mandible morphology	22	7.0003e-5	2.9137e-2
short nasal bone	23	7.0960e-5	2.8251e-2
increased diameter of long bones	25	8.1242e-5	2.9757e-2
abnormal scapula morphology	29	1.1044e-4	3.4872e-2
abnormal limb long bone morphology	35	1.2739e-4	3.3328e-2

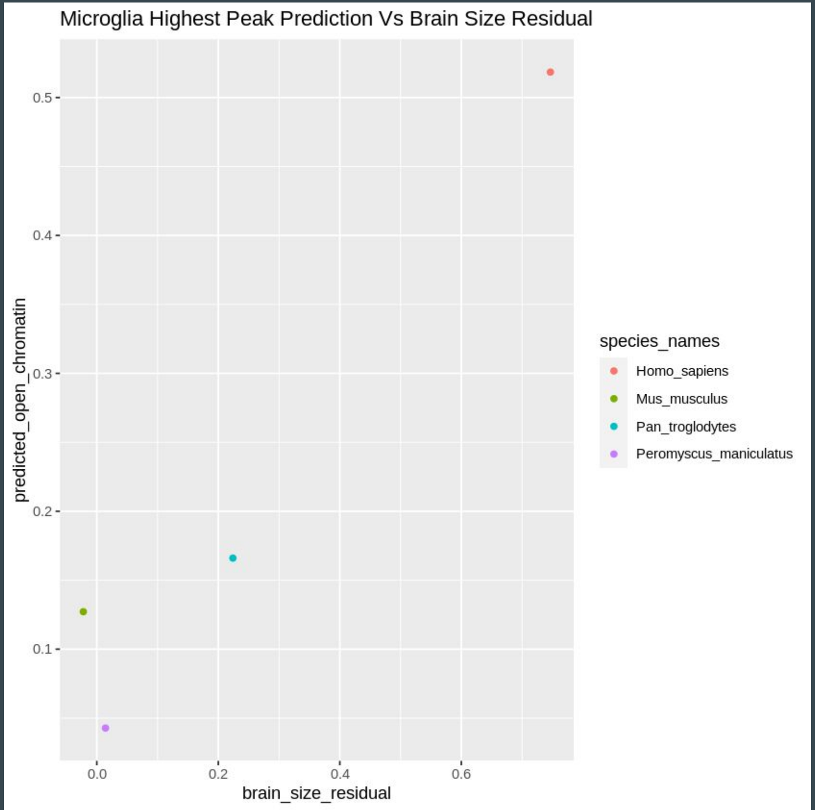
Negative

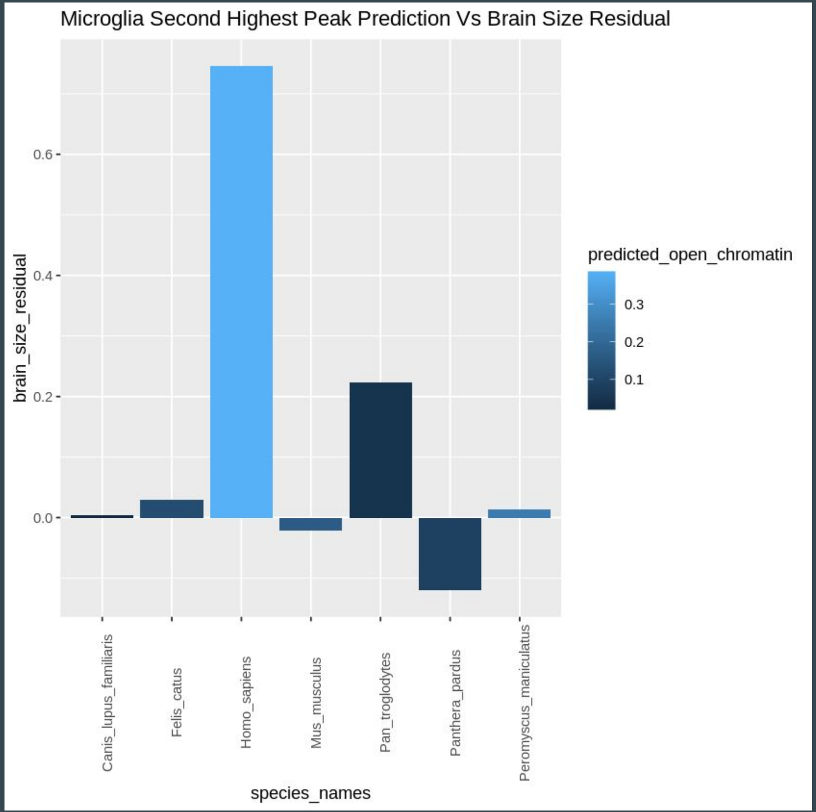
Trait Visualizations - OPC highest peaks



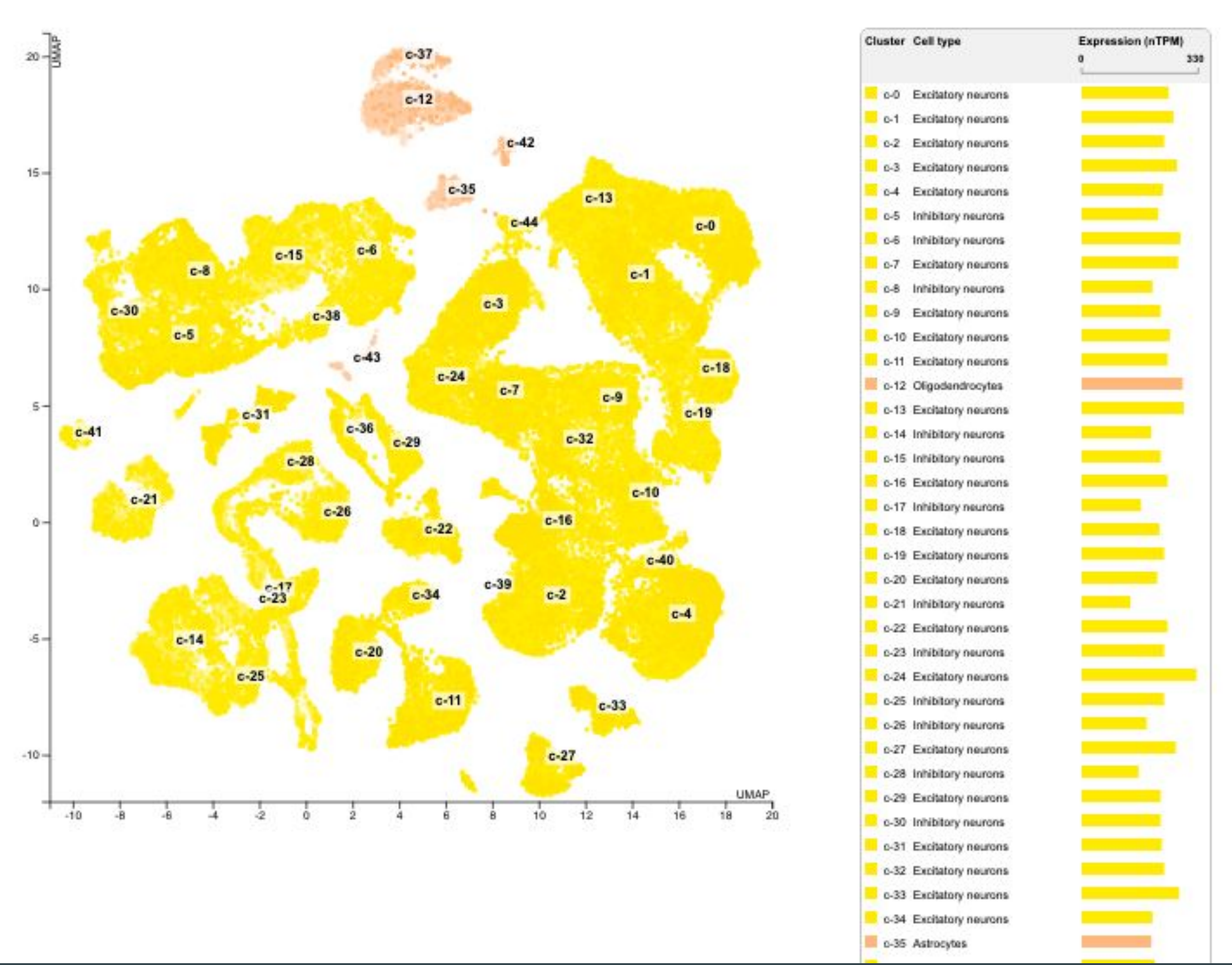


Trait Visualizations - Microglia highest peaks





Cell visualization - Heat Map


UMAP
Cluster Cell type Expression (nTPM)
0
330
c-0 Excitatory neurons
c-1 Excitatory neurons
c-2 Excitatory neurons
c-3 Excitatory neurons
c-4 Excitatory neurons
c-5 Inhibitory neurons
c-6 Inhibitory neurons
c-7 Excitatory neurons
c-8 Inhibitory neurons
c-9 Excitatory neurons
c-10 Excitatory neurons
c-11 Excitatory neurons
c-12 Oligodendrocytes
c-13 Excitatory neurons
c-14 Inhibitory neurons
c-15 Inhibitory neurons
c-16 Excitatory neurons
c-17 Inhibitory neurons
c-18 Excitatory neurons
c-19 Excitatory neurons
c-20 Excitatory neurons
c-21 Inhibitory neurons
c-22 Excitatory neurons
c-23 Inhibitory neurons
c-24 Excitatory neurons
c-25 Inhibitory neurons
c-26 Inhibitory neurons
c-27 Excitatory neurons
c-28 Inhibitory neurons
c-29 Excitatory neurons
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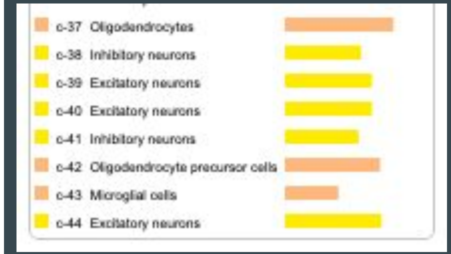
c-32 Excitatory neurons
c-33 Excitatory neurons
c-34 Excitatory neurons
c-35 Astrocytes

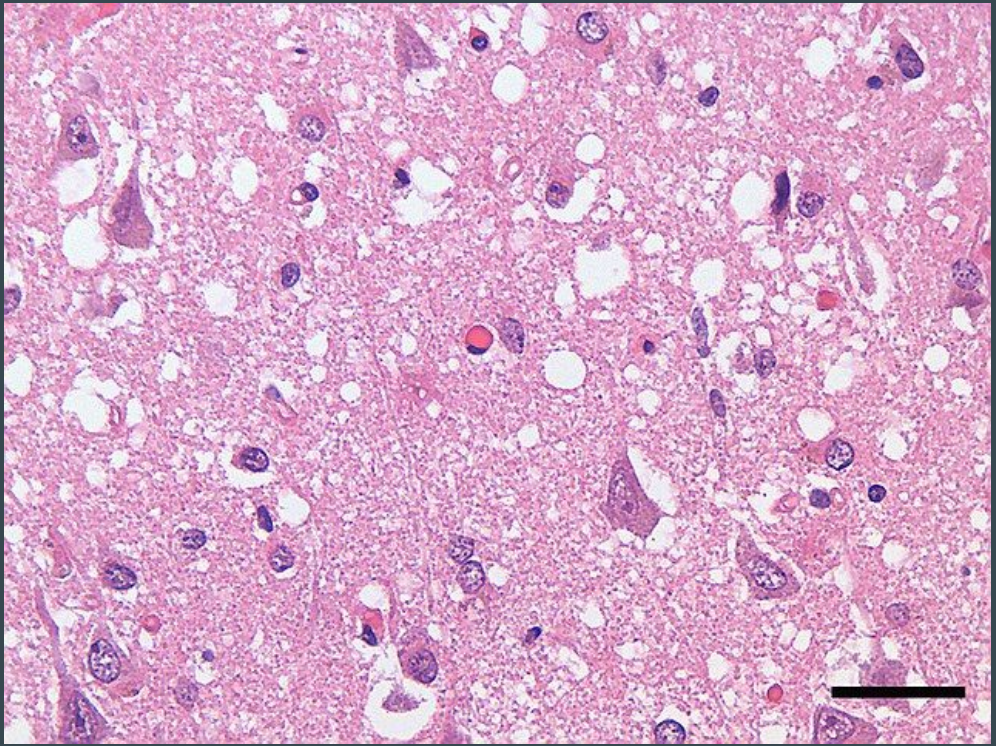

c-37 Oligodendrocytes
c-38 Inhibitory neurons
c-39 Excitatory neurons
c-40 Excitatory neurons
c-41 Inhibitory neurons
c-42 Oligodendrocyte precursor cells
c-43 Microglial cells
c-44 Excitatory neurons

CLASP1

Grad analysis

Prion disease

- Neurodegenerative disease
    - Parkinson’s
    - Alzheimer’s
- Misfolded proteins
- Self-propagating
- Alpha synuclein accumulation
- Sporadic, environmental and genetic basis
- Potential epigenetic markers

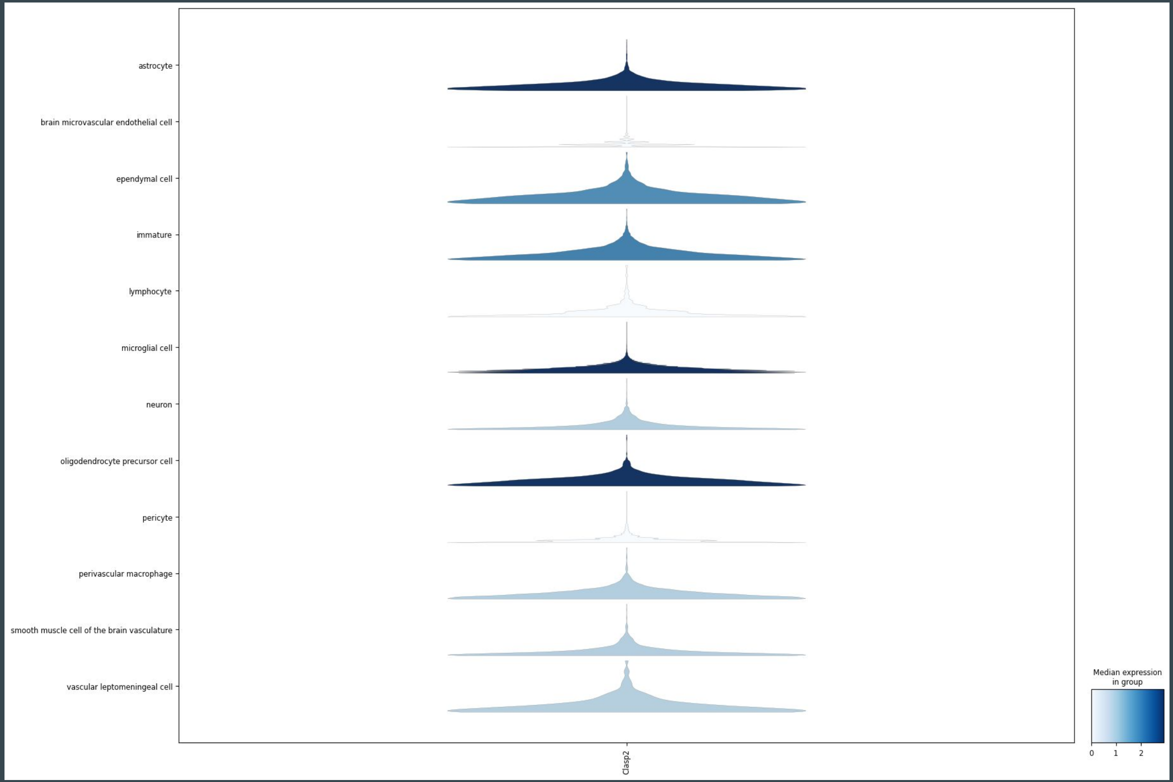


Dataset and Results

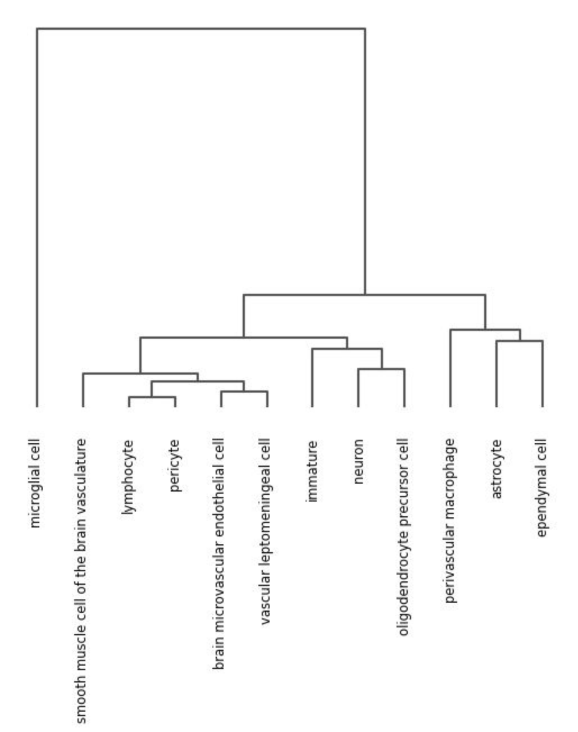
Mouse RNA-seq data

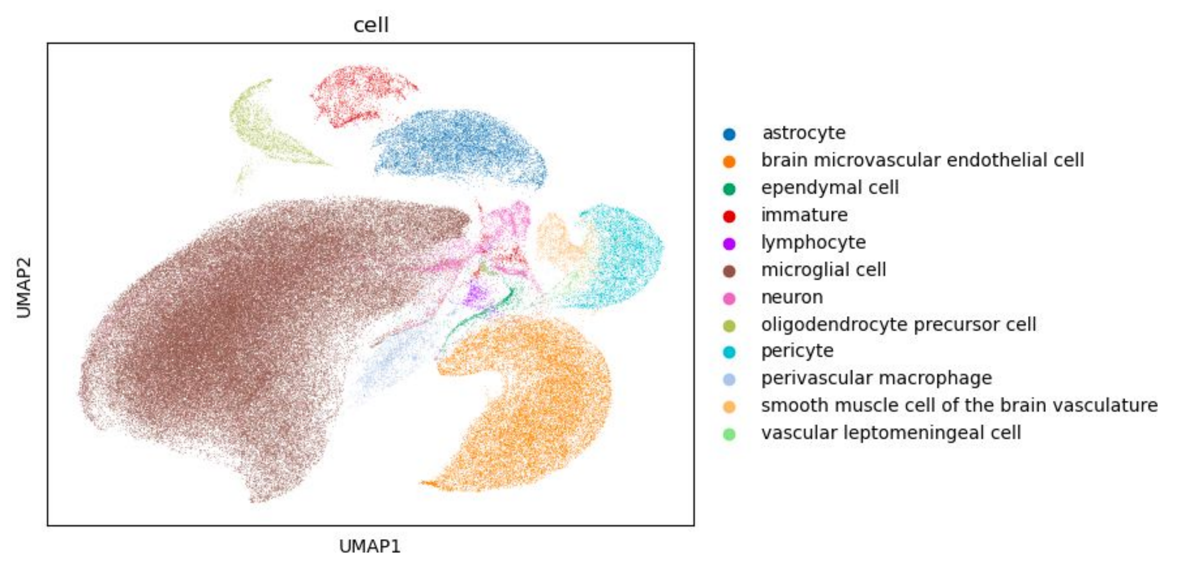
Performed cell-type analysis

Performed disease specific analysis

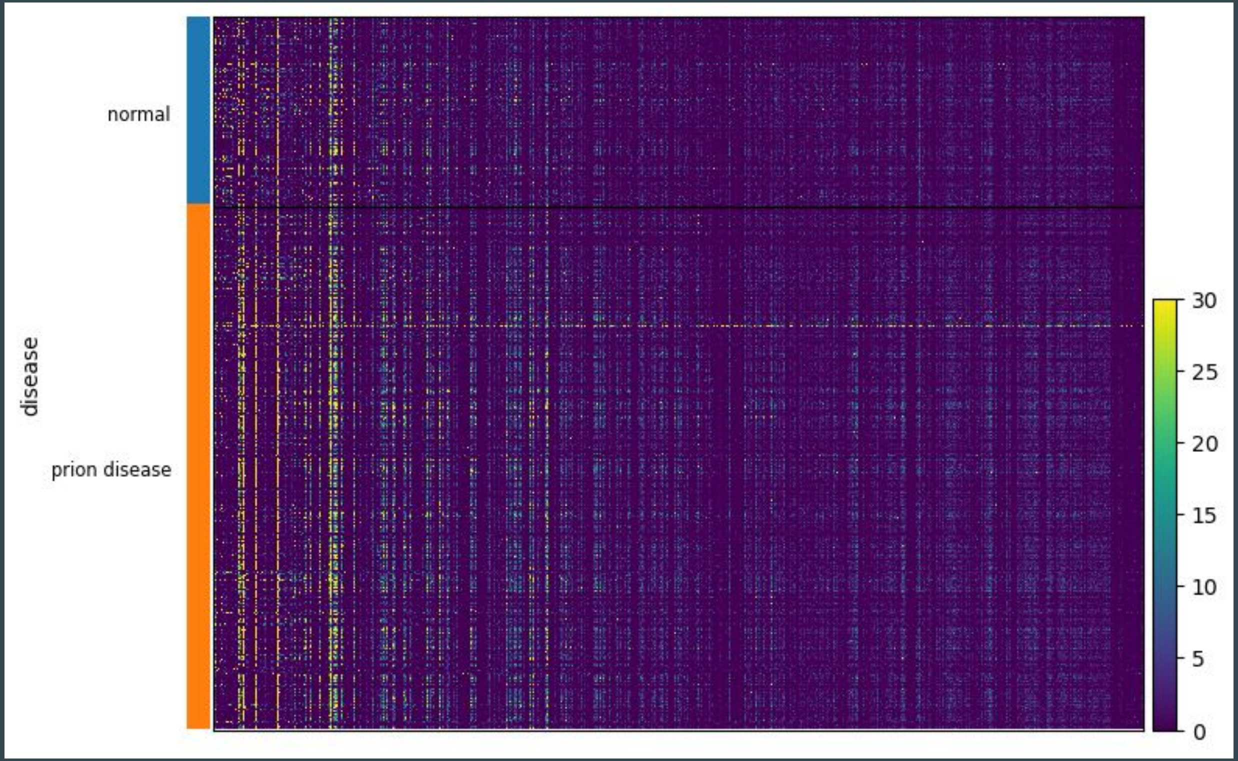


UMAP and Clustering



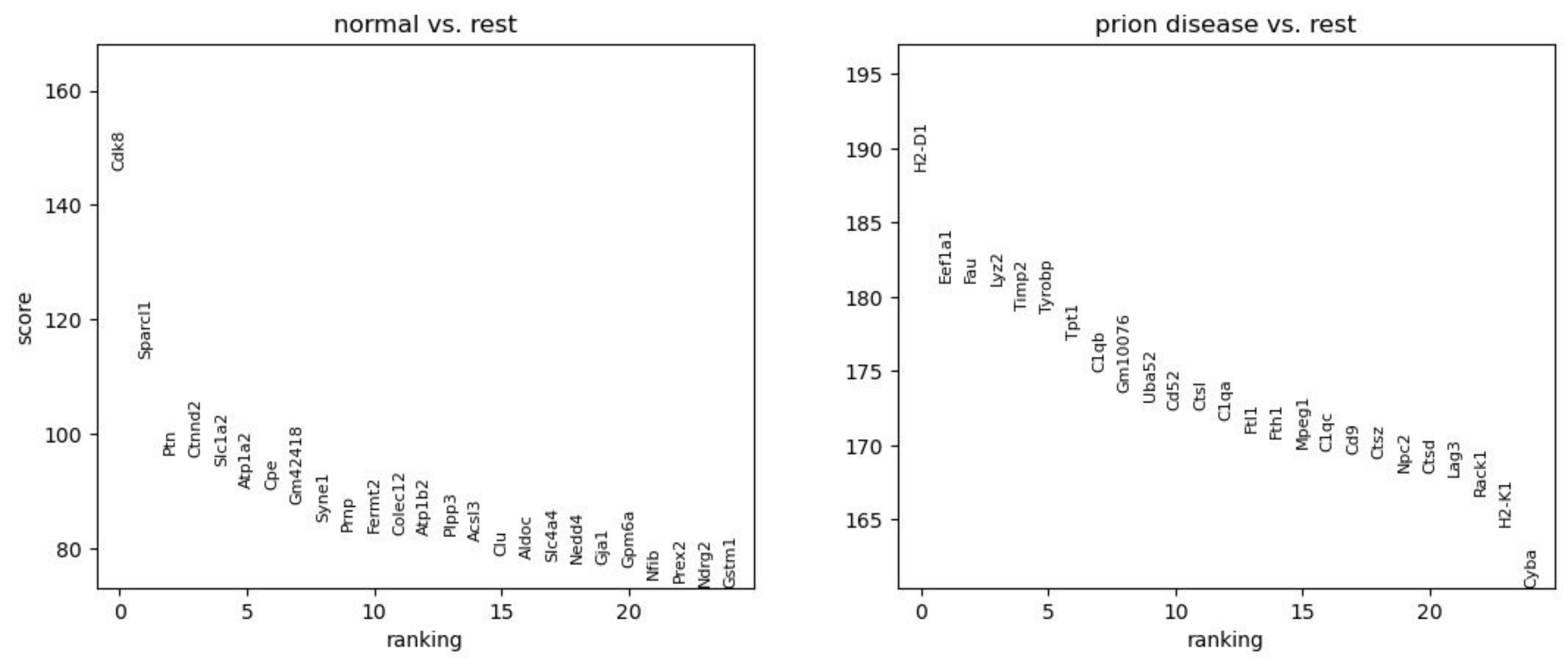


Disease vs non disease



Sum Tests

- Cdk8
- H2D1



Conclusions

- OPCs more closely related to trait
- Relevant results and p values for both cell types
- Link to neurodegenerative disorders and ASD
- Glioblastoma
- Convergent evolution
- Relevance of striatal cell types to prionic disease

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