

An Integrated Mouse Spinal Cord Atlas Revealing Microglia Phenotypes in Health and Injury Conditions

Qi Guo

GRA

Department of Biomedical Informatics

The Ohio State University

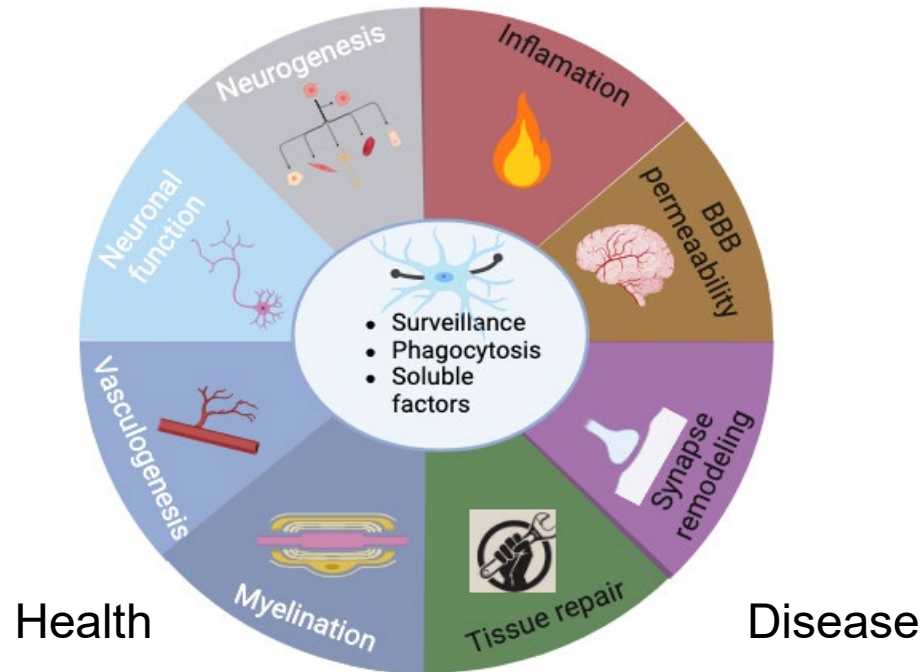
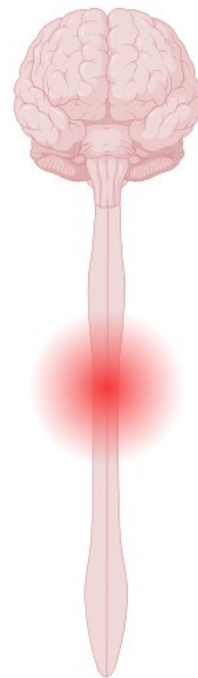
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Thesis advisors: **Dr. Qin Ma**
Dr. Phillip Popovich

1. Background introduction and Challenges

Background Introduction:

- There is no FDA-approved drug or treatment for spinal cord injury.
- Microglia play a central but diverse role in repairing the injured spinal cord. (Brennan F, et al., Paolicelli, R.C. et al.)
- Single-cell RNA sequencing (scRNA-seq) have provided an extraordinary technology to explore tissue heterogeneity.



Challenges:

- Comprehensive microglia subset identification is hindered by limited sample sizes, low microglia proportion (10%) in the CNS and high heterogeneity - Big datasets from 16 studies.
- scRNA-seq datasets from multiple studies cause significant batch effect - scANVI (Xu C, et al.)

2. The Spinal Cord Atlas (SCA) workflow

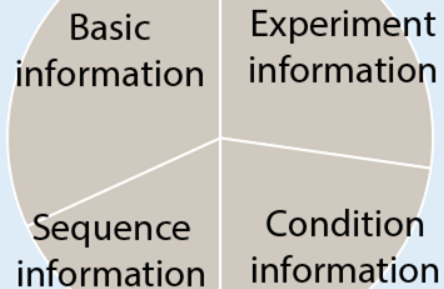
1. Data collection

a. Raw count matrix

	Cell1	Cell2	...	CellN
Gene1	3	2	.	13
Gene2	2	3	.	1
Gene3	1	14	.	18
...
GeneM	25	0	.	0



b. Metadata

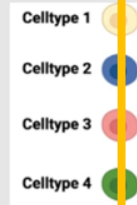


2. Atlas construction

a. Input (Healthy datasets)

	Cell1	Cell2	...	CellN
Gene1	3	2	.	13
Gene2	2	3	.	1
Gene3	1	14	.	18
...
GeneM	25	0	.	0

+



Integration (scANVI)

b. SCA (Health)



c. Mapping

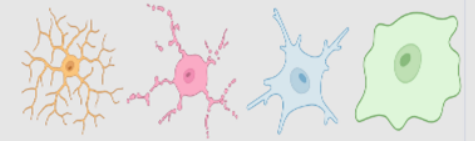


d. Extended SCA (Health+Injury)

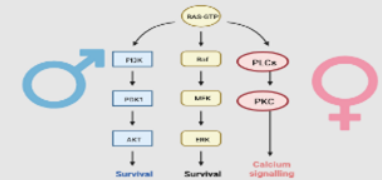


3. Applications

a. Cell type markers



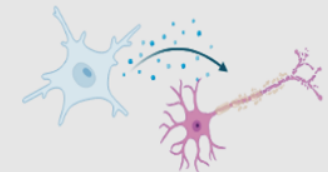
b. Phenotype-related pathways



c. Injury-related cells

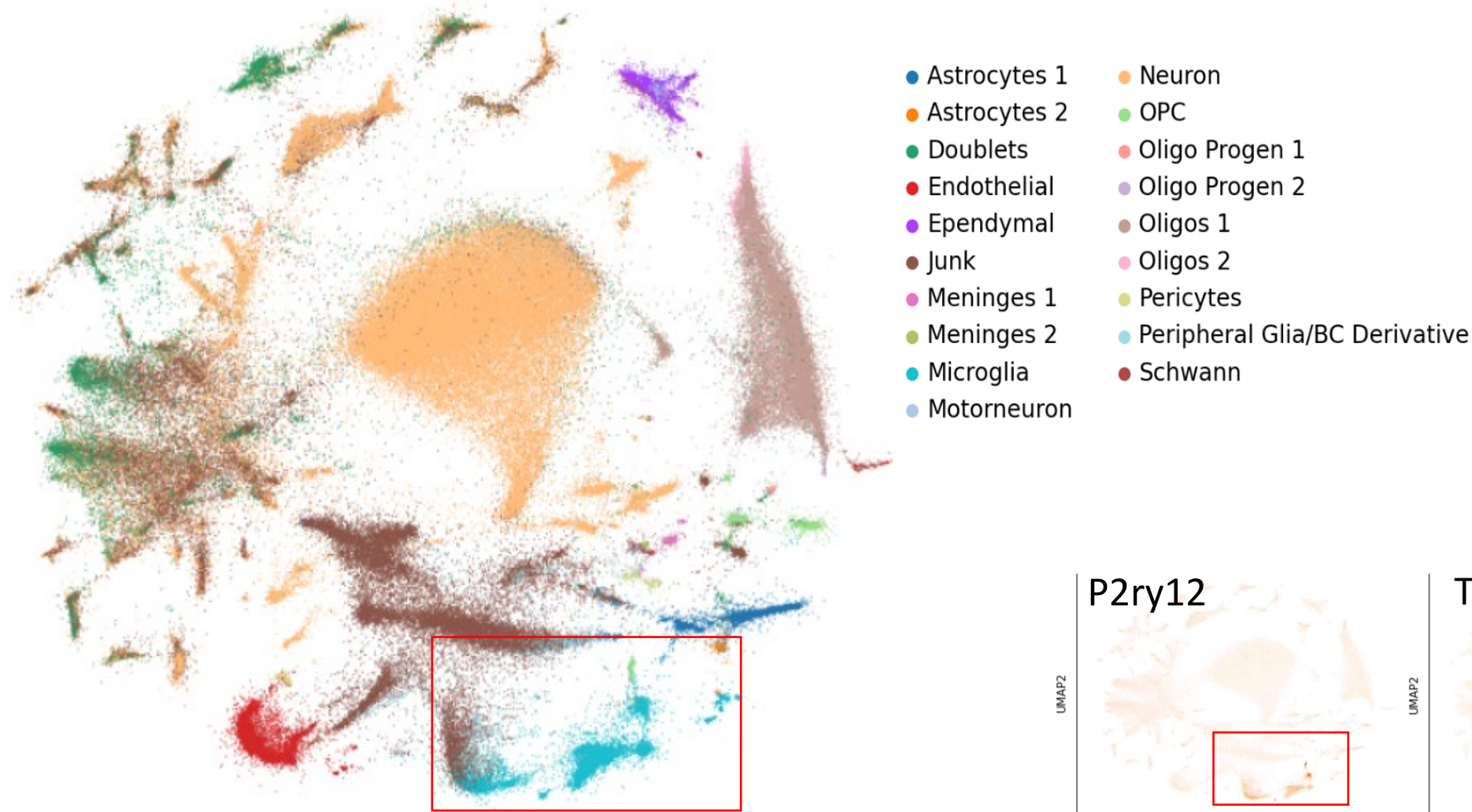


d. Cell-cell communication



3. Preliminary results:

The healthy spinal cord atlas comprises 11 datasets, including 195,875 cells.



The UMAP represents cells' distribution labeled by predicted cell ID based on Russ' dataset (195,875 cells, 7,722 Microglia)

7,722 Microglia have been validated by well-known microglia markers.

4. Take home points

Impact:

- The SCA encompasses 0.2 million cells from 16 major cell types and 7,722 Microglia from 11 studies, which could define microglia heterogeneity.
- Different spinal cord disease (ALS) datasets can be mapped to SCA.

Future study:

- Microglia subsets annotation in healthy condition.
- Mapping disease to healthy atlas.
- Applications.

Thanks for listening!