KAUST Academy Summer Programs - Final Report

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- **Program:** Bioinformatics Specialization - University of Cambridge.
- **Project title:** How does gene expression in different brain cell types relate to proximity to amyloid plaques?
- **Project objectives and goals:** Visualize spatial distribution of cells to help understand the interactions and whether specific genes are differently expressed near plaques.

- **Methodology and Approach:**

1. **Data Preprocessing:** Expression matrix normalized and gene names standardized. Spatial coordinates scaled and matched to expression data.
2. **Distance Computation:** Plaque coordinates extracted. Distances of each cell to nearest plaque calculated using k-nearest neighbor search (nn.dist).
3. **Statistical Analysis:** Wilcoxon rank-sum test: compared expression of nearest 10% vs farthest 10% cells. Spearman correlation: tested monotonic relationships between expression levels and plaque distance.
4. **Visualization:** Scatter plots showing cell locations colored by gene expression. Rolling mean smoothing to visualize trends across plaque distance. Comparisons across young (8-month) vs old (13-month) mice.

- **Preliminary Results or Findings:**

1. **Reactive astrocytes near plaques:** Genes like GFAP and VIM were upregulated in cells located near Aβ plaques.
2. **Spatial enrichment:** Expression peaked at intermediate distances, suggesting a localized "reactive zone."
3. **Age differences:** Younger mice had fewer plaques and lower astrocytic reactivity, while older mice showed higher gene expression and plaque burden.
4. **Disease-associated astrocytes (DAA-like):** A distinct astrocyte subpopulation near plaques, defined by genes upregulation and linked to neuroinflammation and neuronal dysfunction.

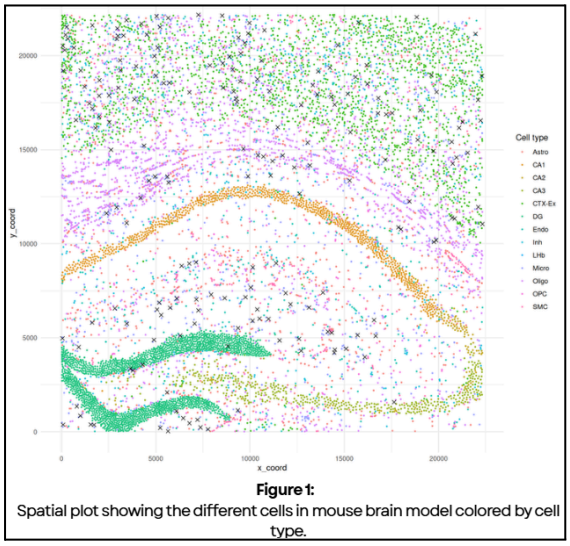


Figure 1:
Spatial plot showing the different cells in mouse brain model colored by cell type.

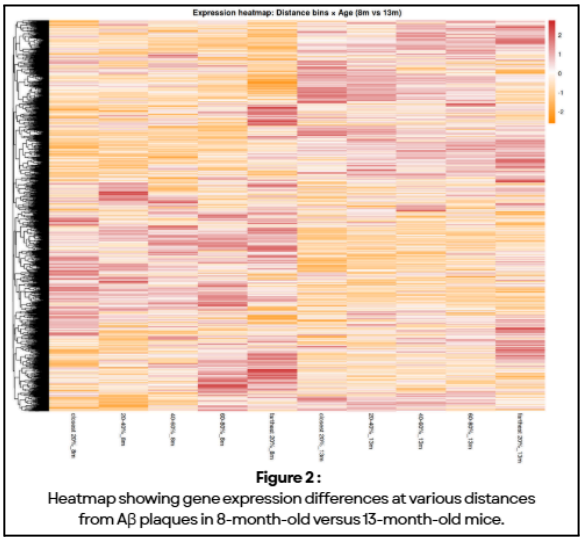


Figure 2 :
Heatmap showing gene expression differences at various distances from Aβ plaques in 8-month-old versus 13-month-old mice.

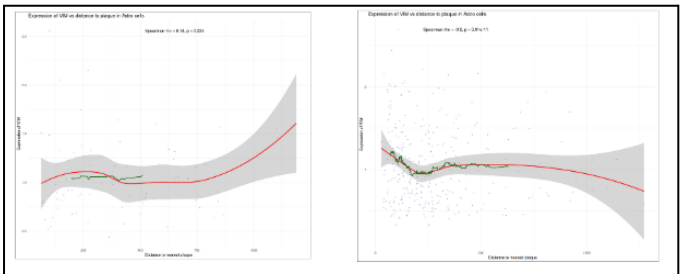


Figure 5 &6 :
VIM expression in astrocytes vs. distance to plaques. Blue points: single-cell values; red line: loess smoothed trend; green line: rolling mean of 50 cells, showing local average expression.

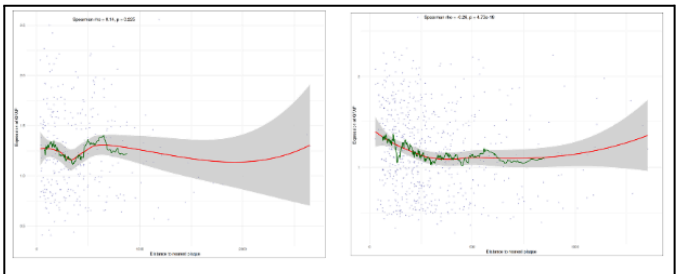


Figure 3 & 4 :
GFAP expression in astrocytes vs. distance to plaques. Blue points: single-cell values; red line: loess smoothed trend; green line: rolling mean of 50 cells, showing local average expression.

- **Challenges and Obstacles Encountered Difficulty:**

1. aligning plaque and cell coordinates due to scaling differences.
2. High biological variability between samples (age-related differences, plaque density).

- **Next Steps and Future Work:**

1. Expand analysis to additional reactive astrocyte genes as modules.
2. Perform clustering to better define plaque-associated astrocyte subpopulations.
3. Explore astrocyte interactions with different cells in plaque microenvironments.

- **Resources and Tools Used:**

  -**Programming Languages:** R.

  -**Packages:** data.table, dplyr, Giotto, ggplot2, viridis, FNN

  -**Resources link:**
  https://docs.google.com/document/d/1CBfr9YCOXSUX5q1WQYfIv0VfplOzgfXVJmVGdrAJfx0/edit?usp=sharing