5.8 million people in the U.S currently have dementia. Dementia is a broad term referring to a loss of cognitive functioning, primarily thinking and memory.

### Introduction

Dementia is a term that encompasses a range of neurological disorders characterized by a significant and persistent decline in cognitive function, typically affecting memory, thinking, language, and judgment. Common types of dementia include Alzheimer's Disease (AD), Vascular Dementia, and Lewy Body Dementia (LBD). These disorders affect millions of people worldwide, impacting not only the individuals with the disease but also their families and caregivers.

### Methods

Gene expression analysis was conducted using single nuclei RNA sequencing (sn-RNAseq) to identify differences in cell function between dementia types. This technique enables the identification of cell type-specific gene expression changes and allows for the clustering of cells into groups based on similar gene expression patterns.

### Results

**Figure 1:** UMAP of endothelial cell type clustering. Cluster 4 is composed of 128 cells where 90% are from the six Alzheimer’s Disease + Vascular Dementia samples.

**Figure 2:** Representation of hippocampus tissue dissection and single nuclei RNA sequencing. NC stands for normal control. Adapted from (Lau et al., 2020).

**Figure 3:** UMAP of endothelial cell type clustering. Cluster 4 is composed of 128 cells where 90% are from the six Alzheimer’s Disease + Vascular Dementia samples.

**Figure 4:** Bar graph depicting the percentage of each sample’s endothelial cells in cluster 4. Percentage ranged from 2.7% to 21.1% of endothelial cells in vascular dementia samples with an average of 11.5%.

**Figure 5:** Average gene expression graphs for two highly upregulated genes in cluster 4 related to vascular calcification. Matrix Gla Protein (MGP) and Dickkopf1 WNT Pathway Inhibitor 2 (DKK2) are part of the WNT3a and BMP pathways that promote calcification (Bundy, Boone, and Simpson, 2021).

**Figure 6:** Types of vascular calcification in the Central Nervous System. Impact of vascular calcification on endothelial cells is especially poorly characterized. (Maheshwari et al., 2022).

### Vascular Calcification

- **Evidence suggests** we have identified brain hippocampus endothelial cells responding to vascular calcification in vascular dementia.
- **These cells** are highly upregulated genes MGP (23-fold increase) and DKK2 (12-fold increase). These two genes are related to calcification response, with MGP being the primary inhibitor of vascular calcification within the human body.
- **Future work** would aim to confirm whether these cells are responding to vascular calcification and explore how calcification contributes to dementia symptoms. The roles of MGP and DKK2 in dementia progression will also be investigated.

### Conclusion and Future Work

- **Evidence suggests** this cluster of 128 cells consists of endothelial cells responding to vascular calcification and is specific to vascular dementia.
- **Future work** would aim to confirm whether these cells are responding to vascular calcification and explore how calcification contributes to dementia symptoms. The roles of MGP and DKK2 in dementia progression will also be investigated.

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