2023 IMPACT CIRCLE

Project Title: **Role of immune aging in the age-related decay of fiber tracts in the brain**

Investigator(s) and collaborations: **David Furman**

Unmet Need/Primary Question:

It is often wrongly assumed that brain aging is a process of loss of neurons with advancement of age. Careful stereology studies have demonstrated that cell loss in the aged brain is a feature of neurodegenerative pathologies while healthy aging does not come with significant loss of cells. The ethos requiring that funding is disease oriented has helped perpetrate this view, and very little is known about non-pathological brain aging. To prevent age-related brain diseases, we need to understand the processes of healthy aging in order to slow down and delay disease. We have developed a cytokine clock that measures chronic levels of low-grade inflammation. The output of this clock correlates with age-related brain atrophy and cognitive decline.

Novel Hypothesis:

We hypothesize that peripheral low grades of inflammation as measured by our cytokine clock directly impact the age-related decay in white matter tracts and lead to age-related cognitive deficits.

Project Proposal:

We propose analysis of our cytokine clock's acceleration and the quality of white matter tracts in 500 participants of the Hilblom cohort of healthy aging. We will generate spectral decompositions of the quality of the subjects' white matter tracts and brain morphometry. These data will be correlated with our cytokine clock to find the interactions between immune aging and connectivity decay in the brain.

Description of Potential Impact:

Building an understanding of the difference between pathological and healthy aging will enable us to seek prophylactic avenues. Brain connectivity is sensitive to cognitive exercise and therefore is amenable to behavioral stimulation therapies. If aided by reducing the acceleration of the inflammation clock, we could be able to develop preventative therapies delaying the aging of the brain and potentially reduce the overall likelihood of developing neurodegenerative pathologies. The originality of our approach is in combining cognitive exercise with prevention of inflammaging. Having the cytokine clock and a direct measurable assessment of brain connectivity will allow for evaluating therapeutic success and adjusting the therapies to the type of fiber loss in the brain.

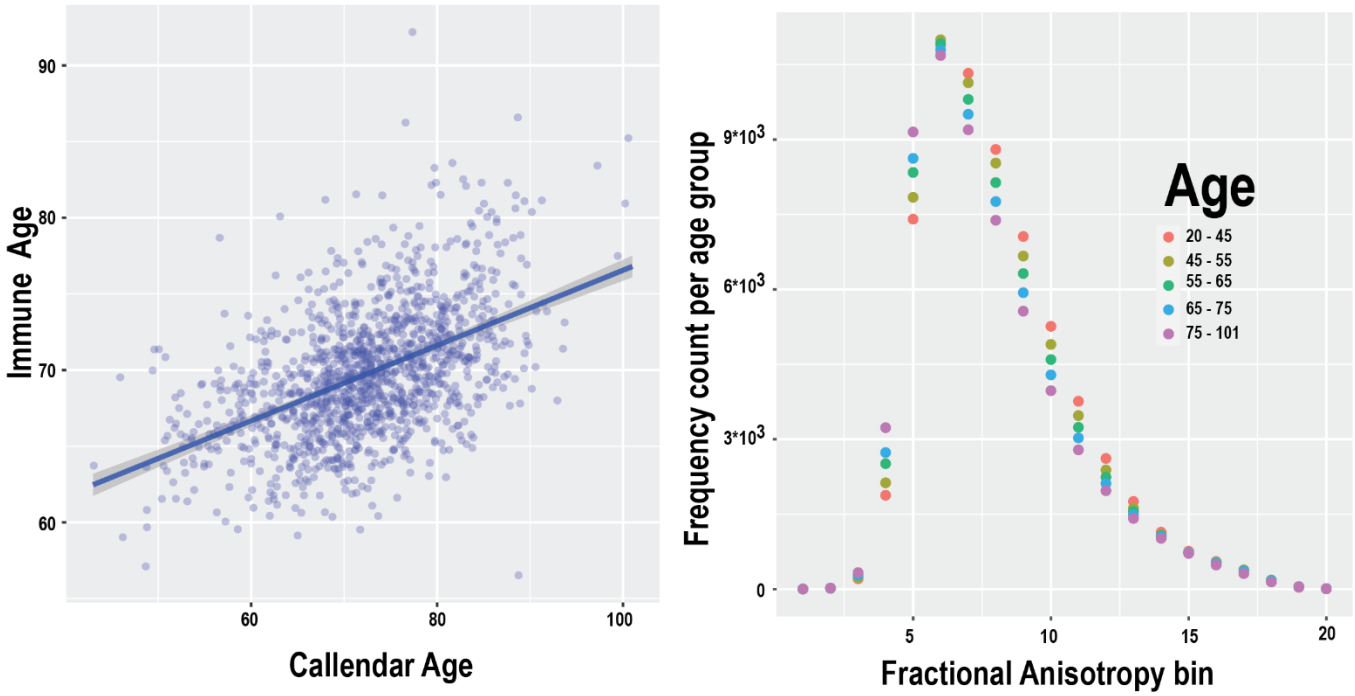

Figure 1 Integration between immune aging and brain aging. Panel A: Immune ageing clock based on a panel of inflammatory cytokines. B: Brain aging of the connectivity spectrum measured by Diffusion Tractography, older individuals have more voxels with low anisotropy and less voxels with high anisotropy indicating loss of fiber pathways in the brain.