Towards a new resource for the MS brain: a cross-brain bank proteomic atlas of non-lesional neocortex

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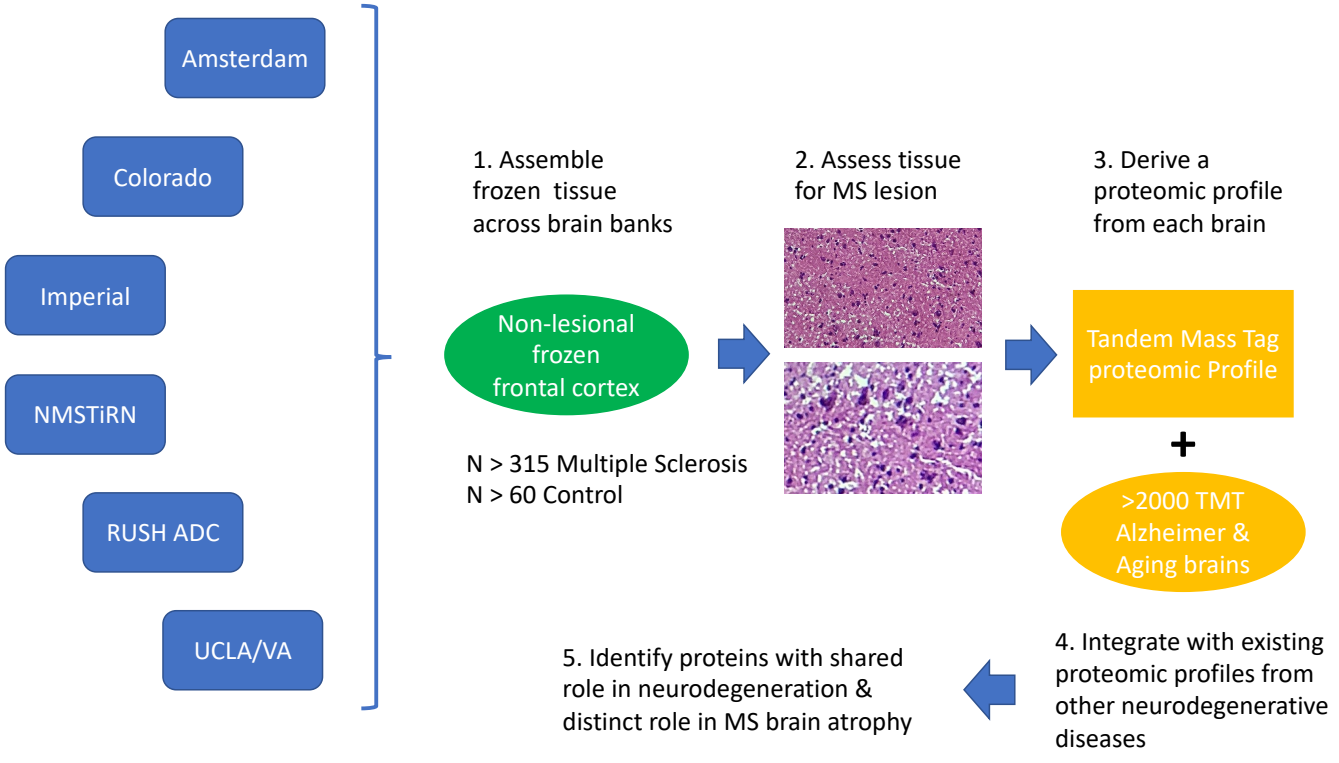
Introduction:
The development of large-scale, publicly available data resource from the target organ (brain) in Alzheimer's disease has led to a marked acceleration in insights into novel mechanisms that can be targeted for drug development. They have also helped to systematically characterize the functional consequences of susceptibility variants. Such resources do not yet exist in the field of MS, where most pathologic studies remain of moderate size.

Aim: To establish the same proteomic profile of non-lesional cortical tissue to explore mechanisms related to the general brain atrophy seen in MS.

Methods:
We have assembled frozen samples from 6 brain banks to create a collection of samples that will undergo the same shotgun proteomic (Tandem Mass Tag-based) profile. Frontal cortex samples were identified in and are being assembled from the Netherlands Brain Bank, the Normal Aging Brain Collection (NABCA), MS society Tissue Bank at Imperial College London, Rocky Mountain MS center brain bank, RUSH University Alzheimer Disease Center, UCLA/Veterans Administration Brain Bank, and the newly established National MS Tissue Registry Network from the US which is funded by the national MS Society.

Results:
In total, we have identified samples of frontal cortex from up to 315 individuals with MS and 60 control individuals; they are being profiled in parallel with samples from aging cohorts (N>2000) that will create a data resource across multiple neurodegenerative and aging-related conditions of Tandem Mass Tag proteomic profiles that are processed in the same manner on the same platform. In each frozen sample, we are assessing whether there is a lesion in the cortex and/or underlying white matter using an H&E stain and a PLP stain. All samples will be profiled in one batch. Deidentified data will be shared through a dedicated portal once pre-processing and quality control analyses are completed. Data generation is anticipated in the winter of 2021/2022. A dataset optimized for repurposing is expected later in 2022.

Conclusion:
We have assembled a large collection of frozen neocortical tissue samples from 6 brain banks to generate a single dataset with harmonized phenotypic information and a coherent set of proteomic data to accelerate discoveries by the MS community. Since it is generated on the same platform with the same protocol as large ongoing studies of Alzheimer's disease and other neurodegenerative diseases, we will be able to assess whether there may be shared and/or distinct pathways that relate to different neurodegenerative diseases (including MS) as well as factors that may represent shared resilience mechanisms. The dataset will also serve as a foundation for more extensive multi-omic profiling of the MS brain, focusing the generalized atrophy of the cortex in MS, a process that remains poorly understood.



Support: Funded by a grant from EMD Serono through its MS Links program