Analysis of age-related changes in gene expression in human microglia

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Research question and background

In this project we investigate the gene expression profile and functional changes in human microglia, and how that is affected by aging. In addition to the high quality fresh post mortem samples from NBB we have collected samples from other European institutes and with collaborators in Brazil.

Gradually we are assembling a sizeable collection of samples. We will compare the gene expression profile and functionality of microglia isolated from human samples with microglia isolated from Rhesus Macaque, mouse and senescence-accelerated mice. The goal of this project is to characterize the human neuroimmune system, how it changes as a consequence of aging and its relation to neurodegenerative diseases.

Methods and tissues used

We have developed and optimized a robust protocol for the acute isolation of human microglia from autopsy brain samples (Olah et al., 2012). We have used parietal cortex samples from control patients (no neurodegenerative disease) and our goal is to isolate microglial cells from young (10-20 years), middle aged (50-60 years), and aged (80 years and older) donors and analyze these samples using RNA sequencing.

With the use of gradient centrifugation in combination with FACS sorting, we are able to isolate CD11b/CD45 positive cells and these double-labeled cells are collected, resulting in pure microglia samples from which we isolate RNA.

For a reliable comparison between young and old microglia we need at least 8 samples in each group with sufficient mRNA yield of high quality.

Results and conclusion

Tissues 2013

In 2013 we obtained 6 samples with the following specifications:
age: 57-101
pH CSF: ≥ 6.01

Only 1 of the samples was from a control donor, 3 of the samples were from donors with neurodegenerative deseases (MS, AD and PD)

Tissues 2014

In 2012 we have obtained 6 samples with the following specifications:
age: 67-111
pH CSF: ≥ 5.96

Total number of samples obtained in 2013-2014

NBB no.	gender	age	clinical diagnosis	pH CSF	pmd
S13-005	female	79	AD	6,5	4:20
S13-019	female	53	MS	6,81	7:15
S13-035*	male	75	COCVA	6,45	7:10
S13-045	male	74	PD	6,3	5:45
S13-067*	male	57	MUSA	6,58	5:45
S13-095*	female	101	control	6,01	6:15
S14-005*	male	67	control	6,48	9:00
S14-027	female	88	AD	6,39	4:40
S14-048*	female	111	control	5,96	8:40
S14-053	female	80	COED	6,55	7:45
S14-051*	male	92	control	6,2	7:04
S14-069*	female	73	control		

Samples marked with an asterisk are used for RNA sequencing and at the moment the data is being analyzed and a manuscript prepared.