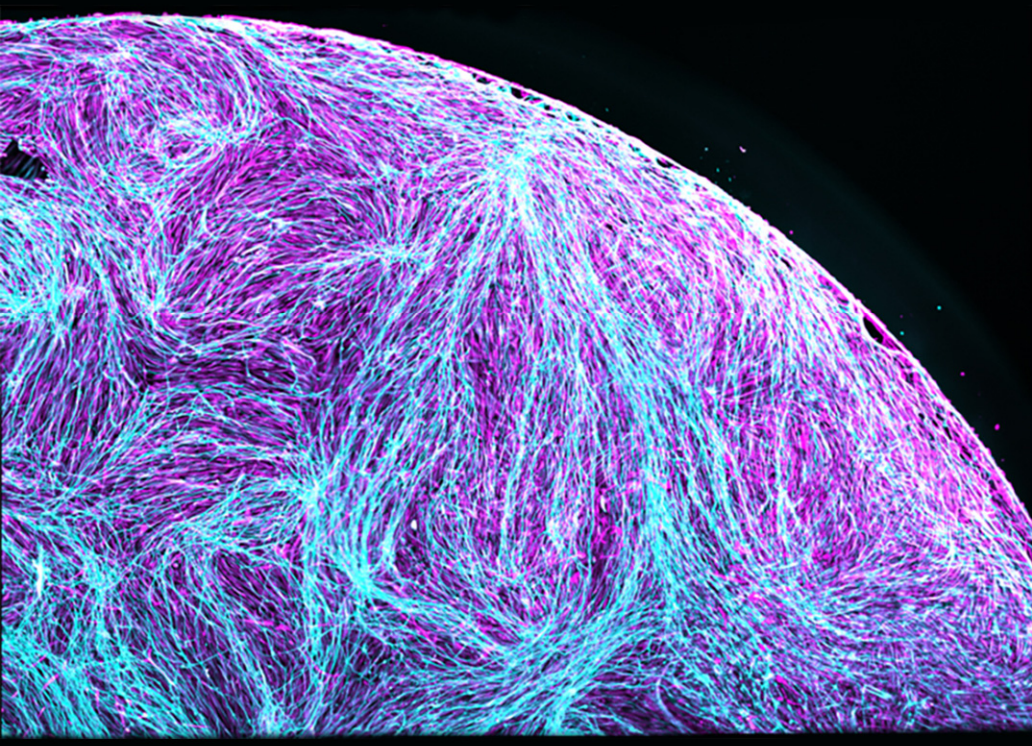
Abstracts of papers presented
at the 2020 *virtual* meeting on

NEURODEGENERATIVE DISEASES: BIOLOGY & THERAPEUTICS

December 2–December 4, 2020



Cold Spring Harbor Laboratory
MEETINGS & COURSES PROGRAM

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NEURODEGENERATIVE DISEASES: BIOLOGY & THERAPEUTICS

December 2–December 4, 2020

Arranged by

Aaron Gitler, *Stanford University*
Richard Ransohoff, *Third Rock Ventures*
Scott Small, *Columbia University*
Li-Huei Tsai, *Massachusetts Institute of Technology*

CSH Cold Spring Harbor Laboratory
MEETINGS & COURSES PROGRAM

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NEURODEGENERATIVE DISEASES: BIOLOGY & THERAPEUTICS
Virtual Meeting
Wednesday, December 2 – Friday, December 4, 2020

Wednesday	10:00 am–11:00 am	Keynote Speaker: Virginia Lee
Wednesday	11:00 am–1:00 pm	**1** Genetics, Genomics and Target Identification in Neurodegenerative Disease
Wednesday	2:00 pm–5:00 pm	**2** Neuroinflammation and Glial Biology of Neurodegeneration
Thursday	10:00 am–1:00 pm	**3** Therapeutic Initiatives in Neurodegenerative Disease
Thursday	2:00 pm–5:00 pm	**4** ApoE and Lipid Metabolism
Friday	10:00 am–12:45 pm	**5** Endolysosomal Dysfunction in Neurodegeneration
Friday	1:30 pm–3:00 pm	**Panel:** Science, Society and COVID-19
Friday	3:00 pm–6:00 pm	**6** New Technologies to Study Neurodegeneration
Throughout Meeting		*Virtual Poster Session*

Virtual Icebreaker, Wednesday, 5:30 pm

StemCell Technologies Workshop: Thursday, 5:30 pm (*p. T-1)*

Closing Social, Friday, 6:00 pm

All times shown are US EST: Time Zone Converter

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COEXISTANCE OF DIFFERENT MYELOID POPULATIONS IN THE FRONTAL CORTEX OF ALZHEIMER´S DISEASE PATIENTS

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Parenchymal microglia are the brain-resident immune cells capable of responding to damage and disease and has been postulated as a critical factor in the Alzheimer´s disease (AD) progression since the identification of several genetic risk factors related to their functions. Apart from microglia, CNS macrophages, like perivascular macrophages (PVMs), are also involved in neurodegeneration. However, the different phenotypes and the implication of myeloid cells in the human pathology have not been determined yet. Here, we analyzed the phenotypic profile displayed by these damage associated myeloid cells in the frontal cortex of AD brains. For this purpose, immunohistochemistry and image analysis approaches have been carried out in postmortem samples from non-demented controls (Braak II) and AD cases (Braak V-VI). Frontal cortex of AD patients showed strong myeloid activation similar to that observed in amyloidogenic mice. Microglial cells of Braak V-VI patients were observed forming clusters and exhibited, both plaque (Iba1+/Trem2+/TMEM119+/CD45high) and inter-plaque (Iba1+/Trem2-/TMEM119+/CD45high) damage-associated phenotype. Moreover, in these individuals the PVMs (Iba1+/CD45high/CD163+/ MCR1-) were localized in the parenchyma, predominantly located surrounding amyloid plaques. On the contrary, Braak II with mild amyloid pathology (CERAD B) cases presented only activated microglial cells, while, immunoreactivity of CD163 was absent (Iba1+/CD45high/CD163-).These strongly activated myeloid cells, could drive the AD pathology and, in consequence, could be implicated in the pathology progression.Taken together, these findings suggest the existence of two populations of myeloid cells associated with Aβ plaques in the frontal cortex in the advanced stages of the pathology and probably due to failures in the integrity of the blood-brain barrier. The differential contribution of these two myeloid populations to the pathogenesis of the disease remains to be elucidated. These results open the opportunity to design targeted therapies, not only to microglia, but also to the population of macrophages, in order to modulate amyloid pathology and provide a better understanding of the immunological mechanisms underlying AD progression.

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