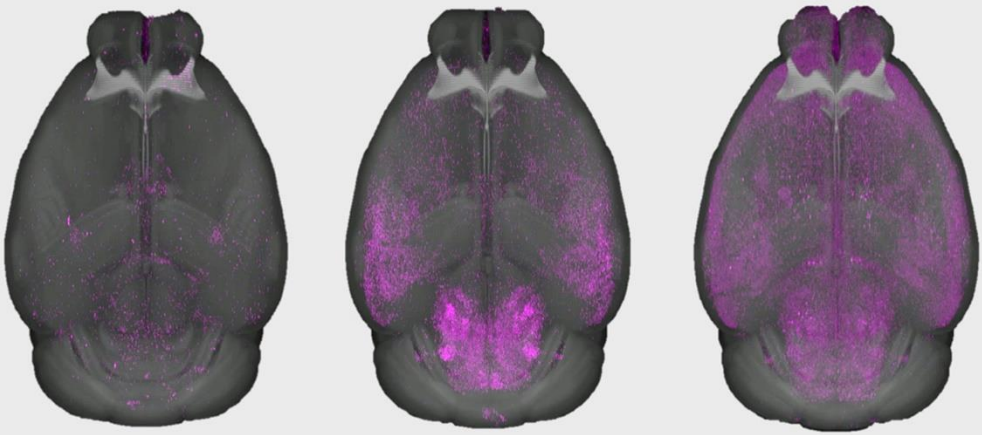
Abstracts of papers presented
at the 2022 meeting on

NEURODEGENERATIVE DISEASES: BIOLOGY & THERAPEUTICS

November 30–December 3, 2022



Cold Spring Harbor Laboratory
MEETINGS & COURSES PROGRAM

Rev-erbα in cellular differentiation of neuronal progenitors to dopaminergic neurons and neuroprotection
Shalini Gupta, Pawan Gupta.
Presenter affiliation: CSIR-Institute of Microbial Technology, Chandigarh, India.
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Elevation of membralin can improve the cognitive decline and β-amyloid pathologies in preclinical Alzheimer's models
LuLin Jiang, Stephanie Myers, Shah Palak, Huijie Huang, Timothy Y. Huang, Randal J. Kaufman.
Presenter affiliation: Sanford Burnham Prebys Medical Discovery Institute, La Jolla, California; Altos Labs, Redwood City, California.
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Discovery of potent cholinesterase inhibition-based multi-target-directed lead compounds for synaptoprotection in Alzheimer's disease
Bengisu Turgutalp, Prabesh Bhattarai, Caghan Kizil.
Presenter affiliation: Columbia University Irving Medical Center, New York, New York; Taub Institute for Research on Alzheimer's Disease, Columbia University, New York, New York.
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Impact of early-life environmental enrichment on episodic memory in APPswe/PS1dE9 mice
Srishti Kushwaha, Smitha Karunakaran.
Presenter affiliation: Centre for Brain Research, Bangalore, India; Manipal Academy of Higher Education, Manipal, India.
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Ultrastructural evidence of mitochondrial pathology in hippocampal reactive astrocytes of β-amyloidosis Alzheimer's transgenic mice
E. Lopez-Oliva, L. Trujillo-Estrada, E. Sanchez-Mejias, M. Mejias-Ortega, J.J. Fernandez-Valezuela, A. Gomez-Arboledas, J.C. Davila, J. Vitorica, A. Gutierrez.
Presenter affiliation: Instituto de Investigación Biomédica de Málaga-IBIMA, Facultad de Ciencias, Universidad de Málaga, Malaga, Spain; CIBERNED, Malaga, Spain.
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Evaluation of neuroinflammation as modulator of tau aggregation in response to repetitive mild traumatic brain injury
Ines Lopez del Castillo, George Edwards III, Laura Vegas-Gomez, Ines Moreno-Gonzalez.
Presenter affiliation: IBIMA, CIBERNED, University of Malaga, Malaga, Spain.
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Ultrastructural evidence of mitochondrial pathology in hippocampal reactive astrocytes of β-amyloidosis Alzheimer's transgenic mice

E. Lopez-Oliva[1,2]., L. Trujillo-Estrada[1,2], E. Sanchez-Mejias[1,2], M. Mejias-Ortega[1,2], J.J. Fernandez-Valezuela[1,2], A. Gomez-Arboledas[1,2], J.C. Davila[1,2], J. Vitorica[2,3] and A. Gutierrez[1,2]

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Astrocytes, the most abundant non-neuronal cell type in the central nervous system, play essential roles in brain homeostasis and neuroprotection, including synaptic plasticity and innate immunity. Many of these activities are highly energy demanding and require large energy input from mitochondria. During the process of Alzheimer's disease (AD), both amyloid-β and phospho-tau pathologies have a detrimental effect on neurons and glial cells, also impairing mitochondria. This could negatively affect neurons, compromising ATP production and leading to a deleterious effect that promotes neurodegeneration. Though mitochondrial dysfunction is thought to be an early event in AD, the majority of studies have focused on neurons, and little is known about the functional characteristics and dynamics of mitochondria in astrocytes. Here, we aim to analyze mitochondrial subcellular features of reactive astrocytes in APP/PS1 mice hippocampus by transmission electron microscopy, immunogold labeling and image analysis. Reactive astrocytes cluster around aβ plaques and display morphological changes. Our results show mitochondrial structural alterations as mitochondrial cristae loss, broken double membrane structure and fragmentation. In addition, an increase in both number and size of mitochondria in this transgenic model compared to WT mice, was found. Since mitochondrial morphology is directly related to mitochondrial fusion/fission, the ultrastructural pathology of astrocytic mitochondria in this model suggests dynamics abnormalities in these organelles that might lead to astroglial functional deficits compromising neuronal survival. Deciphering the mechanisms underlying this pathological phenomenon might help for the development of therapeutic interventions targeted to protect/improve astrocytic mitochondrial function and enhace their neuroprotective support to neurons in AD.

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