



THE ROLE OF THE BRAIN EXTRACELLULAR MATRIX IN BRAIN CLEARANCE

The clearance of toxic macromolecules and metabolic byproducts from the interstitial/extracellular space (ECS) of brain parenchyma via interstitial fluid (ISF) is critical for the maintenance of brain homeostasis. Impairment of brain clearance leads to age-related brain deterioration and neurodegenerative diseases.

The flow rate of brain ISF is dynamically regulated in the sleep/wake cycle, aging, and pathological conditions. However, the mechanism by which ISF flow is regulated is poorly understood. ISF runs through the ECS, which is filled with extracellular matrix (ECM).

The team has developed a novel tool, which specifically labels hyaluronan (HA)-based brain ECM. We attached a fluorescence acceptor tag (HaloTag) to a Link protein that specifically binds to HA chains (H-Link). H-Link reveals the organization of the brain ECM surrounding neurons (perineuronal net), astrocytes, and brain capillary in vivo and in vitro. We will combine this reporter assay, in vivo two-photon brain imaging, and a microfluid chamber system to study how brain ECM is regulated during sleep/wake cycles.

The proposed experiment will for the first time reveal the dynamic changes in brain ECM.

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PROJECT INFO
FUNDED PROJECT AMOUNT
\$30K