TAU PROTEIN AND S100A9 CO-INTERACTION STUDIES

Lukas Krasauskas[1], Andrius Sakalauskas[1], Mantas Ziaunys[1], Vytautas Smirnovas[1]

[1]Amyloid Research Sector, Institute of Biotechnology, Life Sciences Center, Vilnius University, Lithuania
lukas.krasauskas@gmc.vu.lt

Neurodegenerative diseases are one of the most common disorders in the world. Unfortunately, despite intensive research, the understanding of the mechanism of these diseases is limited, and almost all existing treatments are symptomatic [1]. Alzheimerś disease has attracted the most attention from scientists because it is the most common neurodegenerative disease, affecting about 50 million people worldwide. In addition to amyloid plaques composed of amyloid-beta peptides, neurofibrillary tangles formed from the protein Tau are a hallmark of this disease and other tauopathies. Therefore, it is essential to understand the mechanisms at work in this process and determine the best way to curb them. Amyloid-beta aggregates (and alpha-synuclein aggregates in Parkinsonś disease) have been shown to promote Tau aggregation [2]. It has also been observed that the aggregation of these two peptides involves the pro-inflammatory protein S100A9, whose elevated levels in the brain are recorded after various head injuries.
Furthermore, one other tauopathy – CTE (Chronic traumatic encephalopathy) – registers high levels of Tau aggregates, and the exact reasons for their formation are unknown. Researchers observed that this disease is quite prominent in contact sport players (e.g., American football) who experiences chronic head concussions [3]. There has been some speculation from the scientific community that neuroinflammation could induce Tau pathology; thus, it is feasible that S100A9 as a pro-inflammatory protein could be a culprit behind it or at least in part responsible. However, it is strange that there is not much information available or studies performed to confirm or rule out the potential of the S100A9 protein or its aggregates to participate directly in Tau aggregation. Therefore, we examined the ability of the S100A9 protein and its aggregates to promote Tau aggregation. We observed that Tau aggregation is dependent on S100A9 aggregate formation as S100A9 monomers alone do not induce Tau aggregation, while S100A9 aggregates induce notable fluorescence changes in the reaction mixture with Tau protein. Various conditions for S100A9 protein aggregation were examined in the study. Aggregation kinetics were recorded by fluorescence spectroscopy using the amyloidophilic dye thioflavin T. Atomic force microscopy was performed to analyze the morphology of the formed aggregates and FTIR spectroscopy was done to analyze secondary structure change in formed aggregates.

[1] Kametani, F., Hasegawa, M. (2018). Reconsideration of Amyloid Hypothesis and Tau Hypothesis in Alzheimerś Disease. Frontiers in neuroscience, 12, 25

[2] Nisbet, R. M., et al. (2015). Tau aggregation and its interplay with amyloid-β. Acta neuropathologica, 129(2), 207–220.

[3] Marklund, N., et al (2021). Tau aggregation and increased neuroinflammation in athletes after sports-related concussions and in traumatic brain injury patients – A PET/MR study. NeuroImage: Clinical, 30, 102665.