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BOOK OF ABSTRACTS

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Proteasome activation plays role in 18α-glycyrrhetinic acid protective effect in 5xFAD animal model of Alzheimer's disease

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Introduction. Aging represents the most important risk factor for Alzheimer's disease (AD), the most common neurodegenerative disorders worldwide. One of the hallmarks of AD is the accumulation of plaques composed of aggregated amyloid-β peptides (Aβ) which are formed by sequential proteolytic processing of the amyloid-precursor protein (APP).It is well known that different factors can influence amyloidogenic pathway and/or clearance of already formed Aβ. Growing evidence suggest that ubiquitin proteasomal system represents an important factor in AD development and a potential target for the management of disease. Recently it has been shown that several natural compounds, including 18α-glycyrrhetinic acid (18α-GA) protects from protein aggregation-related pathology in AD model system. **Methods.** In order to investigate the protective effect of 18α-GA, we used 5xFAD transgenic mouse AD model, characterized by early amyloid deposition and intra-neuronal Aβ42 aggregation. Both female and male mice were exposed to 18α-GA treatment for one month, started at 2-months of age. This is considered as an early phase of AD pathology, known to be suitable for therapeutics application. In the cortex and hippocampus CT-L, T-L, and PGPH proteasome activities were assayed by hydrolysis of Suc-LLVY-AMC, Boc-LRR-AMC, and Z-LLE-AMC fluorogenic peptides. The number and size of amyloid plaques were determined in these structures. **Results.** This study revealed that 18α-GA treatment influence neuritic dystrophy, increase proteasome activity, decrease Aβ content and number of amyloid plaques in 5xFAD mice. **Conclusion.** These preliminary intriguing data open up new directions using natural compounds for the most efficient treatment of neurodegenerative disorders.

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