particularly α7β2-nAChR, on amyloid-beta is crucial to working towards treatment options and preventative measures.

Figure 1. Receptor mediated internalization of Aβ1-42. SH-EP1 cells stably expressing α7-nAChRs or α7β2-nAChRs, and wild type cells were incubated with oligomeric Aβ1-42, or scrambled peptide followed by incubation with Amido-Glo® dye (Biosensis). Fluorescence intensity was used to compare relative amounts of Aβ1-42 internalization. (A) SH-EP1 cells expressing α7-nAChRs had markedly high levels of internalized Aβ1-42 compared to the (B) same type of cells incubated with a scrambled peptide sequence Aβ1-42 (scrambled), which did not appear to have internalized the peptide. Cells expressing the α7-nAChRs (A) had a higher fluorescence intensity than cells expressing α7β2-nAChRs (C) when incubated with amyloid beta oligomers. These results suggest that α7-nAChRs have a higher internalization rate than α7β2-nAChRs. (Original grayscale images were pseudocolored to show details.).

P4-449 THE ALZHEIMER’S DISEASE-ASSOCIATED R47H VARIANT OF TREM2 HAS AN ALTERED GLYCOSYLATION PATTERN AND PROTEIN STABILITY

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Background: The R47H variant of the triggering receptor expressed on myeloid cells-2 (TREM2) increases the risk of Alzheimer’s disease (AD) similar to apolipoprotein E4. TREM2 R47H has recently been shown to have impaired binding to damage-associated lipid or peptide. Our study aims to characterize biochemical and molecular features of TREM2 R47H mutation.

Methods: Human TREM2 wild type and R47H mutation was inserted into pcDNA5-FRT/TO-HA. All experiments involving human myeloid cells were performed using Lipofectamine 2000. We analyzed by western blotting and Nano-LC/MS analysis.

Results: TREM2 R47H mutation induce increasing terminal glycosylation with complex oligosaccharides in the Golgi apparatus and decreasing sialylation. Different glycosylation of TREM2 R47H mutation are profiled by mass spectrometry. We demonstrated that R47H mutation of TREM2 decreased solubility and increased half-life after treatment cycloheximide.

Conclusions: AD-associated R47H variant of TREM2 have terminal glycosylation impairment, which may disrupt ligand binding, TREM2 proteolysis or phagocytosis of microglia. TREM2 R47H is unstable and resistant to proteosomal degradation. Our study that the biochemical and molecular features of TREM2 are altered by R47H mutation may contribute to the pathogenesis of AD.

P4-450 HIPPOCAMPAL SLICES FROM CALHM1-KO MOUSE, UPON OXYGEN-GLUCOSE-DEPRIVATION, ALTERS HIF-1ALPHA AND AMYLOID β PRODUCTION

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Background: The Ca(2+) channel CALHM1 (Ca(2+) homeostasis modulator 1), was linked with early onset of Alzheimer’s disease (AD). CALHM1 increases production of amyloid beta (Aβ) upon extracellular Ca(2+) removal and its subsequent addback. Despite continuing debate about the Aβ hypothesis, new lines support the concept that an imbalance between production and clearance of Aβ42 and related Aβ peptides is a very early initiating factor in AD. Moreover AD is associated with deficiencies in cerebrovascular functions, e.g., local hypoxia/ischemia could augment the pathogenesis of AD. The literature reveals that exposures to hypoxia/ischemia increase the amyloidogenic processing of Aβ precursor protein (APP) leading to the accumulation of Aβ peptides in brain. Recent studies have indicated that hypoxia-inducible factor-1a (HIF-1a) stimulates the transcription of the b-secretase 1 (BACE1) and Aβ accumulation. Methods: hippocampal slices from Calhm1-knockout (KO) mice and wild type ones, subjected to oxygen-glucose-deprivation (OGD) and glutamate excitotoxicity. Measurements of neuron viability by MTT. Western blot were carried out for measuring HIF-1alpha and beta amyloid Results: Here we provide evidences that in hippocampal slices from Calhm1-knockout (KO) mice, subjected to oxygen-glucose-deprivation (OGD) and glutamate excitotoxicity, Measurement of neuron viability by MTT. Western blot were carried out for measuring HIF-1alpha and beta amyloid. We propose that CALHM1 might influence the outcome of brain ischemia/reperfusion, toward the stimulation of pro-cytotoxic pathways such as HIF-1α activation and Ab accumulation. The pharmacological regulation of CALHM1 could be considered as neuroprotectant drugs in ischemia and in AD.

P4-451 TBI AND AD: SIMILAR TAU-INDUCED NEURODEGENERATION?

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Background: Neurodegeneration following traumatic brain injury (TBI) is well documented, and late-life dementia is directly correlated to the severity or occurrence of TBI. A clinical study done on TBI-exposed US Navy and Marine veterans shows that a moderate TBI doubles the risk, and a severe TBI quadruples the risk for late-life dementia. Unlike a single mild TBI exposure, repetitive mild TBI exposure is also considered to increase the risk for late-life dementia. Recent studies propose that TBI-induced dementia and Alzheimer’s disease might share a Tau induced- neurodegeneration mechanism. Mechanisms underlying TBI-induced neurodegeneration, and the potential role of Tau oligomeric strains in TBI-induced dementia are still unclear. The lack of treatment/preventative methods that protect against TBI-induced dementia necessitates the investigation of the role of Tau oligomers in TBI-induced neurodegeneration. Therefore, in this study, we characterize TBI brain-derived Tau aggregates and investigate their toxicity. Methods: Tau oligomers were isolated by immunoprecipitation...