model used here is a tridimensional one, consisting of two different compartments mimicking cerebral (neurons) and blood compart-
ments, separated by a complex cell layer made of vascular endothelial cells and astrocytes, grown on two opposed faces of the artificial membrane of an insert. Results: In the models presented here, we analyzed the effect of cerebral or blood Aβ1-42 on BBB permeability (fluorescein passage), and the protective effects of β-estradiol and BDNF, under the two conditions (integrity of neurons evaluated by maintenance of neurite network integrity and survival). Additionally, we studied the modification of BBB resistance and physical integrity (detection of occlusive and ZO1) of endothelial layer tight junctions. We showed that circulating Aβ1-42 induced BBB damages (junctions and permeability) with severe consequences on the neuronal integrity. These effect could be partially protected in presence of β-estradiol and BDNF. Conclusions: Our findings link BBB dysfunction with amyloid toxicity. These findings prompt for future studies investigating molecular mechanisms of BBB damages in AD and impact of therapeutic interventions that target these mechanisms.

**P1-191** INVESTIGATING MOLECULAR PATHWAYS INVOLVED IN ALZHEIMER’S DISEASE

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Background: Previously, we developed a Drosophila model of AD. We found that mutant Aβ42 accumulation led to increased dysfunction in the flies. Furthermore, we showed that lithium was able to rescue Aβ42-induced toxicity by blocking translation, and reducing Aβ42 levels. Methods: We carried out microarray analyses in Drosophila, expressing mutant Aβ42 with or without lithium treatment and identified key pathways that were altered - such as neurogenesis, and oxidative or xenobiotic stress pathways. To determine a role for neurogenesis, we expressed Abeta peptide in human hippocampal cell lines and tested for effects on neurogenesis by carrying out immunofluorescence assays. Also, we found in our arrays, that lithium increased the levels of GSTs, which are enzymes involved in xenobiotic stress/antioxidant pathways. To determine a role for xenobiotic stress, we looked at the effect of lithium on Nrf2. Nrf2 functions to activate enzymes such as GSTs and is expected to protect against damage during neurodegeneration. Nrf2 activity is partly regulated by GSK-3, and thus suggests a role for lithium in ameliorating Abeta toxicity via Nrf2 activity - we tested this by carrying out epistatic interactions between lithium and Nrf2 activity in Abeta expressing flies, and measured locomotor dysfunction in the flies. Results: Preliminary results suggest that Abeta toxicity affects neurogenesis by reducing cell proliferation. Further work is needed to confirm this. We found that lithium activates Nrf2 activity, but its protective effect against Aβ42 toxicity is not predominantly mediated by activating Nrf2, but rather by blocking Aβ42 accumulation, reinforcing our previous findings.

**P1-192** WITHDRAWN

**P1-193** DO ANTI-AMYLOID BETA PROTEIN ANTIBODY CROSS REACTIVITIES CONFUNDE ALZHEIMER DISEASE RESEARCH?

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Background: Alzheimer disease (AD) research has focused mainly on the amyloid beta protein (Aβ). However, many Aβ and P3-type peptides derived from the amyloid precursor protein (APP) and peptides thought to derive from Aβ catabolism share sequence homology. Additionally, conformations can change dependent on aggregation state and solubility leading to significant uncertainty relating to interpretations of immunoreactivity with antibodies raised against Aβ. Methods: We reviewed evidence relating to the reactivities of commonly used antibodies including 6F3D, 6E10 and 4G8 and evaluate their reactivity profiles with respect to AD diagnosis and research. Results: Antibody cross-reactivities between Aβ-type, P3-type and Aβ-catabolic peptides confound interpretations of immunoreactivity. More than one antibody is required to adequately characterise Aβ. The relationships between anti-Aβ immunoreactivity, neuropathology and proposed APP cleavages are unclear. Conclusions: We find that the concept of Aβ lacks clarity as a specific entity. Anti-Aβ antibody cross-reactivities lead to significant uncertainty in our understanding of the APP proteolytic system and its role in AD with profound implications for current research and therapeutic strategies.

**P1-194** MRNA EXPRESSION LEVELS OF NMDARS IN PRIMARY CORTICAL NEURONS TREATED WITH 1α-25Dihydroxyvitamin D3

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Background: Ion channels and ion metabolism are the targets that neurodegeneration affect. In neurodegeneration, especially the disruption of Ca²⁺ metabolism and over-stimulation of glutamate receptors trigger neuronal damage. Ca²⁺ which functions in many cell process, particularly plays fundamental role in neural plasticity which is important in learning and memory. Intracellular Ca²⁺ balance which is important for cell survival, maintain by ion channels. Among these ion channels, NMDARs (N-methyl-D-aspartate receptor) which are activated by glutamate, plays critical role in memory formation. NMDARs are tetrameric membrane calcium channels. Vitamin D is a secosteroid hormone that is responsible for regulating more than 1000 genes. Studies have shown that vitamin D has effects on nervous system including neurotrophic factor production, regulation of oxidative stress metabolism and calcium homeostasis. Alzheimer’s disease (AD) is a progressive neurodegenerative disorder. In AD-IDEA protocol, it was shown that treatment of memantine which is a NMDAR blocker, with vitamin D increased MMSE scores in Alzheimer’s patients. This indicates that vitamin D might have a regulatory effects on Ca²⁺ metabolism via NMDARs. In the study, we aimed to investigate the effects of vitamin D on NMDARs mRNA expression levels in primary cortical neurons. Methods: In the study, the primary cortical neuron cultures of Sprague Dawley rat embryos treated with 10⁻³M or 10⁻⁵M 1α-25dihydroxyvitamin D3 (1,25(OH)