

**P061** Potentiation of microglial inflammatory response by protein acetylation

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Inflammation and innate immune reactions are involved in the pathology of several neurodegenerative diseases, such as Alzheimer's disease. Inflammation is a defence reaction against diverse external and internal insults and hence is normally beneficial but, as excessive one, has deleterious effects in brain. Microglial cells are the residential macrophages in brain, and the microglial activation process itself, as well as the stimulators and inhibitors involved, have been intensively studied. Currently, we have studied whether protein acetylation status regulates the extent of microglial activation. It is known that several environmental stresses, aging and diet, which are risk factors for Alzheimer's disease, are involved in the regulation of the protein acetylation status and might regulate the extent of inflammatory responses. Interestingly, we have observed that the increase in protein acetylation induced by histone/protein deacetylase (HDAC) inhibitors, such as trichostatin A (TSA), dramatically potentiated the LPS-induced inflammatory responses in several neural inflammation models, such as mouse N9 and rat primary microglia, neural co-cultures and hippocampal slice cultures. NF- $\kappa$ B signalling inhibitors, helenalin and CAPE, inhibited the induction. TSA-induced potentiation was inhibited e.g. by PI3K inhibitor LY294002, LiCl<sub>2</sub> and dexamethasone. It seems that environmental stress, aging and diet might regulate microglial activation via protein/histone acetylation.