436d Involvement of Saturated Fatty Acids in the Pathogenesis of Alzheimer'S Disease
Sachin Patil and Christina Chan

Alzheimer's disease (AD) is a progressive, neurodegenerative disease characterized by extracellular deposits of amyloid beta (Aâ) protein and intracellular accumulation of neurofibrillary tangles (NFTs). NFTs consist of paired helical filaments of microtubule-associated tau protein that is hyperphosphorylated. The hyperphosphorylation of tau disrupts the cytoskeleton, which leads to degeneration of affected neurons, thus playing an important role in AD pathology. Epidemiological studies suggest that high fat diet significantly increases the risk of AD and the degree of saturation of fatty acids is critical in determining the risk for AD. This is further supported by animal studies in which the mice fed high fat-high cholesterol diet developed AD-like pathophysiological changes in their brain. Despite these accumulating data the basic mechanism behind the causal relationship between fatty acids and the pathogenesis of AD has not been established.

In this context, we show for the first time that saturated fatty acids (FFAs), palmitic and stearic acids, cause Alzheimer-like hyperphosphorylation of tau in primary rat cortical neurons. The observed FFA-induced effect is mediated through astroglia-induced oxidative stress. How FFA metabolism in astrocytes results in the aforementioned effects in neurons is not clear. We are currently applying metabolic flux analysis (MFA) to gain some insight into the metabolic profiles of primary cortical astroglia and neuronal cultures in the presence of saturated FFAs. This may help to identify the metabolic pathways involved in the observed FFA-induced, AD-specific phenotypes in the neurons, as well as, novel targets related to FFA metabolism, for therapeutic intervention in AD.