P-1.48

Unraveling the Role of Cytochrome C in the Pathogenesis of Alzheimer's Disease

Katarina Siposova [1], Eva Valusova [1], Viktoria Fedorova [1], Andrey Musatov [1]

[1] Institute of Experimental Physics, Slovak Academy of Sciences, Kosice, Slovakia (slovak Republic)

The etiology of Alzheimer's disease is complex and multifaceted, and the precise mechanisms underlying its onset remain incompletely understood. Numerous hypotheses propose various molecular targets believed to influence disease progression. One such hypothesis involves oxidative stress, which may not only induce oxidative damage, such as lipid peroxidation through membrane permeabilization, but also enhance Aβ production by activating β-secretase. These processes may contribute to a "circular cascade" of Aβ peptide accumulation and oxidative damage through intricate interactions between amyloid beta and membrane components. Within this, an exceptional role may be played by cytochrome c (Cyt c), which has diverse biological functions. Motivated by this, we investigated the effect of Cyt c on Aβ(1-40) amyloid aggregation, as well as the stability and morphology of fibrils. Our results demonstrated a significant anti-amyloidogenic potential of Cyt c, suggesting a key role for lysine residues. To validate this, we further examined the effects using apo-Cyt c, lysine, and poly-lysines. This study may provide new insights into the role of Cyt c in the age- and Aβ-related pathology of Alzheimer's disease, adding a new dimension to its biological significance. Acknowledgments: This work has been supported by grants APVV23-0013, VEGA 2/0034/22, and MVTS SK-TW Supra-Sight.