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One hundred years of Alzheimer's tangles*State of the Art***From Tangles to Tau Protein**

Iqbal K, Novak M 341

Alois Alzheimer could not have chosen a name more appropriate than neurofibrillary tangles when one hundred years ago he presented this histopathological hallmark of the progressive dementing disorder, which got named after him as Alzheimer disease. Both, the structure and as well as the molecular composition of neurofibrillary tangles have baffled neuroscientists for many years.

*Topical Review***The tangled story of Alois Alzheimer**

Zilka N, Novak M 343

In 1907, Bavarian psychiatrist Alois Alzheimer, who is considered to be a founding father of neuropathology, was first to describe the main neuropathologic characteristics of the peculiar disease in the brain of a woman showing progressive dementia when she was in her early 50s.

*State of the Art***Post-translational modifications of tau protein**

Pevalova M, Filipcik P, Novak M, Avila J, Iqbal K 346

Microtubule-associated protein tau is a phosphoprotein whose expression and phosphorylation is developmentally regulated. Whereas in adult mammalian brain several isoforms are produced from a single gene by alternative splicing, in fetal brain only a single isoform exists, corresponding to the smallest of the tau isoforms. Main physiological function of tau is the promotion of assembly and stabilization of microtubular network, which is essential for normal axonal transport of vesicles within the neuron.

*Systematic Review***Intrinsically disordered tau protein in Alzheimer's tangles: a coincidence or a rule?**

Skrabana R, Skrabanova M, Csokova N, Sevcik J, Novak M 354

Tau protein, the major constituent of neurofibrillary tangles in Alzheimer's disease and related tauopathies, is classified as intrinsically disordered protein (IDP). IDPs in contrast to globular proteins contain high proportion of polar and charged amino acids in their sequence, which results in the absence of a well-defined three-dimensional structure of the free protein.

*In Depth Reviews***Biological markers in Alzheimer's disease**

Grundke-Iqbal I, Rolkova G, Konstekova E, Iqbal K 359

Alzheimer's disease is the most common type of dementia occurring in human population. The disorder is characterized clinically by memory loss and histopathologically by the presence of neurofibrillary tangles and senile plaques in patient's brain. Accuracy of the clinical diagnosis of Alzheimer's disease is quite variable (~60 to 95 %), leaving a significant number of Alzheimer's disease patients undiagnosed or falsely positively diagnosed.

The hunt for dying neurons: Insight into the neuronal loss in Alzheimer's disease

Zilkova M, Koson P, Zilka N 366

Neuronal loss is one of the major pathological hallmarks of neurodegenerative disorders including Alzheimer's disease. Using rigorous quantitative methods, the distinct pattern of neuronal loss in pathological conditions such as neurodegeneration and in normal aging was clearly shown. Furthermore, the decrease of total neuronal numbers correlated in a considerable extent with the presence of neurofibrillary degeneration in the same brain regions.

*Systematic Reviews***Neuroinflammation in Alzheimer's disease: protector or promoter?**

Zilka N, Ferencik M, Hulin I 374

Alzheimer's disease is an irreversible, progressive and degenerative disorder that destroys the higher structures of the brain. Prominent neuropathologic features of Alzheimer's disease are senile plaques, neurofibrillary tangles, synaptic and cell loss. There is mounting evidence that chronic inflammatory processes play a fundamental role in the progression of neuropathological changes of Alzheimer's disease. It has been shown, that there is a reciprocal relationship between the local inflammation and senile plaques and neurofibrillary tangles.

The role of oxidative stress in the pathogenesis of Alzheimer's disease

Filipcik P, Cente M, Ferencik M, Hulin I, Novak M 384

Oxidative stress has been implicated in the pathogenesis of Alzheimer's disease as a relevant marker of neuronal degeneration. However it plays an important role not only in the pathogenesis of neurodegenerative diseases but also in other critical disorders like heart diseases, carcinogenesis and others. Oxidative stress is also associated with normal aging. In this review we discuss a crucial question: to what extent oxidative stress may be a causative factor in pathogenesis of Alzheimer's disease type of neurodegeneration.

*In Depth Review***Neural network plasticity, BDNF and behavioral interventions in Alzheimer's disease**

Hubka P 395

Alzheimer's disease is characterized by a gradual and hierarchical decline in cognition that is essentially connected with the functional properties of brain areas with the highest degree of plasticity. Corresponding brain regions are mostly affected by histological determinants of Alzheimer's disease. Crucial pathways involved in maintaining the neural plasticity were also shown to be impaired in Alzheimer's disease.