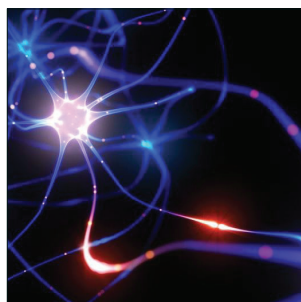
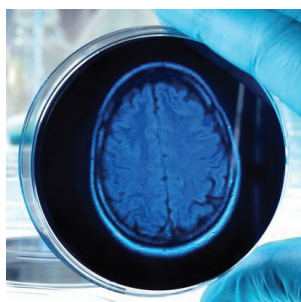

Keynote Forum September 16, 2019

Dementia 2019



13th World Congress on
Dementia and Alzheimer's Disease
September 16-17, 2019 | Paris, France

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Autoantibodies in Alzheimer's disease

Alzheimer's disease (AD) is an age-related multifactorial progressive neurodegenerative disorder manifested by memory loss, spatial disorientation, and gradual deterioration of intellectual capacity. Its etiology is unknown. Pathological changes including synaptic and neuronal loss, oxidative damage, activated inflammatory cells and protein depositions such as extracellular amyloid plaques composed by misfolded amyloid beta (A β) peptide and intracellular neurofibrillary tangles comprised of hyperphosphorylated aggregates of the microtubule-associated protein Tau (τ) are observed.

Compromised blood brain barrier (often observed at AD) may permit increased contact of immune cells with components released from dying neuronal cells, as well as the transfer of various brain proteins into the blood and induction of autoimmune response against them. Immune system activation is frequently reported in patients with AD. Some autoantibodies are naturally occurring antibodies produced without extrinsic stimuli, originated from B1 cells and reacting with various components of neural system; however, antibodies derived after antigenic stimulation by "self" might be produced by B2 cells as well. Antibodies against A β , τ , neurofilament light and heavy chains, S100B, cholinergic, adrenergic and glutamatergic receptors, as well as some other brain-derived antigens were reported in patients with various neurodegenerations. It should be stressed that some level of autoantibodies are commonly found at healthy individuals and incomplete and often controversial results are reported

about CNS immune/autoimmune responses during AD. Although autoantibodies might be sometime causing or aggravating pathology, naturally occurring autoantibodies may maintain physiological homeostasis, play key roles in the clearance of self molecules and apoptotic cells, protect from pathologically altered structures like oxidatively damaged, aggregated, and non-functional lipids and proteins. It is conceivable as well, that impaired/exhausted immune system of AD patients may contribute to pathology. It is worth mentioning that autoantibodies (or their specific profile) may serve as valuable biomarkers of various neurodegenerative diseases.

In our report we will focus on autoantibodies against τ in AD, MCI and some other dementias, their characterization in healthy subjects, AD, MCI patients and some other neurodegenerations, male/female differences and potential application of intravenous immunoglobulin (IVIg) treatment of neurodegenerative diseases.

Speaker Biography

Jan Ricny graduated from Faculty of Sciences, University of J.E. Purkyne, Brno, Czechoslovakia in 1975 and obtained PhD from Institute of Physiology, Czechoslovak Academy of Sciences, Prague in 1983. After postdoctoral training at McGill university at Montreal and Max-Planck Institut für Biophysikalische Chemie at Göttingen works as researcher and senior researcher at Institute of Physiology of Academy of Sciences and National Institute of Mental Health, Czech Republic. Author of about 80 publications, H index 16. His main interests are cholinergic neurochemistry and neurodegenerative diseases.

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Reduction of Alzheimer's disease prevalence and progression using multi-target therapeutic strategies

Prevalence of Alzheimer's disease and Risk Factors: Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive and irreversible nerve cell death throughout the brain including cerebral cortex, basal forebrain and hippocampus thus, leading to memory loss and cognitive impairment. It represents a pressing worldwide health problem with major socioeconomic burden. The disease is ultimately fatal and cell loss progress finally to a kinetic - mute state. Mutation in genes which increase production of amyloid β -peptides as well as which promote amyloid deposition, neurotoxicity, oxidative stress, neurofibrillary tangle formation, and increasing brain inflammation are reported to be associated with the disease. Alzheimer's disease progresses gradually, brain shrinks dramatically over time but still there is a lack of data about its progression. Scientists hope to model stages for AD for more prediction of the disease progression, expectation of its symptoms and to enhance the power to find real treatment. Major attention has been paid to AD risk factors especially modifiable ones as heavy smoking, excessive alcohol drinking and low education as well as cognitive and physical inactivity. History of depression and stress has been also suggested as possible risk factors, in addition to several environmental agents as dietary and malnutrition factors, metals and pesticides as well as brain injuries. Diagnosis mainly based on clinical assessment; however lab tests and neuroimaging are used to exclude other disorders.

Multi-target Therapeutic Strategies: For the complexity involved in the mechanism of AD progression consequently, multi-target therapeutic strategies are a must for providing symptomatic and disease modifying benefits. Lifestyle and healthy aging through reducing stress and increasing cognitive engagement, physical activities, healthy food as well as dietary supplementation of natural antioxidants, vitamins, polyphenols, and zinc in combined treatments showed marked protective effects rather than individual

treatments. The deleterious effect of stress on the brain can be also counteracted by using both epigallocatechin-3-gallate (EGCG) and diazepam. In experimental AD models, multi-target therapeutic strategies showed promising results and provided protection especially in the presence of different risk factors as stress, isolation and protein malnutrition. Moreover, the impact of EGCG, cocoa, pomegranate, coenzyme Q10, wheat grass, propolis and vinpocetine either each alone or in combination can greatly enhance the protective power of physical and mental activity. On the other hand, there are many challenges to developing vaccines that help to prevent the disease in the early stages, which should be efficacious regardless of patient immune status.

Speaker Biography

Azza A Ali has completed her PhD specialized in Pharmacology and Toxicology from Faculty of Pharmacy, Cairo University, Egypt. She developed research line of behavioral pharmacology in Egypt and participated as Advisory Board Member of the Arab Association for Pharmacy Development and its conference (AIPC 2019). She is member of many scientific societies as (AAPS) and Alzheimer's Association (ISTAART). She is also an Editorial Board Member of many international Journals as Brain Disorder & Therapy, Acta Psychopathologica, EC Pharmacology and Toxicology as well as Organizing Committee Member and Chairperson at many international Conferences as the International Conference on Brain Disorders & Dementia Care, Canada (2017) and International Conference on Parkinson's Disease & Movement Disorders, USA (2017, 2018). She published more than 60 papers in reputed journals, supervised and discussed more than 90 PhD and MSc thesis and actively participated by workshop, oral and posters presentations at many international conferences especially on Dementia and Parkinson's disease and in the Alzheimer's Association International Conference (AAIC 2016, 2017). She has many appreciation certificates and certificate of best presentation award at 19th International Conference on Environmental Pollution and Pollution Control, London, UK (ICEPPC 2017). Now she is a Head of Pharmacology and Toxicology Department and Member of the Committee for the Promotion of Professors at Al-Azhar University, Egypt.

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New biomarkers of Alzheimer's disease in Cerebrospinal fluid

Causes of Alzheimer's disease is not known and ideal biomarkers (100% sensitivity, 100% specificity) of this type of dementia have not been revealed yet. Current biomarkers (levels of amyloid beta 1-42, tau and phospho-tau) in cerebrospinal fluid are often estimated in a combination in order to increase their sensitivity and specificity. Recently, we evaluated new diagnostic biomarkers in cerebrospinal fluid (the ratio of Thioflavin-T-based fluorescence to intrinsic amyloid fluorescence (sensitivity 61.1%, specificity 70.8% compared to nondemented controls), levels of mitochondrial 17beta-hydroxysteroid dehydrogenase type 10 – amyloid beta 1-42 (sensitivity 41.1%, specificity 83.3% compared to nondemented controls), levels of mitochondrial 17beta-hydroxysteroid dehydrogenase type 10 – mitochondrial cyclophilin D (sensitivity 92.9%, specificity 91.7% compared to nondemented controls but only 26.2% compared to Frontotemporal lobar degeneration). Significant changes of all our prospective biomarkers were observed already in early stages of disease (the group of mild-cognitive impairment related to Alzheimer's diseases), however, specificities failed when compared to other types of dementia. Nevertheless, we can recommend the ratio

of Thioflavin-T based fluorescence to intrinsic amyloid fluorescence (reflecting oligomers to aggregates rate) in cerebrospinal fluid as the relatively cheap and easily accessible supportive diagnostic biomarker of Alzheimer's disease. Moreover, the above-mentioned complexes of two mitochondrial proteins (17beta-hydroxysteroid dehydrogenase type 10 and cyclophilin D) in cerebrospinal fluid seem to be the highly sensitive biomarker of neurodegeneration. Supported by AZV project of Ministry of Health of the Czech Republic (16-27611A).

Speaker Biography

Neurochemist Zdenka Kristofikova studied at Czech Technical University in Prague (Ing., Department of Nuclear Chemistry) and at University of Defence, Faculty of Military Health Sciences in Hradec Kralove (PhD, Department of Toxicology), both in the Czech Republic. At the present time, she works as a researcher and a head of working group in Department of Experimental Neurobiology of National Institute of Mental Health, Czech Republic. She has over 100 publications that have been cited over 600 times, and her publication H-index is 15. She is interested in cerebrospinal fluid or serum/plasma biomarkers and various animal models (genetic as well as pharmacological) of Alzheimer's disease for a long time.

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