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Editorial

Alzheimer's disease: Making the point

The Workshop at the Charles University of Prague has been held under the Auspices of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), the European Federation of Laboratory Medicine (EFLM), the Czech Society of Clinical Biochemistry, the CSF Society and the RAGFP-Trasformational Impact Committee.

It has been a specialized workshop on Alzheimer's Disease which covered traditional and innovative diagnostic approaches. The aim was to promote collaborative relationships between clinicians, researchers and laboratory scientists in highly specialized areas that are underserved by clinical laboratories.

Alzheimer's Disease is still an incurable, progressive, neurodegenerative condition which accounts for over 50–70% of dementias, afflicting 5% of men and 6% of women over 60 years old worldwide (World Health Organization 2010). As age is the principal risk factor, the general ageing of the global population, means that the total number of people suffering from Alzheimer's dementia is likely to still be increasing. The prevalence increases exponentially with age as Alzheimer's dementia affects < 1% of people aged 60 to 64 years old and 24% to 33% of those aged over 85 years.

There are around 36 million patients worldwide with Dementia and the extimated worldwide patients population by 2050 is 115 million. About two thirds are Alzheimer's Disease Patients! Alzheimer's is a complex multi-factorial disease, clinically characterized by cognitive impairment and late dementia, and representing one of the greatest epidemic and health challenges today. The pathological brain changes may begin 20–30 years before the onset of the clinical symptoms. Thereafter, the symptomatic phase of AD can last from about 5 up to 12 years. Today we have only few drugs to counteract AD and unfortunately they are able only to delay the progression of symptoms but do not modify the disease process. Nevertheless to achieve the optimal efficacy, any therapy should be initiated as early as possible. The identification of early diagnostic and progression biomarkers, as well as novel targets for drug design, are needed. Despite a great amount of research, AD still has mysterious aspects and an open problem for both researchers and clinicians.

To detect in vivo the pathological process underlying progressive cognitive and behavior impairment, the Internationals guidelines recommend the use of biological and topographical markers, which can reflect neuropathological modifications in brain. In cerebrospinal fluid (CSF), decrease of amyloid Beta 1–42 ($A\beta_{42}$) and a low ratio of $A\beta_{42}$ with amyloid Beta 1–40 ($A\beta_{42}/A\beta_{40}$), together with the increase of both total tau protein (t-tau) and phosphorylated tau (p-tau), contribute to define the “Alzheimer's signature”.

From the laboratory point of view it should be pointed out that to date the overall variability of available biomarkers (both diagnostic and prognostic markers) remains too high to allow assignment of universal biomarkers cut off values for a specific intended use.

In particular, with the increasing utility of CSF biomarkers including $A\beta_{1-42}$, t-Tau and phospho-Tau, the pre-analytical phase of testing has become an important variable in consistent measurement from laboratory to laboratory. To minimize pre-analytical variability standard operating procedures have been proposed, and importantly recommend the use of polypropylene collection tubes over glass or polystyrene. The recent development of fully automated methods determined a great improvement in reducing the variability of the preanalytical phase.

These improvements, together with the establishment of some certified reference materials (CRMs) [1] and Proficiency Processing Schemes [2] recently introduced in clinical laboratories, make possible an harmonization between different methods in the next future.

At the same time the integration of the data from the routine laboratory with other laboratory techniques (proteomics, genomics, flow cytometry) and diagnostic tools (radiology, pathology) is desirable.

Moreover other roles of biomarkers have to be considered in Alzheimer's Disease clinical trials as diagnostic accuracy, stratification of patients, characterization of the mechanism of action and the biochemical effects of drugs, monitorization of the progression, and assessment of the response to treatment.

Finally new approaches in biomarker discovery are on the horizon to support the Diagnosis of Alzheimer's Disease; in particular proteomics and metabolomics even if they often showed conflicting results due to differences in analytical platforms, matrices, panel of metabolites studied, clinical cohorts, and preanalytical confounding factors.

This Omics attempt to investigate the global and dynamic molecular changes under different normal and pathological conditions, and thus represent a promising approach for the study of the Alzheimer's Disease. Advances in technologies have led to a new system of analysis, named the “Omics era”, which integrates the opportunity of collecting various data and information at the molecular levels together with the simultaneous development of novel computational tools needed to analyze and filter such data with the aim of discovering novel diagnostic biomarkers and potential drugs.

References

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