

BIOBANKING FOR DIAGNOSTIC MARKERS IN NEUROLOGICAL DISORDERS

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The diagnosis of neurological disorders is severely hampered by the absence of reliable bio markers that can be measured in body fluids such as blood, urine and cerebro-spinal fluid (CSF). The search for diagnostic bio markers obtained from living donors has contributed a vast amount of data. When using autopsy material, we have to cope with significant data fluctuation due to rapid post-mortem changes. The role of amyloid and Tau as early diagnostic markers in the pathology of dementia has been reported in differential involvement in Alzheimer's disease (AD), late onset Alzheimer disease (LOAD), Lewy Body dementia (DLBD), Vascular dementia, fronto-temporal lobar degeneration (FTLD), Mild Cognitive Impairment (MCI) and non neurological controls.

In the coming decennia Brain /Tissue /Bio banks (BTB-banks) will collect, preserve and type RNA and DNA extracted from brain /tissue /body fluids in order to update the pathological hallmarks of dementing disorders.

The variability in the known/ clinically applied Bio markers in dementia which can be identified and incorporated into clinical drug trials is immense. We evaluated the validity of these bio markers in reflecting the typical hallmarks of neurological diseases and healthy non-dementing controls and definitively validate them at autopsy.

Neurodegenerative disorders are classified according to clinical criteria. Accumulating knowledge and understanding on the underlying mechanisms leading to these disorders has created increased interest the search and identification of disease-specific biomarkers in cerebrospinal fluid (CSF). The brain-specific proteins amyloid β_{42} protein, tau and hyperphosphorylated tau have been widely investigated in the differential diagnosis of dementia syndromes.

These biomarkers are widely used in the classification of various dementia disorders. Due to the overlap in pathophysiological hallmarks of the various syndromes, we are looking for possible common markers which are present in CSF; a panel of these markers can be used for early and differential diagnosis.

The current wide use of new techniques (e.g. proteomics) may lead to identification of new biomarkers which in turn will be applied in the differential diagnosis of neurodegenerative disorders. Any given medical intervention that can delay the onset or progression of chronic diseases will have an enormous public health.

Biochemical markers (biomarkers) present in the in CSF have been reported to help in improving the accuracy of the clinical diagnosis (Blennow, 2001); reference values for both CSF-tau and CSF-A β 42 have been reported (Sjögren et al, 2001a,b).

In our studies we combined the use of CSF-tau and CSF- A β 42 markers for to assist in differential diagnostic procedures. Although it is presently clear that no single biomarker can absolutely discriminate between AD and other dementias, a judicious combination of several biological markers may substantially increase the sensitivity and specificity of the diagnosis. If the results from a panel of biomarkers are added to the findings derived from a classical work-up, diagnostic accuracy can be further increased (Ravid 2008 a,b).

References

- Andreasen, N et al. Cerebrospinal fluid levels of total-tau, phospho-tau and A β 42 predicts development of Alzheimer disease in patients with mild cognitive impairment. *Acta Neurol Scand* 2003;107(suppl 179):1-5.
- Blennow K. CSF markers for the diagnosis of Alzheimer's disease. *Clinical Laboratory International*, October 2001:8-10.
- Blennow, K. et al. CSF markers of incipient Alzheimer's disease. *Lancet Neurol* 2003;2:605-613.
- Kapaki, E et al. Highly increased CSF tau protein and decreased β -amyloid (1-42) in sporadic CJD; a discrimination from Alzheimer's disease? *Neurol Neurosurg Psychiatry* 2001;71:401-403.
- Maddalena, A et al. Biochemical diagnosis of Alzheimer's disease by measuring the cerebrospinal fluid ratio of phosphorylated tau protein to β -amyloid peptide₄₂. *Arch Neurol* 2003;60:1202-1206.
- Ravid R – Standard operating procedures, ethical and legal regulations in BTB (brain/tissue/bio) banking: what is still missing? *Cell Tissue Bank*;9(2):121-37, 2008.
- Ravid R, Grinberg LT. How to run a brain bank-revisited. *Cell Tissue Bank*.;9(3):149-50, 2008.
- Sjögren, M et al. Tau and A β 42 in cerebrospinal fluid from healthy adults 21-93 years of age: establishment of reference values. *Clinical Chemistry* 2001a;47:10:1776-1781.
- Sjögren, M et al. Both total and phosphorylated tau are increased in Alzheimer's disease. *Neurol Neurosurg Psychiatry* 2001b;70:624-630.