



Press release

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For the first time, a new Biomarker test enables early detection of Alzheimer's dementia in blood.

Hennigsdorf, 15.05.2009. A recent study published in the journal "Biological Psychiatry" substantiates the interrelation between the variations in the microcirculation and the Alzheimer's disease. With the aid of the new Biomarker tests, these variations can be measured and Alzheimer's diseases can be diagnosed with greater accuracy. Chances for therapy can be highly improved with early diagnosis of the disease.

Correlation between micro vascular variations and the occurrence of Alzheimer's dementia (AD) has already been established. The B·R·A·H·M·S AG has now developed a test procedure to measure the concentration of the Biomarker MR-proANP (Mid-regional Pro-Atrial Natriuretic-Peptide), MR-proADM (Mid-regional pro-adrenomedullin) and CT-proET-1 (C-terminal pro-Endothelin-1) in blood.

Based on a clinical trial carried out by the diagnostic company in cooperation with the Ludwig-Maximilians-University, Munich and the Trinity College, Dublin, it has now been established that measuring these three parameters can lead to early detection of Alzheimer's disease. The Biomarkers are focused on the factors that control the dilatation and constriction of the cerebral micro vascular system and thereby control the cerebral perfusion. This is vital for the maintenance of adequate supply of oxygen and nutrients to the brain as well as for the elimination of toxic substances from the brain.

In this first major clinical trial in which 94 patients with probable Alzheimer's dementia (AD) and 53 healthy test subjects as controls had taken part, the new blood test differentiated between the clinically diagnosed patients suffering from Alzheimer's dementia and the healthy test subjects (controls) with about 81 percent accuracy. The results suggest that systematically measured micro-vascular variations can prove to be a highly sensitive diagnostic tool for early detection of Alzheimer's dementia. The manuscript, in which these results have been reported, has recently been published in the esteemed *Biological Psychiatry* technical journal.

One of the distinct advantages of this test is that it is based on the simple blood test that can be easily carried out by a general practitioner and that which is an easily accessible screening tool for him. Until now, the available Biomarkers with good clinical accuracy for the detection of Alzheimer's dementia are based on the cerebrospinal fluid (Cerebrospinal fluid [CSF]) or on



imaging procedures including MRT or PET that are relatively difficult and expensive for general practitioners. The measurement of CSF- Biomarkers as well as imaging procedures the best validated methods for early diagnosis of Alzheimer's dementia currently, since these show high sensitivity in preclinical stages such as mild cognitive impairments (Mild Cognitive Impairment [MCI]).

Biomarker tests, based on the blood tests, are applied at an even earlier stage of development and are already considered to be vital in routine-screening for early detection of Alzheimer's disease and prevention of dementia. The new test procedure is a promising prospect as a diagnosis tool based on blood tests and is currently tested in a large clinical study for mild cognitive impairments (Mild Cognitive Impairment [MCI]) – a clinical syndrome related to increased Alzheimer's risk.

Background of Alzheimer-dementia:

Alzheimer's dementia is a neurodegenerative disease and its outbreak can be due to various etiological factors and mechanisms. Vascular variations, including arteriosclerosis, high or low blood pressure as well as diabetes, are some of the significant risk factors. It is presumed that vascular risk factors account for at least 50 percent of all cases of dementia. Moreover, micro vascular variations at the blood-brain barriers are associated with the occurrence of Alzheimer-dementia. The clinical diagnosis of Alzheimer's is based mainly on ruling out other causes of dementia and still requires a multitude of examinations that are complex, long and expensive. Only a histopathological examination of the brain post-mortem can confirm the presence of Alzheimer's dementia with absolute certainty. Furthermore, the disease is diagnosed only at a later stage. Hence, a diagnosis even at the preclinical phase would be of greater significance. This extends over a period of 10-40 years and is often accompanied with only mild symptoms. An early treatment can significantly improve the success rate and linger the progress of the disease.

Currently about 1.1 million people in Germany suffer from dementia, approximately 600,000 of them suffer from Alzheimer's, the most common form of dementia. The variations in the ageing structure of the population would result in increased number of the population being affected by the disease. According to a census of Federal Statistical Office, the population of those above 65 years of age is estimated to go up by another 7 million by 2050. Since majority of the people affected by the disease are from this age group, making up to 97 percent of them, the number of people who would be affected might be more than 2.6 million by this period.

**Background of the Biomarker:**

The Atrial Natriuretic Peptide (ANP) is produced mainly in the atria of the heart and is associated with natriuresis, diuresis, vascular dilatation and regulation of the cardio vascular system. Since peptide is very unstable, the test measures a fragment of the corresponding prohormone, the Mid-regional Pro-atrial Natriuretic Peptide (MR-proANP), which as surrogate marker, helps in consistent measurement of the concentration of the hormone.

Adrenomedullin (ADM) is a multifunctional peptide that is mostly synthesised from tissues, especially those of the heart and the kidneys. It is effective in vascular dilatation and influences the cardio vascular system, the hormone secretion and the respiration. Since the mature hormone ADM, similar to ANP, cannot be accurately measured in blood due to its instability, this test detects the mid-regional fragment of ADM-precursor molecule, Mid-regional Pro-Adrenomedullin (MR-proADM) as stable surrogate.

Endothelin-1 (ET-1) is however a peptide hormone, which on the basis of its vascular constricting effect for the regulation of blood pressure, is considered to be a direct opponent to ADM. The new test in this case measures a C-terminal fragment of ET-1-precursor molecule (CT-proET-1), which is similar to MR-proANP and MR-proADM, having a much higher stability when compared to mature ET-1-Hormone.

Background of B·R·A·H·M·S:

The B·R·A·H·M·S AG conducts researches, develops, produces and markets innovative diagnostic biomarkers. It is one of the three largest biotechnology companies in Germany. The company sells its products in more than 65 countries via its own subsidiary companies and sales organisations as well as laboratory systems from its own production via the globally operating licensees. The headquarters of B·R·A·H·M·S is at Hennigsdorf in Berlin, where about 220 employees out of 400 of the world wide employees of the company are posted.

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