

Distinguishing True Alzheimer's Disease from Lyme Neuroborreliosis Mimicry via the Practical Application of MicroRNA Molecular Markers are Especially Important in Areas Endemic for Tick Borne Disease

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"Lyme Neuroborreliosis manifesting Alzheimer's Disease like symptoms can be successfully treated with antibiotics if diagnosed early".

Dementia is a disease most frequently associated with individuals of advancing age [1]. Alzheimer's disease (AD) is most commonly associated with dementia in elderly patients [1]. This disease is "morphologically characterized by extracellular beta-amyloid plaque deposition, intra-neuronal tau pathology, neuronal death, vascular dysfunction and inflammatory processes" [1].

Chemokine markers (CCL2, CXCL8, and CXCL10) are present in the CSF of AD patients, and have been found to be useful markers of pathology for this disease [1]. The chemokine CCL2 has been shown to be involved in the pathogenesis of AD. The CCL2 chemokine has been also found to be useful as a supplemental biomarker for observing the progress AD [1]. In order to obtain these markers, however, one has to perform a spinal tap. It would be ideal to have markers found in both the CSF and in Serum/Plasma specimen types.

Additional markers for AD, called "microRNAs" have being discovered [2,3]. MicroRNA markers provide new and useful information to our understanding of the mechanisms associated with AD. Such information is needed in order to foster an earlier diagnosis and subsequent treatment of this neurological disorder [2,3].

MicroRNAs (miRNAs) are small non-coding RNA's which have been demonstrated to regulate the expression of a gene [2-4]. When microRNA expression has been altered, research investigations have shown that these markers to be linked to pathological processes, which also have included neurodegeneration [3,4]. These microRNAs have been found to be present in both the CSF and in the Serum/Plasma of AD patients [3,4].

There are several species of microRNA's that are deregulated in the brain, and have been found also in both the CSF, as well as, in the serum/plasma of patients with AD [5].

Galimberti, *et al.* had discovered that the microRNA's: miR-23a, miRNA26, and miR-125b could serve as useful indicators when these investigators compared 18 non-inflammatory and 8 inflammatory neurological controls and 10 patients with frontotemporal dementia [4]. These investigators discovered that in CSF of AD patients there occurred a "significant down-regulation of miR-125b and miR-26b versus the Non-Inflammatory Disease Control Patients (NINDC) [4]. When these investigators looked at "serum specimens" they found that miR-125b expression was distinctly different in AD patients when compared with NINDC patients [4]. This investigation showed that miR-125b microRNA levels of AD patients in serum were decreased when compared with NINDC patients [5] and that they were thus able to distinguish AD patients from NINDC patients using serum samples with "an accuracy of 82%" [4].

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Shaik, *et al.* stated that “some of the miRNAs found to be dysregulated in AD” have been reported to “correlate with neuropathological changes, including plaque and tangle accumulation”, as well, as altered expressions of microRNA species that are known to be involved in AD pathology [5].

Neurological Lyme Disease or Lyme Neuroborreliosis and its mimicry of the clinical manifestations of such neurodegenerative diseases as Amyotrophic Lateral Sclerosis (ALS), Multiple Sclerosis (MS), Alzheimer's Disease, and Parkinson's Disease have been responsible for cases of misdiagnosis in areas that are endemic for Lyme and related Tick Borne Diseases [6]. Sadly, if diagnosed early, Lyme Neuroborreliosis can be successfully treated and reversed with antibiotics. By contrast, true cases of ALS, MS, Alzheimer's Disease, Parkinson's haven't any cure at the present time [6]. Thus, it is crucial to have available an expanded arsenal of markers that enable a clinician to distinguish Lyme Neuroborreliosis Mimicry from true forms of neurodegenerative diseases (i.e. ALS, MS, Alzheimer's Disease, and Parkinson's Disease). Lyme Neuroborreliosis caused by *Borrelia burgdorferi* can be persistent and can result in “extensive health care costs” [6,7].

Neurological Lyme Disease has been found to cause “lingering symptoms that persist in up to 20% of those afflicted” despite treatment with antibiotics [7]. The research investigations of Brissette at the University of North Dakota, have been focusing upon the application of microRNA markers that are associated with Lyme Neuroborreliosis, and have found that *Borrelia burgdorferi* “can induce changes in the microRNA expression of miR-122-5p, miR-135a-3p, miR-146b-5p [7].

Additional research investigations involving specific microRNA species expression changes in both True Alzheimer's Disease, and Lyme Neuroborreliosis Mimicry with Alzheimer's like clinical manifestations are urgently needed in order to be able to properly diagnose and treat patients, and to avoid misdiagnosis especially in Tick Borne Disease endemic areas. This latter point is of the utmost importance because Lyme Neuroborreliosis manifesting Alzheimer's Disease like symptoms can be successfully treated with antibiotics if diagnosed early!!!

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