Biological Markers in the Diagnosis of Multiple Sclerosis

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Multiple Sclerosis (MS) is a disease that affects the central nervous system. Patients with multiple sclerosis often face symptoms of numbness, fatigue, pain, and coordination problems, as well as many other issues. Through years of effort, researchers have found numerous biological markers (biomarkers) that have helped in the diagnosis of the disease. Several biomarkers have been found by examining the cerebrospinal fluid. Furthermore, the use of magnetic resonance imaging (MRI) is another tool used for discovering MS biomarkers. Gene expression profiling is a new, up-and-coming method diagnosing MS. Clinicians and researchers have found that patients with MS express certain genes differently. Finding these genes may lead to the profound discovery of many biomarkers. By spotting such biomarkers efficiently, doctors can begin the prognosis treatment sooner, ultimately saving the lives of those affected by Multiple Sclerosis.

Introduction

Clinician classify Multiple Sclerosis as an autoimmune disease, in that, the body's immune system attacks and destroys the myelin sheath that surrounds nerve cells of the central nervous system (CNS). Typically, the pathology of the disease is recognized by this demyelination accompanied by inflammation and axonal damage (Stoop et al., 2008). Damage to the myelin sheath and nerve fibers will hinder nerve signals sent from the brain to the spinal cord and the peripheral nerves. This delay, or in some cases complete disruption of the nerve signal, will lead to the symptoms seen in MS patients. There is a lengthy list of symptoms including: fatigue, numbness, walking & balance coordination, vision loss, paralysis, bladder/bowel dysfunction, cognitive dysfunction, emotional changes, and depression. The symptoms for each patient vary greatly, and not every patient experiences all the symptoms. Experiencing such symptoms can render a patient disabled.

MS is a disease that is not prejudice to any one type of people. However, there were some trends found from studying the epidemiology of the disease. Young adults, mostly women, are diagnosed with MS after experiencing some symptoms of Multiple Sclerosis (Tumani et al., 2009). Ongoing research has yet to discover why females are diagnosed more often than males. Although MS is not hereditary, it is believed that one can be genetically predisposed to the disease. Research has shown when a patient is diagnosed with MS they typically have a close relative whom also has the disease, which displays that certain genetic factors found in relatives can trigger the autoimmune response (Jager & Hafler, 2004). It is the goal of researchers and clinicians to discover which 'genetic factors' contribute to the diagnosis of MS. To diagnose MS, a physician will look for biomarkers that could possibly be found through various tests, such as: MRI, cerebrospinal fluid (CSF) assessment, and gene expression profiling (Stoop et al., 2008).

Recent Progress

Multiple Sclerosis is a very complex disease, where, not one distinct genetic biomarker has been found in order to diagnosis MS (Hong et al., 2004). However, most patients have been diagnosed on the basis of displaying different symptoms characterized by MS. Careful neurological examination via an MRI is highly recommended when diagnosing MS. In most cases, an MRI will display lesions found in the brain and/or spinal cord of the patient. MS lesions are rarely biopsied, so CSF analysis is

one of the few accurate and practical tools for diagnosis and pathology (Tumani et al., 2009). Stoop et al. (2008) claims that, "…because the disease process in MS is located in the CNS, cerebrospinal fluid (CSF) is a promising body fluid in which to search for biomarkers and disease-associated proteins and peptides." Assessing the CSF, clinicians look for an array of inflammatory molecules (cytokines,chemokines, their receptors and molecules related to T cell adhesion/trafficking and apoptosis) that are produced by inflammatory cells and T cells during the autoimmune process (Hong et al., 2004). Further studies have ventured into gene expression profiling, also known as microarrays. Several researchers have examined the peripheral blood of MS patients and have identified several genes that are expressed differently when compared to control patients (Jager & Hafler, 2004). After mapping a "molecular fingerprint" of MS, one can study the peripheral blood cells to determine if a patient is likely to have MS. However, this study has its limitations. Due to the variability of the disease, results are very difficult to recreate. Further research on the molecular pathways of the disease must be accomplished in order to make the power of microarray technology efficient and accurate (Jager & Hafler, 2004). Although researchers are hopeful for new findings in the field of gene expression profiling, Hong and coworkers (2004) state, "special requirements for sophisticated equipment and sample processing and the cost issue are among the major limitations associated with current microarray technology.

Discussion

Physicians and researchers are making great strides trying to understand the pathology of Multiple Sclerosis. MRI technology has advanced and has greatly aided in the diagnosis of MS by detecting lesions found in the brain and the spinal cord. CSF analysis is a great tool that can examine the cerebrospinal fluid for inflammatory cells that are caused by the autoimmune process (demylenation & axonal damage) of the disease. Tumani et al. (2004) claim, "CSF is an invaluable research tool that allows to access as proximally as practically possible the neighborhood of the target organ of the autoimmune attack. Its study has contributed to gaining important insights into the immunopathogenesis of MS." Gene expression profiling is becoming highly sophisticated, and with increased research clinicians will be able to find a number of genes that are MS-related. Although there is not a single distinguishable biomarker that can determine the diagnosis of MS, it seems that clinicians can diagnose the disease based upon a multitude of distinct properties that MS displays. There is no doubt that with further research efforts many more biomarkers of MS will be found, which will inevitably benefit the lives of those affected by Multiple Sclerosis.

References
1. Hong J., Zanga Y., Huttona G., Rivera V.M., and Zhang J.Z. 2004. Gene expression profiling of relevant biomarkers for treatment evaluation in multiple sclerosis. Journal of Neuroimmunology. 152, 126-139.
2. Jager P.L., & Hafler D.A. 2004. Gene expression profiling in MS: what is the clinical relevance? The Lancet Neurology. 3, 269.
3. Stoop M.P., Dekker L.J., Titulaer M.K., Burgers P.C., Sillevis Smitt P.A., Luider T.M., and Hintzen R.Q. 2008. Multiple sclerosis-related proteins identified in cerebrospinal fluid by advanced mass spectrometry. Proteomics. 8, 1576-1585.
4. Tumani H., Hartung H.P., Hemmer B., Teunissen C., Deisenhammer F., Giovannoni G., Zettl U.K., and The BioMS Study Group. 2009. Cerebrospinal fluid biomarkers in multiple sclerosis. Neurobiology of Disease. 35, 117-127.