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Humoral Immunity Profiling of Subjects with Myalgic Encephalomyelitis Using a Random Peptide Microarray Differentiates Cases from Controls with High Specificity and Sensitivity

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Abstract Myalgic encephalomyelitis (ME) is a complex, heterogeneous illness of unknown etiology. The search for biomarkers that can delineate cases from controls is one of the most active areas of ME research; however, little progress has been made in achieving this goal. In contrast to identifying biomarkers that are directly involved in the pathological process, an immunosignature identifies antibodies raised to proteins expressed during, and potentially involved in, the pathological process. Although these proteins might be unknown, it is possible to detect antibodies that react to these proteins using random peptide arrays. In the present study, we probe a custom 125,000 random 12-mer peptide microarray with sera from 21 ME cases and 21 controls from the USA and Europe and used these data to develop a diagnostic signature. We further used these peptide sequences to potentially uncover the naturally occurring candidate antigens to which these antibodies may specifically react with in vivo. Our analysis revealed a subset of 25 peptides that distinguished cases and controls with high specificity and sensitivity. Additionally, Basic Local Alignment Search Tool (BLAST) searches suggest that these peptides primarily represent human self-antigens and endogenous retroviral sequences and, to a minor extent, viral and bacterial pathogens.

Keywords Antibody · Chronic fatigue syndrome · Immunosignature · Myalgic encephalomyelitis · Peptide array

Introduction

Myalgic encephalomyelitis (ME), also commonly referred to as chronic fatigue syndrome or ME/CFS, is a heterogeneous illness characterized by a number of physical symptoms and comorbid conditions including neurocognitive dysfunction,

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