Genomic organization and single-nucleotide polymorphism map of desmuslin, a novel intermediate filament protein on chromosome 15q26.3

ABSTRACT

The absence of mutations in the desmuslin gene did not impact its function. Nevertheless, the single-nucleotide polymorphisms mapped in this study are highly disequilibrated and can be used for disambiguation studies of this region of chromosome 15q26.3.

INTRODUCTION

A chronic debilitating autoimmune disease called Rheumatoid arthritis causes synovitis (synovial swelling) of the joints, bursae and tendon sheaths, but is not often manifested as a synosomial disease; instead, immunologic processes appear to mediate these systemic and articular manifestations. The presence of synovial abnormalities in rheumatoid arthritis is marked by synosympathetic cell proliferation, neoangiogenesis, and inflammatory cell infiltration involving the myeloid, macrophage, or lymphoidin lineages. There has been considerable debate over the relevance of the specific cell types (and their products) to inflammation in rheumatoid arthritis, but it seems likely that all these cell kinds play some role in disease pathogenesis. Rheumatoid arthritis is supported by the identification of certain types of T cells in blood and synovial tissue that express specific surface membrane proteins or express a limited range of antigen receptors. To exemplify, clonal amplifications of CD8+ CD57+ T cells are frequently found in the repertoire of T-cells from rheumatoid arthritis patients. Similarly, CD4+CD28- T cell replications occur in both the blood and synovial compartments or tumor sites of these patients and appear to be auto-reactive. Ultimately, the T-cell receptors for antigen expressed by these and other T-cell subsets often display bias in favor of receptor that expresses some V gene expression (in contrast to the detailed studies of T cell clonality in rheumatoid arthritis), but much remains unclear about the extent to which B-cell diversity varies in this disease. The interpretation that the B-cell repertoire is also restricted is supported by previous studies. Circulating B cells were found to have oligoclonality according to flow cytometry, and cell culture experiments revealed the spontaneous secretion of immunoglobulins of restricted heterogeneity by synovial tissue explants as defined by immunological subclass, isoelectric focusing, or idiotype expression. Molecular studies of immunoglobulin genes found in the synovial tissue of rheumatoid arthritis patients provide new evidence for these concepts. These findings are significant because they reveal an ongoing immune response that targets specific (auto)antigens at low and high levels of B- and T-cells. By using the length of the third complementarity determining region (CDR3) of this rearranged copy of an enzyme called HCDR3, we were able to study the level of genetic alterations in B cells affected by rheumatoid arthritis through our current investigation. The immunoglobulin VH gene fingerprinting method, which has been used to identify the diversity of B cells and T cells in multiple clinical trials, was modified to address this problem. Recent findings indicate that B-cell clonal expansion is a typical and widespread feature of rheumatoid arthritis, that it includes both non-responsive and activated cells, and that this can persist for several months. These results provide support for the notion that autoimmune responses are involved in underlying chronic (auto)immune responses.

Research on gene expression in the postnatal developing murine brain has revealed that only 1% of genes transcribed are regulated by development. The aim of this study is to provide researchers with an alternative approach to identify specific transcripts with unique developmental consequences without having to perform a comprehensive screening. RNA fingerprints that contain a subset of developmentally controlled transcripts are presented here, with all the information required for isolation and identification of individual transcripti. We have identified 131 developmentically controlled transcriptions in three major expression profiles, totaling 141. Roughly 7% of the participants were categorized as C, and the rest were classified as A (61) or B (61). Our research supports the idea that modifying DDRT-PCR expression profiles indicates actual changes in expression levels during brain development. Remember that alterations in expression profiles are linked to changes in RNA level per microgram total ARN throughout the brain and, given that the postnatal brain is not a homogeneous system (i.e.