Clonal expansion is a characteristic feature of the B-cell repertoire of patients with rheumatoid arthritis

ABSTRACT

The aim of this study was to determine the degree of B-cell clonal diversity in individuals with rheumatoid arthritis by using HCDR3 (third complementarity determining region of the rearranged heavy chain variable region gene) length as a reference. The fingerprinting of the immunoglobulin VH gene was achieved through a modified approach that involved the use of genomic DNA or complementary (c)DNA sourced from peripheral blood, synovial fluid, and tissues from patients with rheumatoid arthritis. The detection and differentiation of activated but unactivated B-cell clones from numerically expanded ones were made possible by these assays. Based on current evidence, B-cell clonal expansion is a prevalent and distinctive characteristic of rheumatoid arthritis, with increasing frequency from the blood to the synovial compartments and narrowing of the cDNA repertoire at the level of both joints. Resting, apparently memory B cells, and activated B cell types can both serve as clonal expansions. Furthermore, some of these expansion events may persist for days or weeks. The outcomes reinforce the idea that a persistent (auto)immune response is active in rheumatoid arthritis, and that this response, particularly at the B-cell level, may be distinct to particular joint types. A determination of the targets of these autoimmune reactions may offer valuable information to understand the immunopathogenesis of this condition.

INTRODUCTION

Tumor necrosis factor and lymphotoxin- (LT-) are both cytokines that have pleiotropic biological functions, including inducing programmed cell death and controlling immune cell proliferation and differentiation. Plasma levels of TNF or LT- have been found to be associated with specific autoimmune and infectious diseases, as well as solid and hematologic malignancies, according to various studies. It is also believed that genetic polymorphisms within their genes located tandemly on the long arm of chromosome 6 within the MHC class III region may affect the secretion of these molecules. Located in the TNF promoter region at nucleotide position-308, one of the most well-documented polymorphisms affects a consensus sequence for AP-2's binding site, with guanine defining the common TNT1 allele and tensing the underlying molecule to glycine and then forming agadenine. A polymorphism at nucleotide 252 within the first intron of the LT- gene was reported to affect plasma levels of LD-0, which is associated with a single nuclide ester-responsive element. This effect differs between two alleles that have been designated as IL-10.5 and il--20.5. The TNF2 and LT- (5.5 kb) alleles have been found to be associated with elevated levels of both Tnf2 AND lentiviral factor-converting enzymes (TL-A), suggesting that elevated plasma levels also correlate with an elevated level of TNTNF or LD->1 target/Ln–.Note: This disease is particularly relevant to us in terms of autoimmune diseases and infectious diseases, and has also been shown to negatively affect lymphoid malignancies. In this study, we genotyped a group of 64 patients with childhood acute lymphoblastic leukemia (ALL) in both matched case-control studies and identified genetic polymorphisms within TNF and LT- genes to determine their predictive power for ALL relapse.

CONCLUSION

By describing the building blocks of protein complexes in skeletal muscle and heart, with emphasis on information about genotype-phenotype relationships, we can better understand the pathophysiology of human muscle diseases. Our recommendation is for other groups to test for the C598T DMN mutation in their human patient samples affected by muscular and cardiac diseases. The generation of desmuslin null animal models will also help us comprehend the role of this protein in muscle and cardiovascular disease.