Soluble Class I HLA Antigens in Patients with Rheumatoid Arthritis and Their Families

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ABSTRACT. ***Objective.*** To study Class I soluble HLA in black patients with rheumatoid arthritis (RA) and their families, and to compare the findings to a group of healthy families of the same racial background.
Methods. ELISA was developed to measure soluble HLA Class I (sHLAI) in the serum of 25 patients with RA. Family studies were performed in seven patients with RA and their 28 first degree relatives. These family studies were compared to similar measurements from 66 members of 13 healthy families.
Results. Mean sHLAI values were higher in patients with RA than those observed in healthy black individuals. Patients with RA were characterized by elevated serum HLAI, while no change was observed between patients with RA positive or negative for rheumatoid factor. The relatives of patients with RA had high concentrations of sHLAI, compared to families without RA. Highest serum concentrations of sHLAI were found in individuals who were HLA-A23 or HLA-Aw33 positive.
Conclusion. sHLAI may play a role in the pathophysiology of RA, and there is an association between either augmented release or production of sHLAI and specific HLA allotypes. (*J Rheumatol 1995;22:1025–31*)

Key Indexing Terms:
SOLUBLE HLA CLASS I
ELISA
MAJOR HISTOCOMPATIBILITY COMPLEX
RHEUMATOID ARTHRITIS

In humans, HLA are prominently expressed on the surface of lymphoid and other nucleated cells. Although the antigen is mostly exterior to the surface of the membrane, it is anchored in the cell membrane by a transmembrane domain and has a short intracellular polypeptide domain. We and others have demonstrated that HLA molecules not only are expressed on the cell surface, but also can be identified in a soluble or shed form[1-7]. Technical advances have made it possible to study soluble HLA in more detail by using monoclonal antibodies (Mab)[1,7-9] to capture as well as to identify these glycoproteins on a solid support substance.

Results of recent studies have shown that soluble HLA levels may be influenced by MHC genes, and that soluble HLA class I (sHLAI) levels may vary with particular alleles determined by major histocompatibility complex (MHC) genes[10,11]. Segregation analyses suggest Mendelian inheritance of sHLAI, but with variation of sHLAI allotype expression.[12].

sHLA may play a role in the maintenance of self-tolerance[13-16]. However, there are many questions about its function, such as its role in both normal and abnormal immunologic states. These questions cannot be addressed without obtaining additional normative data and comparable information in states of disordered immunity.

The function and biologic significance of sHLA in autoimmune conditions is unknown. sHLAI levels have not been examined extensively in autoimmune rheumatic diseases.

We sought to determine whether high or low (or both high and low) concentrations of sHLAI were controlled by either specific alleles or haplotypes of the MHC, as well as whether these levels related to an autoimmune state, namely rheumatoid arthritis (RA).

MATERIALS AND METHODS

Fifty-three serum samples were obtained from patients with RA (n = 25) and from first degree relatives (n = 28) of 7 of these patients. Samples were obtained after procurement of written informed consent during the course of larger studies of genetic polymorphisms in populations of African descent[17,18]. All patients fulfilled the American Rheumatism Association 1987 revised criteria for RA[19]. Records of all 25 patients with RA were reviewed to determine disease onset and activity. Sixteen of 25 patients with RA were seropositive for rheumatoid factor. Patients were not selected for severity of rheumatoid organ disease or form of treatment. Serum samples were also obtained from 13 healthy families (n = 66) with no history of rheumatic disease. All serum samples were studied for sHLAI.

Because there is a high degree of racial variation in the gene frequencies of HLA[20], we limited study participation to Afro-American and Afro-

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