

# Serum Beta-2 Microglobulin Explained

by Dr. Guy Sherwood

The purpose of the body's immune system is not only to recognize "foreign" antigens but also to be able to determine between self and not self. The problem with cancer is that the body does not recognize these malignant cells as being "foreign." Rather, the body thinks that they are just one of the regular guys and leaves them alone.

In the vast majority of cells in the body, especially cells with a nucleus (nucleated cells), there exist large cell surface proteins that are called Class I antigens. These Class I molecules/antigens are abundantly expressed on lymphoid cells, less so on liver, lungs, and kidneys, and only sparsely on brain and skeletal muscle. In the human, the surface of very early embryonic tissue does not display these molecules.

These Class I antigens are also called the classic transplantation antigens. Indeed, these molecules were originally recognized through their ability to provoke vigorous rejection of grafts exchanged between different members of a species (think organ transplant medicine).

Class I antigens are one of three types of surface recognition sites that are required for cells participating in immune response to function normally. They are a type of "ID badge" that notify cells of the immune system as to whether or not the cells are self or not self. Beware if the immune cells do not recognize the Class I antigen on a cell!

The Class I antigens contain a heavy protein chain and a light chain. The heavy chain is produced by multiple genes. Some of these genes in humans resemble, in an uncanny fashion, certain similar genes in mice (murine genes). The light protein chain is chemically bound to this heavy chain. This light chain, which is coded for on chromosome 15, does not vary - as opposed to the heavy chains. This light protein chain is also shed by the cell and is therefore found in the blood serum and urine. It is 12,000 Daltons in size. (IgM is 900,000 Daltons in size; the smallest immunoglobulin IgG is 150,000 Daltons in size).

This light chain is called serum beta-2 microglobulin because it was initially discovered as a serum protein before its role as part of the Class I antigen was elucidated.

Multiple myeloma, Waldenstrom's evil cousin, is characterized by malignant proliferation of plasma cells. There are three stages of this disease: Stage I early disease (low production of monoclonal protein and low production of beta-2 microglobulin), Stage II (between Stage I and Stage III, and Stage III (extensive disease, many cancer cells and production of monoclonal protein, lots of protein "spilled" in the urine, and high levels of beta-2 microglobulin).

The degree of elevation of serum beta-2 microglobulin correlates well, therefore, with the extent of disease and tumor burden.