Antigenic Targets of Serum IgM in Waldenström's Macroglobulinemia and IgM MGUS

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Objective: To define antigenic targets of serum IgM antibodies in 392 patients with Waldenström's macroglobulinemia (WM) or IgM monoclonal gammopathies of unknown significance (MGUS).

Methods: We studied 3 series of patient samples, including: 1. A prospectively collected, consecutive set of serums with IgM M-proteins identified by immunofixation methodology in the clinical immunology laboratory at Barnes-Jewish Hospital in St. Louis (#58), 2. Serums (#173) obtained over 2 decades from patients with WM by an oncologist at Baylor University in Houston, and 3. Serums (#163) obtained from self-identified patients with WM who attended 2 national educational seminars. ELISA assays measured IgM binding to 16 purified antigens that included glycolipids, oligosaccharides, proteins and glycoproteins. Western blotting examined IgM binding to proteins in myelin, and neuronal nuclei and cytoplasm.

Results: High titer IgM binding (>10,000) to one or more antigens was found in 40% of serums. The most common antigenic targets (27%) were a series of oligosaccharide-containing antigens that have not previously been reported to bind to IgM M-proteins. IgM binding was found to myelin-associated glycoprotein in 3%, and to gangliosides in 13%, of WM serums. The most common ganglioside target antigen was GalNAc-GD1a. Western blotting identified IgM binding to several unknown antigenic targets, some of which appeared to be more common in WM than in MGUS serums.

Conclusions: Antigenic targets of IgM binding can be found in many WM and MGUS serums. Binding to neuropathy-associated antigens, such as MAG and gangliosides occurs 16% of WM serums. Further study is required to define correlations of targets of serum IgM binding with clinical features in WM and MGUS.