

Treatment of multiple myeloma by antibody mediated immunotherapy and induction of myeloma selective antigens.

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BACKGROUND: In view of the successful use of serotherapy in many B-cell malignancies, we and others have sought to identify tumor selective antigens for the serotherapy of plasma cell dyscrasias (PCD) including multiple myeloma (MM), and Waldenstrom's macroglobulinemia (WM). We recently identified Muc-1 core protein as a MM selective antigen. Though Muc-1 core protein is abundantly expressed on most MM plasma cells, expression of this antigen can be absent, or weak on some plasma cells which could potentially result in the selection of Muc-1 core protein negative clones following serotherapy of PCD. In addition to Muc-1 core protein, we have also been examining the use of CD20 directed serotherapy for PCD. **DESIGN:** As part of these efforts, we recently initiated a phase II clinical trial examining the use of Rituximab (Rituxan, MabThera) as a single agent in MM patients; as well several WM patients have been treated with Rituximab at our Institutions. **RESULTS:** In previous studies, we have shown that CD20 is abundantly expressed on the plasma cells of most WM patients; in contrast, CD20 is expressed on plasma cells from a minority of MM patients, and in these patients expression of CD20 can be weak or heterogeneous with both CD20+ and CD20- plasma cells present. As such, we have sought out clinically useful inducers of Muc-1 core protein, and of CD20 on malignant plasma cells. **CONCLUSIONS:** These efforts resulted in the identification of dexamethasone (Dex) as a potent inducer of Muc-1 core protein on MM plasma cells, and interferon-gamma (IFN-gamma) as a potent inducer of CD20 on MM plasma cells and B-cells. Importantly, these agents induced their respective antigens at pharmacologically achievable doses.