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M-protein Binding Peptides from Phage Display Libraries as Biomarkers in Multiple Myeloma: a Paradigm for Early Detection of Disease Relapse

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The detection of specific biomarkers with simple laboratory tests can may important implications in the diagnosis, treatment and survival of patients. An example is Multiple Myeloma (MM), an incurable B-cell leukemia. With the use of new drugs, most MM patients now enter into a period of remission; however they inevitably relapse. MM tumor cells derive from a single clone of plasma cells that usually express and secrete excess amounts of clonotypic immunoglobulin (M-protein). Within each patient, M-protein V_H gene sequences differ suggesting that these antibodies are directed against different antigens. Currently, electrophoresis and gel immunofixation are used to identify the presence and isotype of M-proteins in serum, however these methods are both tedious and insensitive. Particularly with regards to early intervention in patients in remission, a more sensitive method that heralds the presence of the specific M-protein biomarker would indicate disease relapse, leading to earlier resumption of treatment and potentially enhanced patient survival. To this end, we have used phage display peptide libraries to isolate peptides that bind M-proteins from MM patients. Bioinformatic analyses of the peptide sequences determined their homology to natural proteins of clinical significance including proteins from bacterial species associated with respiratory infections and food poisoning. These peptides can then be conjugated to fluorescent or other reporter molecules and used in simple immunoassays to follow the reappearance of the patient's M-protein in serum. The isolation of biomarker-binding peptides and their use in sensitive immunoassays is a platform approach that can be applied to development of improved methods for the monitoring of patients.