Familial predisposition to monoclonal gammopathy of unknown singificance (MGUS), multiple myeloma (MM) and Waldenström's macroglobulinaemia (WM)

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Hereditary predisposition is not generally considered to play a major role in the development of the antibody-producing neoplasias, monoclonal gammopathy of unknown significance (MGUS), multiple myeloma (MM) and Waldenström's macroglobulinaemia (WM). Around 130 families with multiple cases of such disorders have been described in the medical literature, including 43 with WM and MGUS. Only 3 families had all three disorders and it appears likely that MM and related MGUS are separate entities from WM and IgM-MGUS. High levels of immunoglobulin-M in blood have been noted in unaffected relatives in several WM family studies. In Iceland eight families with multiple cases of MM and/or MGUS and/or WM have been identified. One of these families has been studied over many years. Progression has been observed from MGUS to WM and lymphoma. Testing of lymphocytes from blood samples from healthy family members showed that 10 out of 35 produced increased amounts of immunoglobulins compared to controls, identifying these persons as hyper-responders. One of the hyper-responders was also diagnosed with MGUS. In conclusion, Waldenström's macroglobulinaemia can occur on the basis of a familial predisposition. The study of rare families with a strong family history could give clues to the understanding of the development of WM, starting from a slight error in regulating a normal immune response. Studies are in progress investigating B-lymphocyte responses in a culture model.