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A Monoclonal Antibody Specific for Free Human Kappa Light Chains Induces Apoptosis of Multiple Myeloma Cells and Exhibits Anti-Tumor Activity *In Vivo*.

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Abstract

Despite high dose chemotherapy and autologous stem cell transplant, multiple myeloma (MM) remains an incurable malignancy, with a median 5 year survival of less than 20%. With the exception of idiotype, few antigen targets have been identified that would facilitate specific immunotherapy of MM. We have previously described a murine monoclonal antibody that recognizes a conformation-dependent epitope on free human kappa light chains and a cell surface antigen, KMA, expressed on kappa MM plasma (MM_{κ}) cells (Raison, RL and Boux, HA Mol Immunol 1985 22:1393). Here we show that the murine antibody, designated **mKap**, bound specifically to a range of MM_{κ} cell lines and inhibited the *in vitro* growth of these cells. Flow cytometric analysis (Annexin-V and PI staining) of MM_{κ} cell lines incubated with **mKap** demonstrated a dose dependent induction of apoptosis. Furthermore, the presence of activated caspases in **mKap** treated cells was detected using the CaspACE™ FITC-VAD-FMK reagent. The induction, by **mKap**, of apoptosis in MM_{κ} cells occured in the absence of cross-linking second antibody or effector cells. *In vivo*, anti-tumor activity by **mKap** was demonstrated in a SCID mouse tumor xenograft model. Tumor growth was measured by quantitation of secreted myeloma Ig over a period of 6 weeks. From week 4 onwards, significantly lower serum concentrations of myeloma Ig were detected in animal groups receiving 3.0, 1.5, 0.3 and 0.15 mg total **mKap** compared to the untreated control ($P<0.005$ at week 4; $P<0.0001$ at week 5). The tumor-restricted specificity of **mKap**, coupled with its ability to inhibit MM_{κ} cell growth *in vitro* and *in vivo*, suggests the potential use of either a chimeric or humanised version of this antibody, alone or in combination with chemotherapy, for the treatment of kappa MM.