

Oral Presentation

Increased circulating LDL cholesterol increases myeloma tumour burden in vivo

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Multiple myeloma (MM) is a fatal malignancy characterized by an expansion of malignant plasma cells in the bone marrow (BM) and associated with osteolytic bone disease. MM is preceded by the benign condition, monoclonal gammopathy of undetermined significance (MGUS). Understanding MGUS progression and development of MM bone disease is key for patient management. We and others have previously demonstrated that diet-induced obesity promotes myeloma progression, but the mechanisms underlying this remain unknown. The aim of the current study was to determine the effect of dietary cholesterol on MM development. A 2% cholesterol diet was used to increase circulating LDL in mice. Mice were randomly distributed to either a) cholesterol diet 4 weeks prior to 5TGM1 MM inoculation (pretreatment) or b) cholesterol diet 4 weeks prior to MM inoculation and continued for the entire experiment (continuous). Mice on the continuous cholesterol diet had increased

tumour burden, associated with an increase in lipid droplet content of MM cells. No differences in tumour burden were seen in those mice where cholesterol diet was halted at time of MM inoculation. In vitro, myeloma cells cultured with delipidated FBS had a 50% reduction in viability after 72 hours. Rich cholesterol content lipoproteins (LDL) but not VLDL could restore MM cell viability, suggesting that cholesterol is responsible for this lipid-depletion effect. Taken together, our results show that high cholesterol promotes myeloma and results in a higher lipid content in myeloma cells, ultimately increasing BM tumour burden. Pretreatment with a cholesterol diet did not alter disease progression suggesting a direct pro-tumourigenic effect of cholesterol. These results demonstrate both the detrimental effect of cholesterol on myeloma progression and the potential for dietary intervention approaches.