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ATM mutations occur in multiple myeloma tumours at a low frequency

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Ataxia Telangiectasia (AT) patients have biallelic inactivation of the *ATM* gene and exhibit a 200 fold increased frequency of lymphoid tumours, commonly occurring at a young age. *ATM* mutations have been found in a number of adult lymphoid malignancies but there is no data on the occurrence of *ATM* mutations in multiple myeloma.

We report here a 50 year old patient with a milder A-T phenotype who developed multiple myeloma. We also screened sporadic cases of multiple myeloma for *ATM* mutations using denaturing high performance liquid chromatography analysis (HPLC) and DNA sequencing. In one tumour the missense mutation 7181C>T (S2394L) was identified. The S2394L substitution was modelled in an expression system and the protein was shown to have no ATM kinase activity. This patient also had sequence change P1054R. Two further myeloma patients had the *ATM* splice site mutations IVS40-1G>C and IVS18-6T>C, leading to loss of exons 41 and 19 respectively. A further 3 of the 45 tumours were found to have other *ATM* sequence changes in the *ATM* gene that were either known polymorphisms or shown here to be new polymorphisms.

This study shows that *ATM* mutations can occur at a low frequency in sporadic multiple myeloma tumours and may indicate a role of *ATM* mutations in the pathogenesis of some multiple myelomas