**Molecular cytogenetics of Waldenström's macroglobulinemia (WM) indicate lack of 14q32 translocations, genomic stability and frequent 6q deletions**

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***Introduction:*** The genetics of WM are still poorly understood. Since rare reports have suggested that WM sometimes is associated with 14q23 translocations, deletions of 6q, and t(11;18)(q21;q21) we tested for these abnormalities in WM cells. We also tested for deletions of 13q14, 17p13, and numerical chromosomal abnormalities. In addition we tested for IgH switch region recombination, *p53* mutations, *p16* methylation and somatic hypermutation.

***Patients and methods:*** Patients with clinico-pathologic diagnosis of WM (all had an IgM >1.5g/dL) were eligible. Southern blot assay was used to detect legitimate and illegitimate IgH switch rearrangements. In addition to conventional cytogenetic (CC) and multicolor metaphase FISH (M-FISH) analyses, we used interphase fluorescent in-situ hybridization (FISH) to screen for t(9;14)(p13;q32) and other IgH translocations, t(11;18)(q21;q21), and also 6q21, 13q14 and 17p13 deletions. Genomic stability was also assessed using chromosome enumeration probes for chromosomes 7, 9, 11, 12, 15 and 17 in 15 patients. Methylation of p16 was assessed with standard methods (sodium bisulfite MS-PCR).

***Results:*** WM do not have legitimate or illegitimate IgH rearrangements or translocations, by the Southern blot assay ($n$ = 12), CC ($n$ = 37), M-FISH analyses ($n$ = 5), and interphase FISH ($n$ = 42). We did not find any case with t(9;14)(p13;q32) or t(11;18) translocations. Although tumor cells from most patients were diploid for the chromosomes studied, deletions of 6q21 were observed in 42% of cases. Methylation of *p16* was rare. Somatic hypermutation was invariable. Deletions of 13q14 and 17p13 are rare at the time of diagnosis and only seen in a small fraction (~ 15%) of patients at progression.

***Conclusion:*** WM tumor cells, which appear to be diploid or near diploid, often have deletions of 6q21. IgH translocations, including the t(9;14)(p13;q32), and t(11;18) are not found commonly in WM. Unlike myeloma and B-CLL WM does not harbor 13q14 and 17p13 deletions at the time of diagnosis.