Genome Wide SNP array analysis in Waldenstrom's macroglobulinemia.

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Background: Waldenstrom's macroglobulinemia (WM) is a rare lymphoproliferative disorder. Approximately 50% of patients (pts) with WM exhibit a normal karyotype using either conventional chromosome banding analysis (CBA) or FISH approach. Comparative genomic hybridization (CGH) array delineated the minimal deleted region on 6q deletion, the most frequent aberration in WM, and pointed out the role of NFKB pathway key regulator genes. Partial uniparental disomy (UPD) induced by copy neutral loss of heterozygosity (LOH) are important mechanisms for tumour suppressor gene inactivation or oncogene activation in cancer. had been Our aim was to identify new genetic aberration involved in WM pathogenesis using Single Nucleotide Polymorphism (SNP) arrays described as a high resolution method allowing both the detection of UPD/LOH and copy number alteration (CNA) analysis in the same experiment.

Material and methods: DNA was extracted following CD19 B cells selection from 31 bone marrow samples with WM. Paired samples (tumor / normal T lymphocytes) were used as an intra-individual reference to identify germline polymorphisms. We used Genome-Wide Human SNP Array 6.0 Affymetrix chips. Size, position and location of genes were identified with UCSC Genome Browser HG18 assembly, LOH and CNA using genotyping console 3.02 software (Affymetrix) and Partek genomic suite.

Results: Overall, SNP array detected a genetic aberration in 85% of patients. We observed 59 CNA in 65% of patients. New cryptic genetic aberrations were detected as 25% of CNA were < 5 mb in size, the lower limit of detection by CBA. We observed 69 LOH in 67% of cases. The LOH observed in the absence of CNA loss are consistent with UPD in 80% of the cases. Interstitial or telomeric UPD regions varied in size, from 0.4 to 154 mb were described.

In conclusion, we described new cryptic genetic aberrations and the existence of UPD, a mechanism that might contribute to the inactivation of tumour suppressor genes by mutations or epigenetic alterations using SNP array in WM. Update of this study will be provided at the International Workshop on Waldenstrom's Macroglobulinemia.