[ABSTRACT WM3.2]

THE GENE EXPRESSION SIGNATURE OF CLONAL CELLS FROM WALDENSTROM'S MACROGLOBULINEMIA: DIFFERENCES AND COMMONALITIES WITH THE NORMAL CELL COUNTERPART AND OTHER RELATED LYMPHOPROLIFERATIVE DISORDERS

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Aims. We have used genome-wide expression profiling (GEP) to investigate the transcriptomic signature of WM related to normal status, as well as to explore the differences and similarities in expression patterns of clonal cell populations from WM and from those of chronic lymphocytic leukemia (CLL) and multiple myeloma (MM). Material and Methods. Bone marrow samples from 10 patients with WM, 12 with MM and 11 with CLL, along with 8 normal B lymphocytes samples (NBL) obtained from peripheral blood and 5 normal plasma cells (NPC) samples obtained from the bone marrow of healthy donors, were used for the analysis. The isolation of clonal B lymphocyte and plasma cell populations was carried out by multiparameter flow cytometry sorting with the appropriate monoclonal antibodies. Total RNA (100 ng) was amplified and labeled according to Affymetrix technology and hybridized to "Human Genome U133A" microarray. Results. The comparative analyses of the gene expression profile of WM-BL vs NBL identified a set of 171 genes expressed differentially between the two groups. Three members of the activator protein 1 (AP-1) group, JUN, FOSB and BATF, and genes involved in B cell development, such as BTK, CD69, CD83, IRF8 and ITPR1 were deregulated in WM-BL. When comparing the expression profile of WM-PC with that of NPC, a total of 498 genes (mostly included in RNA post-transcriptional modification, DNA replication and cellular assembly and organization categories) were up-regulated in WM-PC group. Interestingly, a set of 4 genes (LEF1, MARCKS, ATXN1 and FMOD) was able to discriminate clonal BL from WM and CLL. The most important genes that discriminate PC from WM and MM were those involved in plasma cell differentiation such as PAX5 (overexpressed in WM-PC), and IRF4 and BLIMP1 (underexpressed in WM-PC). We also investigated the relationship between the three B lymphoproliferative disorders. One of the most significant overexpressed genes, both in WM and CLL, was the IL10 receptor (IL10RA). Conclusions. These results delineate a distinct transcription signature of clonal cells from WM, which is genetically different from the MM and CLL cell-counterpart. The differentially expressed genes have important functions in the B-cell differentiation and oncogenesis. Supported by Spanish Myeloma Network (G03/136) and "Ministerio de Ciencia y Tecnologia" (SAF04/06587) and "Junta de Castilla y Leon" grants (SA032/04)