Session IV: Micro-environment and Immune Regulation in WM

Abstract 123

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T cell immunity in Waldenström's Macroglobulinaemia and Myeloma. D.E. Joshua, Ross D. Brown, Daniel M. Y. Sze Suilin, Mo J. Gibson, and P. J. Ho. Institute of Haematology, Royal Prince Alfred Hospital, Sydney, AUSTRALIA.

There is now considerable evidence that the presence of expanded CD8+ CD57+ TCR Vβ-restricted cytotoxic T-cell clones in the peripheral blood of patients with multiple myeloma confers a favourable prognosis. The clonality of these TCR Vβ expansions was previously verified by CDR3 length analysis and direct sequencing. For patients with Waldenström's Macroglobulinaemia (WM), clinical evidence suggests that T-cells play an important role in maintaining the stability of the disease as there is an increased rate of transformation to aggressive lymphoma after the use of T-cell suppressive agents such as Cladribine and Fludarabine. We postulate that while these act as anti-tumour agents, their effect on existing cytotoxic T-cell clones may lead to the loss of the host's immunological control of the disease.CD8+ CD57+ TCR Vβ-restricted cytotoxic T-cell expansions were present in 74% of patients with WM (n=19) which is similar to the incidence in myeloma, (n=221) but their prognostic importance has yet to be determined. These expansions cover a wide spectrum of the TCR Vβ repertoire. The lack of CD8+ CD57+ TCR Vβ-restricted cytotoxic T-cell expansions correlate with nucleoside analogue therapy (χ^2= 13.8; p<0.001). Treg cells have been reported to be increased in patients with myeloma. We determined the number of Treg cells (CD4+ $CD25^{hi}$+ CD127-) in the blood of patients with WM and age matched controls. The mean % Tregs in the WM patients (7.0±1.8) was not different from the normal group (7.0±2.1) although there was a significantly lower absolute number of Tregs in WM patients. (3.2±2.4 and 5.1±2.1 $x10^7$/L respectively)Trogocytosis involving CD80 and CD86 expression on T cells occurs in 30% of patients with myeloma (n=45) and has been suggested to be one mechanism of tumour escape. In contrast there was no detectable trogocytosis in the blood samples from 11 patients with WM (χ^2= 4.1; p<0.05).Cytotoxic T-cell clones in WM were flow-sorted into CD57+ and CD57-clones, and assayed by microarray and real time PCR for clonality analysis and gene expression .Three of the six most significantly overexpressed genes in the CD57+ population in an Affymetrix 133plus microarray were related to T cell cytotoxicity and included perforin1, granzyme B and H .These findings are consistent with the concept of T cell disease control in WM.