

THE CANCER TESTIS ANTIGEN CT7 (MAGE-C1), BUT NOT NY-ESO-1 IS FREQUENTLY EXPRESSED IN PLASMA CELL MYELOMAS AND A COMBINED NUCLEAR-CYTOPLASMIC EXPRESSION IS ASSOCIATED WITH A WORSE CLINICAL OUTCOME.

*M. Tinguely¹, B. Lopes¹, B. Jenni^{1,6}, S. Cogliatti², U. Schmid², C. Dommann-Scherrer³, R. Maurer⁴, V. Rousson⁵, D. Korol⁶, A. Knights⁷, A. Curioni⁷, A. Knuth⁷, N.M. Probst-Hensch⁶, H. Moch¹, A. Zippelius⁷

*Institutes of Pathology, University Hospital Zurich¹, St.Gallen², Winterthur³ and Triemli⁴;
Institute of Social and Preventive Medicine⁵, Dep. of Molecular Epidemiology/Cancer
Registry, University Zurich; Division of Oncology⁶, University Hospital Zurich, Switzerland*

Introduction Plasma cell myelomas (PM) exhibit clinical and molecular heterogeneity with a mean survival of 3-5 years. Cancer/testis (CT) antigens are encoded by genes, that are normally expressed only in human germ cells and silenced in other somatic tissues. However, they are preferentially expressed in certain tumor types. Therefore, these immunogenic proteins represent ideal candidates for therapeutic vaccination strategies. NY-ESO-1 and CT7 (MAGE C1) were found to be expressed in PMs by gene expression profiling and in some cases by immunohistochemistry.

The aim of our study was 1) to determine the frequency and prognostic impact of CT-7 and NY-ESO-1 protein expression 2) compare their role with established prognostic factors (degree of maturity, proliferation index (Mib1), t(4;14) and t(11;14)).

Materials and Methods Fixed, paraffin embedded, decalcified biopsies from 209 patients were investigated on TMAs. 8 cases of MGUS and 4 reactive BMs were used as controls. IHC was done for: CD138, Mib1, CT7-33 (MAGE-C1) and NY-ESO-1, I-FISH for t(4;14) and t(11;14).

Results 92% (193/209) of PMs were mature, 8% (16/209) immature. 57.4 % (97/169) PMs were positive for CT7, 69 % (60/97) showing a nuclear and cytoplasmic (n/c) expression. NY-ESO-1 was positive in 8.4% (17/203). A simultaneous expression of CT7/NY-ESO-1 in 12 pts (6 mature, 6 immature PMs) was associated with a shorter median survival of 14 months, a high proliferation rate (mean Mib1 of 36%) and a strong expression of both markers in all tumour cells. Immature morphology (p = 0.0147), age >65yr (p <0.001), Mib >10% (p < 0.001) and n/c CT7 positivity (p = 0.039) are significantly associated with a worse outcome. CT7 was found in scattered cells of MGUS, whereas NY-ESO-1 was negative.

Conclusion CT7 is frequently and strongly expressed in most tumour cells of PMs. Besides a immunotherapeutic target, CT7 (MAGE-C1) might serve as prognostic marker in PMs.