Circulating Tumor Cells and Detection of the Melanoma-Associated Antigen HMW-MAA in the Serum of Melanoma Patients

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TO THE EDITOR

In the September issue of this journal, Vergilis *et al.* (2005) report that the high-molecular weight-melanoma-associated antigen (HMW-MAA) also known as the melanoma chondroitin sulfate proteoglycan (MCSP) can be present in the blood of healthy donors and melanoma patients. Defining a threshold of $1 \geqslant U$ as elevated by their double-sandwich ELISA assay they found significant differences in positivity for HMW-MAA/MCSP antigen among controls and melanoma patients (29 *vs* 3% positivity). The authors propose ''shedding of the antigen by both malignant cells and normal cells but in greater amount by cancer cells'' as a mechanism for its appearance in the serum without specifying possible sources of the HMW-MAA/MCSP antigen.

Our recently published data demonstrate circulating melanoma cells as a potential source of the HMW-MAA/MCSP antigen found in the serum of melanoma patients (Figure 1). In our prospective study, we detected HMW-MAA/MCSP-positive cells with morphological features of tumor cells in the blood of 43 (26%) of 164 melanoma patients, whereas all 50 controls were negative (Ulmer *et al.*, 2004). The malignant origin of the HMW-MAA/MCSP-positive cells in our study was demonstrated unambiguously by single-cell comparative genomic hybridization. As we noted a faint positivity for the HMW-MAA/MCSP antigen on few granulocytes, one might speculate that these cells may contribute to the low levels of serum HMW-MAA/MCSP antigen measurable in controls.

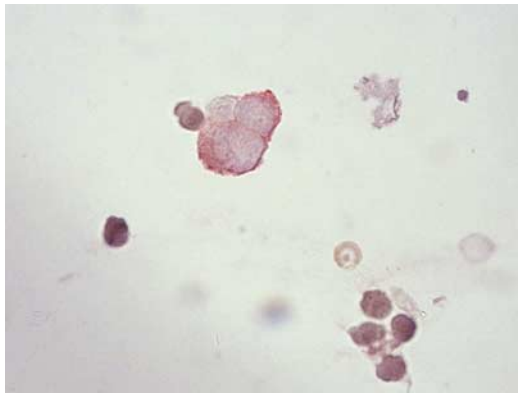

Figure 1. High-molecular weight-melanoma-associated antigen/melanoma chondroitin sulfate proteoglycan (HMW-MAA/MCSP)-positive cells (red) may be detected in peripheral blood of melanoma patients (alkaline phosphatase-anti-alkaline phosphatase; original magnification: ×100).

In contrast to the study published by Vergilis *et al.* (2005), we found a significant association between a positive result and the number of tumor cells detected, respectively, and the stage of the patient. The presence of two or more HMW-MAA/MCSP-positive tumor cells in our study had a negative impact on survival in patients with metastatic disease, whereas elevated levels of HMW-MAA/MCSP did not correlate with the clinical outcome of patients in the study reported by Vergilis *et al.*

The reason for these differences remains unclear. One might speculate that patient characteristics (selected patients included in a vaccination protocol with a probably low tumor load in most cases (Vergilis *et al.*, 2005) *versus* a broad range of patients including patients with stage II and III melanoma with non-resected tumors (Ulmer *et al.*, 2004)) might account for these differences.

To further evaluate these results, we suggest one to include both methods in future experimental designs.

CONFLICT OF INTEREST

The authors state no conflict of interest.

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Abbreviations: HMW-MAA, high-molecular weight-melanoma-associated antigen; MCSP, melanoma chondroitin sulfate proteoglycan