MELANOMA AND MELANOCYTIC NAEVI

MINIMAL RESIDUAL DISEASE IN MELANOMA: MOLECULAR CHARACTERIZATION OF CUTANEOUS TRANSIENT METASTASES AND CIRCULATING MELANOMA CELLS IDENTIFIES A DISEASE PROGRESSION EXPRESSION PANEL

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Background: Measuring circulating melanoma cells (CMCs) before they are clinically detectable, represents a potential powerful method to monitor patients with malignancies that have a minimal morbidity. Immuno-magnetic enrichment utilizes the immuno-cytochemical properties of circulating cells to select and isolate them. Melanoma-specific-epitopes should be still defined. Upregulation of endothelial antigen MCAM/MUC18/CD146 is strongly associated with disease progression. We reported that MCAM/MUC18/CD146 expression predicts clinical relapse, whereas absence or persistent loss is associated to stable disease or to disease-free status. Our findings motivate us to further study the reliable role of MCAM/MUC18/CD146 in MM progression, analyzing the Long, Short and 5'-portion expression in CMCs and cutaneous transient metastases (CTM). We selected CMCs by using immuno-magnetical enrichment in melanoma patients staged ≥pT1b AJCC (transition from radial to vertical phase) that concurrently developed CTMs during follow-up. Moreover, we performed a gene expression panel comprising the angiogenic factors (VEGF, bFGF), some differentiation markers (Tyrosinase, MART1), cell-cell adhesion molecules (MCAM/MUC18/CD146, E-Cadherin, N-Cadherin, VE–Cadherin) and matrix-metallo-proteinases (MMP2 and MMP9).

Materials and methods: We collected CTM and CD45-CD146+ CMCs from 4 MM (median age 62 yrs) staged AJCC IIb (2), IV (1) and occult (1). Three out of 4 patients, submitted to immunotherapeutic trials, showed stable-disease status. Primary melanoma cell lines and healthy blood samples were included as positive and negative controls.

Results: Molecular expression analysis documented that, respect to high expression of

almost all investigated genes detected in CTM, CMCs shared negativity for angiogenic factors, specific melanoma-differentiation markers and cell-adhesion molecules, except for bFGF, VE-CADH and MMPs. MCAM/MUC18/CD146 was detected only in CD45-CD146+ CMCs from patient showing disease progression.

Conclusions: MCAM/MUC18/CD146 as melanoma-specific antigen results to be correct target to enrich CMCs. Preliminary observation indicates that enriched CD45-CD146+CMCs express few markers such as bFGF, VE-CADH, MMPs and MCAM/MUC18/CD146 that could define a “warning” disease progression panel.