



## **Involvement of HERV-K in stemness and malignancy of human melanoma**

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Malignant melanoma is an aggressive metastatic tumor characterized by chemoresistance and poor patient prognosis. Tumor cell plasticity and the putative cancer stem cell subpopulations, that express stem cell markers, such as CD133, have been associated with melanoma tumor initiation and progression. We already demonstrated that Human Endogenous Retrovirus-K (HERV-K) is associated to aggressiveness and immune evasion of metastatic melanoma, and that mechanisms leading to abnormal HERV-K gene expression seem to involve the microenvironment alteration. Thus, we then investigated the potential role of HERV-K activation in cellular plasticity and stemness features of melanoma cells upon the modification of the microenvironment. Flow cytometry, RT-PCR analysis, RNA interference, sphere-forming and migration/invasion assays were used to assess cell phenotypic modifications, expression of HERV-K, stemness and metastatic features of the cell lines, respectively. Using the highly heterogenic human melanoma cell line TVM-A12, isolated in our laboratory from a patient, and other commercial cell lines, we found that melanoma cell plasticity and generation of the CD133+ putative cancer stem cell subpopulation under stress condition are HERV-K dependent. Interestingly, TVM-A12-CD133+ cells displayed a significantly higher self-renewing, migration and invasion capacity than the heterogeneous TVM-A12 cell lines, and were affected by antiretroviral treatment. These results provide new molecular basis for understanding the biological features of melanoma, but are also a useful resource for the identification of new therapeutic targets and diagnostic biomarkers.