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## Gene expression profiling of inflammation dependent and independent primary and metastatic lesions from patients with cutaneous melanoma

Cutaneous melanoma comprises multiple clinical forms and understanding the functional implications of specific genes associated with primary and metastatic lesions at different sites is crucial to identify new prognostic biomarkers and to select patient candidates for new target-oriented therapies and immune-based therapies. Previously, we reported that interleukin (IL)-1beta and IL-18 promote experimental melanoma metastasis via vascular endothelial growth factor (VEGF)-induced VLA-4 (α4β1) integrin. We also reported that IL-18 regulates human melanoma VLA-4 integrin activation through a hierarchized sequence of inflammatory factors. The cascade involves PGE2 production from melanoma cells induced by IL-18-dependent TNFα; next, PGE2-induces IL-1β via VEGF secretion, which in turn induces VLA-4 activation via COX-2-dependent H2O2. Interestingly, this sequence operated in IL-18R/VLA-4/VEGF-expressing melanomas, but not in those melanoma cells without this phenotype. Hence, we next determined signature genes from human IL-18-treated melanoma cell lines with and without IL-18R/VEGF/VLA-4 phenotype and verified their expression in primary and metastatic lesions from patients with melanoma. Signature genes associated to melanoma cell response to soluble VCAM-1 were also determined and their expression in primary and metastatic lesions from melanoma patients verified. Altogether, VCAM-1- and IL-18-dependent melanoma genes represent a panel of clinically-verified genes that may help to identify and treat patients with inflammation-dependent and independent melanomas; second, they may also help to predict prometastatic risk in patients with early stage inflammation-dependent melanoma; and third, they may be a source of new potential targets for the specific treatment of primary and metastatic cutaneous melanoma developed via inflammation-dependent mechanisms.

### Biography

Fernando Vidal-Vanaclocha is a full Professor and Chair of the PhD program in Translational Medicine and the Master degree in Regenerative Medicine and Cell Therapies, at the CEU-San Pablo University and HM-Hospitals School Medicine, Madrid. As a Medical Doctor with PhD training in Pathology, he has been involved in cancer metastasis research over more than 30 years. In 2010, he has founded the Institute for Applied Molecular Medicine (IMMA). He is also an Adjunct Professor of Molecular Medicine, George Washington University School of Medicine, Washington-DC and Editor of the *Cancer Microenvironment Section, Journal Translational Medicine*.

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