



Article

Sorting Transcriptomics Immune Information from Tumor Molecular Features Allows Prediction of Response to Anti-PD1 Therapy in Patients with Advanced Melanoma

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Citation: Trilla-Fuertes, L.; Gámez-Pozo, A.; Prado-Vázquez, G.; López-Vacas, R.; Zapater-Moros, A.; López-Camacho, E.; Lumbreras-Herrera, M.I.; Soriano, V.; Garicano, F.; Lecumberri, M.J.; et al. Sorting Transcriptomics Immune Information from Tumor Molecular Features Allows Prediction of Response to Anti-PD1 Therapy in Patients with Advanced Melanoma. *Int. J. Mol. Sci.* **2023**, *24*, 801. <https://doi.org/10.3390/ijms24010801>

Academic Editor: Mohammad Rahimi-Gorji

Received: 7 November 2022

Revised: 21 December 2022

Accepted: 27 December 2022

Published: 2 January 2023



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Abstract: Immunotherapy based on anti-PD1 antibodies has improved the outcome of advanced melanoma. However, prediction of response to immunotherapy remains an unmet need in the field. Tumor PD-L1 expression, mutational burden, gene profiles and microbiome profiles have been proposed as potential markers but are not used in clinical practice. Probabilistic graphical models and classificatory algorithms were used to classify melanoma tumor samples from a TCGA cohort. A cohort of patients with advanced melanoma treated with PD-1 inhibitors was also analyzed. We established that gene expression data can be grouped in two different layers of information: immune and molecular. In the TCGA, the molecular classification provided information on processes such as epidermis development and keratinization, melanogenesis, and extracellular space and membrane. The immune layer classification was able to distinguish between responders and non-responders to immunotherapy in an independent series of patients with advanced melanoma treated with PD-1 inhibitors. We established that the immune information is independent than molecular features of the tumors in melanoma TCGA cohort, and an immune classification of these tumors was established. This immune classification was capable to determine what patients are going to respond to immunotherapy in a new cohort of patients with advanced melanoma treated with PD-1 inhibitors. Therefore, this immune signature could be useful to the clinicians to identify those patients who will respond to immunotherapy.