Proceedings International
Platinum Open Access Journal (ISSN 2668-6384)

Proceedings, Abstract
Volume 5, Issue 1, 2023, 4
https://doi.org/10.33263/Proceedings51.004

Portrayal of Antigen-presenting Cells in Cutaneous Melanoma - Innovative Pillars for Harnessing Immunotherapy †

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† Presented at 2nd Edition of the OncoHub Conference – Connecting Scientists and Physicians for Next Generation Cancer Management, Poiana Brașov, Brașov, 21-23 September 2022

Received: 10.12.2022; Accepted: 20.12.2022; Published: 5.01.2023

Abstract: Lack of personalized treatment in different melanoma stages is an important issue facing public health programs. The complexity of the disease implies several specialties of physicians and researchers. Therefore, the multi, inter-, and trans-disciplinary approach to melanoma is essential. Valuable scientific information was acquired on immune mechanisms involved in melanoma growth, allowing the development of immune-related drugs (ipilimumab, nivolumab, pembrolizumab), but still, a percentage of patients do not respond and/or gain resistance to these new therapies. Thus, a better understanding of immune mechanisms in melanoma and finding immune markers that predict response to a specific (immune)treatment is wanted. Mature dendritic cells (DCs) process antigens (Ag), and this function is essential for initiating an effective immune response. Based on our findings, new research avenues that focus on the antigen-presenting cells (APCs) compartment can be a nodal point of immune response in melanoma. As Langerhans cells (LCs) sustain the immunological synapse within the tumor and are actively involved in the specific anti-tumoral response, this APC can control the local anti-tumoral response and hence the immune-therapy efficacy. The dual role of DCs is still to be explored. Hence immature DCs do not present Ags and can suppress antitumor T-cell activity. Even mature, functional DCs without appropriate costimulatory molecules can generate pro-tumoral reactions. One of the latest emerged hallmarks of cancer is "avoidance of immune destruction" and there is an increased possibility that LCs encompass the disease-specific "avoidance" predictive markers that can identify common features of histologically/genetically different melanomas. Moreover, establishing an APC pattern of immune response in melanoma patients can lead to the development of improved immune-therapies treatments based on the blockade of the immune hindrance of Ag presenting functions and/or of activation of the LC functions.

Keywords: skin melanoma; Langerhans cell; immune therapy.

Funding

Research is funded by PN-III-P4-PCE-2021-0549.

Acknowledgments

This research has no acknowledgment.

Conflicts of Interest

The authors declare no conflict of interest.