ImmunoTools *special* Award 2023

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Towards efficient cancer immunotherapy by developing artificial dendritic cells

The immune system plays a major role in protecting the body against tumor cells through tightly regulated processes. An effective antitumor immune response comprises a range of events, from the capture and processing of tumor antigens by antigen-presenting cells (APCs) to their presentation to naïve T cells with subsequent priming and activation of effector T cell responses against tumor-specific antigens. However, immune surveillance is an extremely complex and dynamic process, and cancer cells often evade or subvert the immune response, leaving the host vulnerable to tumor development *[1]*. In this regard, the immune modulation of both innate and adaptive immune responses has attracted significant attention.

The accelerated development of antitumor immunotherapies in recent years has brought immunomodulation into the spotlight. These include immunotherapeutic treatments with autologous dendritic cell (DC)-based vaccines which can elicit tumor-specific immune responses and prolong survival *[2]*. However, this personalized treatment has several drawbacks, including being costly, labor-intensive, and time consuming [3]. This has sparked interest in producing artificial dendritic cells (aDCs) to open up the possibility of standardized "off-the-shelf" protocols.

We synthesized and characterized an artificial dendritic cell in detail. Our future goal is to evaluate whether our aDC can effectively induce the polarization of CD4 T cells towards a Th1 phenotype and prime CD8 T cells *in vitro*. The reagents from the ImmunoTools special award will enable us to:

1. Functionalize the obtained aDC with antibodies anti-human CD11a Biotin - conjugated and anti-human CD45RA Biotin-conjugated to favor the establishment of the immunological synapse and potentiate the activation of T cells.
2. Analyze the impact of loading aDC with rh IL-12 on the polarization of T cells towards the desired anti-tumoral Th1 phenotype.
3. Discriminate between the T cell subsets activated, by flow cytometry using anti-CD4-APC, anti-CD8-PE, anti-FoxP3-PE and anti-CD25-FITC.
4. Distinguish between naïve and memory T cell subsets, by flow cytometry using anti-CD45RA-FITC and anti-CD45RO-PE, respectively.
5. Evaluate the cytolytic activity of antigen-specific CD8+ T cells obtained using Annexin-V-APC.

[1] Chen, Daniel S.; Mellman, Ira - Oncology meets immunology: The cancer-immunity cycle. Immunity. 39:1 (2013) 1–10. doi: 0.1016/j.immuni.2013.07.012.

[2] Villadangos, José A.; Schnorrer, Petra - Intrinsic and cooperative antigen-presenting functions of dendritic-cell subsets in vivo. Nature Reviews Immunology. 7 (2007). 543-555. doi : https://doi.org/10.1038/nri2103

[3] Hlavackova, Eva *et al.* - Dendritic cell-based immunotherapy in advanced sarcoma and neuroblastoma pediatric patients: Anti-cancer treatment preceding monocyte harvest impairs the immunostimulatory and antigen-presenting behavior of DCs and manufacturing process outcome. Frontiers in Oncology. 9:1034 (2019) 1–15. doi: 10.3389/fonc.2019.01034.

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