Exploring the anti-inflammatory effect of $Mo_2Ti_2C_3$, Ta_4C_3 and Nb_4C_3 in murine monocytes and macrophages.

Giorgia Longo[1,2], Linda Giro[2,3], Laura Fusco[3,4], Natalya Resto-Trujillo[2], Mohammad Oliaeimotlagh[2], Amir Khan[2], Benjamin Chacon[4], Christopher Shuck[4], Martina Pigazzi[2], Yuri Gogotsi[4], Lucia Delogu[3,5], Klaus Ley[2], **Marco Orecchioni[2]**

1. Women and Child Health Department, Haematology-Oncology Clinic and Lab, University of Padova, Padova, Italy;
2. Immunology Center of Georgia, Augusta University, GA, USA
3. Department of Biomedical Science, University of Padua, Padua, Italy;
4. A. J. Drexel Nanomaterials Institute and Department of Materials Science and Engineering, Drexel University, Philadelphia, PA, USA;
5. Department of Biological Sciences, Khalifa University of Science and Technology, Abu Dhabi, UAE.

morecchioni@augusta.edu

Abstract

Macrophages are innate immune cells with varying phenotypes and functions that are influenced by their microenvironment. The distinction between the classical M1 and M2 phenotypes, even if with limitations, has been crucial in understanding their involvement in inflammation[1]. Recently, single-cell technologies have revealed a complex range of macrophage activation states, each contributing differently to maintaining physiological balance and affecting the development and progression of diseases. Identifying the origins and function of these macrophage subsets and effectively modulating their phenotype remains a complex challenge. MXenes, a new category of two-dimensional transition metal carbides and nitrides, show promise in the biomedical field owing to their notable features, such as biocompatibility [2]. MXenes' unique chemical properties allow for their detection at the single-cell and tissue level using mass cytometry (CyTOF), which shows great promise for biomedical applications[3]. We found that MXenes can be internalized by myeloid cell precursors, monocytes, and macrophages without affecting their survival or differentiation. Early evaluations of MXenes uptake by monocytes have shown their detectability even after 30 minutes of incubation, which is partially driven by Clathrin-mediated endocytosis. RNA sequencing and CyTOF analysis also found that MXenes can modulate both monocytes and macrophage phenotype, driving an anti-inflammatory M2-like response by reducing proinflammatory markers expression (**Figure 1**) and driving anti-inflammatory markers like CD28[4]. In vivo, peritoneal macrophages exhibit similar phenotype shifts upon MXenes uptake. These findings position MXenes as exciting new tools for detecting and regulating macrophage function, with promising implications for future biomedical applications.

References

[1] Orecchioni M., Ghosheh Y., Pramod A. B., & Ley K. Macrophage polarization: Different gene signatures in M1(Lps+) vs. Classically and M2(LPS-) vs. Alternatively activated macrophages.
[2] A. Vahid Mohammadi et al. The world of two-dimensional carbides and nitrides (MXenes). Science, 2021
[3] L. Fusco et al. Immune Profiling and Multiplexed Label-Free Detection of 2D MXenes by Mass Cytometry and High-Dimensional Imaging. Adv. Mater. 2022
[4] Lizbeth Estrada-Capetillo et al. CD28 is expressed by macrophages with anti-inflammatory potential and limits their T-cell activating capacity. Eur J Immunol 2021

Figures

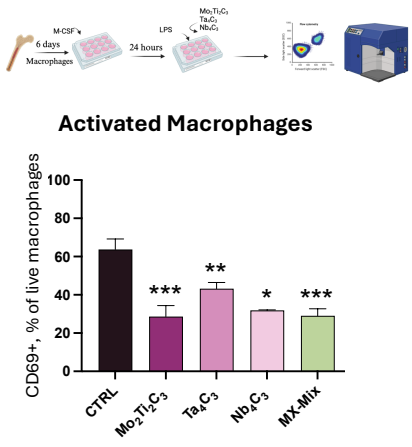

Figure 1: MXenes inhibit the activation of bone marrow-derived macrophages treated with LPS