Single-Cell Insights into MXene Oxidation and Biocompatibility in Immune and Skin Models

Laura Fusco[1], Benjamin Chacon[2], Erfan Rezvani Ghomi[2], Divij Matthew[3], Beatriz Estrada-Hernaez[4], Linda Giro[1], Roberta Cagliani[5], Kara Spiller[4], Flavia Vitale[6], Yury Gogotsi[2], Lucia Gemma Delogu[5,1]

[1]*Department of Biomedical Sciences, University of Padua, Padua, Italy*
[2]*A. J. Drexel Nanomaterials Institute and Department of Materials Science and Engineering, Drexel University, Philadelphia, PA, USA*
[3]*Department of Systems Pharmacology and Translational Therapeutics, University of Pennsylvania, Philadelphia, PA, USA*
[4]*School of Biomedical Engineering, Science and Health Systems, Drexel University, Philadelphia, PA, USA*
[5]*Department of Biological Sciences, Khalifa University, Abu Dhabi, UAE*
[6]*Department of Neurology, University of Pennsylvania, Philadelphia, PA 19104, USA*

Laura.fusco@unipd.it

Abstract

Transition metal carbides, nitrides, and carbonitrides (MXenes) are emerging as promising candidates for a growing list of biomedical applications. [1-5] However, the biological properties and the impact of the potential oxidation of these materials on their biocompatibility are poorly understood.

Here, we selected three different materials ($Mo_2Ti_2C_3$, Nb_4C_3, and Ta_4C_3) to evaluate the immune and biological interactions of their oxidation at the single-cell level. To this end, we applied LINKED, our recently proposed label-free single-cell detection strategy based on single-cell mass cytometry by time-of-flight (CyTOF), [1] which enables the detection of nanomaterials and the simultaneous measurement of multiple cell markers.

We demonstrated the ability of oxidized MXenes to be internalized by peripheral blood mononuclear cells (PBMCs) and their biocompatibility on all the immune cell subpopulations identified, regardless of the extent of oxidation. We confirmed the biocompatibility of MXenes on primary human monocyte-derived macrophages (HMDMs). In addition, we expanded the LINKED strategy by demonstrating the ability of this methodology to detect MXene oxidation while revealing its biological effects. To this end, $Mo_2Ti_2C_3$, Nb_4C_3, and Ta_4C_3 were detected in the ^{93}Nb, ^{95}Mo, and ^{181}Ta channels, respectively, while the spillovers resulting from metal isotopes forming oxides were detected in channels representing the background signal due to the oxidization of the corresponding metal isotopes at 16 mass units (^{16}O) higher than the mass of the primary isotope (M+16). Finally, in view of the promising applications of MXenes at the skin level, we evaluated the effects on different cutaneous models, confirming the absence of toxicity and skin irritation.

These results shed new light on the biological and chemical characterization of MXenes, enabling exciting new opportunities in biomedicine.

References

[1] L. Fusco et al. Immune Profiling and Multiplexed Label-Free Detection of 2D MXenes by Mass Cytometry and High-Dimensional Imaging. *Advanced Materials*, 2022, 2205154.
[2] L. Fusco et al. V_4C_3 MXene immune profiling and modulation of T cell-dendritic cell function and interaction, *Small Methods*,2023, 2300197.
[3] A. Vahidmohammadi et al. The world of two-dimensional carbides and nitrides (MXenes). *Science*, 2021, 372.
[4] Y Gogotsi. & B Anasori. The Rise of MXenes. *ACS Nano*, 2019, 13, 8491.
[5] L Fusco. et al. Graphene and other 2D materials: a multidisciplinary analysis to uncover the hidden potential as cancer theranostics. *Theranostics*, 2020, 10, 5435.