

MXene nanomaterials as a new frontier in immunomodulation for human health: from earth to space explorations

Olla Elkhatib^{1*}, Maha Alhosani^{1*}, Benjamin Chacon^{2*}, Roberta Cagliani¹, Linda Giro^{3,5}, Immacolata Greco⁴, Carlo Iorio⁴, Laura Fusco^{2,3}, Marco Orecchioni⁵, Antonio Bencomo⁶, Jiranuwat Sapudom⁷, Jeremy Teo⁷, Yarjan Abdul Samad⁸, Yury Gogotsi², and Lucia Gemma Delogu^{1,3*}

* Those authors contributed equally to this work

1. Department of Biological Sciences, Khalifa University of Science and Technology, Abu Dhabi, UAE.

2. J. Drexel Nanomaterials Institute and Department of Materials Science and Engineering, Drexel University, Philadelphia, PA, United States

3. Department of Biomedical Science, University of Padua, Padua, Italy

4. Centre for Research and Engineering in Space Technologies, Université Libre de Bruxelles, Brussels, Belgium

5. Immunology Center of Georgia, Augusta University, Augusta, Georgia

6. Abu Dhabi Stem Cells Center (ADSCC), Abu Dhabi, UAE

7. Laboratory for Immuno Bioengineering Research and Applications, Division of Engineering, NYU Abu Dhabi, Abu Dhabi, UAE

8. Department of Aerospace Engineering, Khalifa University of Science Technology and Research, Abu Dhabi, UAE

lucia.delogu@ku.ac.ae

MXenes, a novel family of 2D nanomaterials, are gaining attention for their biocompatibility, antimicrobial properties, and applications in cancer therapy, diagnostics, and tissue engineering [1-3]. However, their biological effects under microgravity conditions remain unexplored. Astronauts face compromised immune systems and impaired wound healing during spaceflight, largely due to the sensitivity of immune cells like peripheral blood mononuclear cells (PBMCs) to gravitational changes [4-6]. To address these challenges, we are investigating whether MXenes can modulate immune function and promote tissue repair under microgravity conditions. Based on the nanoimmunity-by-design approach [7], we assessed the impact of MXenes on PBMC populations in simulated microgravity using random positioning machine. Additionally, we explored MXenes' potential to enhance skin regeneration, addressing critical health concerns for astronauts on long-duration space missions. Preliminary results from our analysis in simulated microgravity show that this environment does not affect the viability of PBMCs treated with MXenes. Monocytes and dendritic cells demonstrate significantly higher uptake of MXenes under microgravity conditions, indicating a gravity-dependent impact on cellular interaction. Furthermore, Nb₄C₃ MXene is non-irritating and non-toxic to skin cells, promoting regeneration in a dose

dependent manner up to 200 µg/mL. Further data from parabolic flight experiments are currently under analysis to validate these results. This research could lead to novel strategies for enhancing astronaut health and open new biomedical applications for MXenes in both space and terrestrial environments.

References

- [1] Vahid Mohammadi A, Rosen J, Gogotsi Y. The world of two-dimensional carbides and nitrides (MXenes), Science, 2021.
- [2] Fusco L, Gazzi A, Shuck CE, Orecchioni M, Alberti D, D'Almeida S, Rinchai D, Ahmed E, Elhanani O, Rauner M, Zavan B, Grivel J-C, Keren L, Pasqual G, Bedognetti D, Ley K, Gogotsi Y, Delogu LG*. Immune Profiling and Multiplexed Label-Free Detection of 2D MXenes by Mass Cytometry and High-Dimensional Imaging, Advanced Materials, 2022.
- [3] Fusco L, Gazzi A, Shuck CE, Orecchioni M, Ahmed EI, Giro L, Zavan B, Yilmazer A, Ley K, Bedognetti D, Gogotsi Y, Delogu LG*. V4C3 MXene Immune Profiling and Modulation of T Cell-Dendritic Cell Function and Interaction. Small Methods, 2023
- [4] ElGindi, M.; Sapudom, J.; Ibrahim, I. H.; Al-Sayegh, M.; Chen, W.; Garcia-Sabaté, A.; Teo, J. C. M. May the Force Be with You (Or Not): The Immune System under Microgravity. Cells 2021
- [5] Spatz, J.M., Fulford, M.H., Tsai, A. et al. Human immune system adaptations to simulated microgravity revealed by single-cell mass cytometry. Sci Rep 11, 2021
- [6] Akiyama, T., Horie, K., Hinoi, E. et al. How does spaceflight affect the acquired immune system?. npj Microgravity 6, 2020
- [7] Gazzi, A.; Fusco, L.; Orecchioni, M.; Ferrari, S.; Franzoni, G.; Yan, J. S.; Rieckher, M.; Peng, G.; Lucherelli, M. A.; Vacchi, I. A.; Chau, N. D. Q.; Criado, A.; Istif, A.; Mancino, D.; Dominguez, A.; Eckert, H.; Vázquez, E.; Ros, T. D.; Nicolussi, P.; Palermo, V.; Schumacher, B.; Cuniberti, G.; Mai, Y.; Clementi, C.; Pasquali, M.; Feng, X.; Kostarelos, K.; Yilmazer, A.; Bedognetti, D.; Fadeel, B.; Prato, M.; Bianco, A.; Delogu, L. G. Graphene, Other Carbon Nanomaterials and the Immune System: Toward Nanoimmunity-by-Design. J. Phys. Mater. 2020