Impact of Protein Corona on MXene Immune and Biological Interactions

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Abstract

Understanding how nanomaterials interact with biological systems is essential for their successful integration into biomedical applications [1]. When exposed to biological fluids, nanomaterials acquire a layer of biomolecules, forming a protein corona that redefines their biological identity and influences their interactions with immune cells [2,3]. In this study, we investigated how the surface chemistry of three distinct MXenes (Nb_4C_3, $Mo_2Ti_2C_3$, and Ta_4C_3) affects protein corona composition and subsequent immune cell engagement. Using advanced proteomics and lipidomics, we analyzed the protein coronas formed around each MXene after exposure to human plasma and serum [4,5]. Each material developed a unique protein profile. In particular, Ta_4C_3 strongly attracted immune-related proteins, such as complement factors and antibodies, suggesting it may actively engage the immune system. In contrast, Nb_4C_3 primarily adsorbed proteins linked to metabolic signaling. Hierarchical clustering of 64 abundant proteins revealed that the composition of the protein corona closely matched the identity of each MXene, with distinct functional interactomes forming around each material. In detail, Ta_4C_3 was associated with proteins like VTN, CFD, SERPING1, and PCOLCE, $Mo_2Ti_2C_3$ with endosomal/raft-sorting proteins, and Nb_4C_3 with IGF/adipokine signatures. These distinct protein profiles may influence how cells interact with MXenes, including potential differences in cellular uptake routes (clathrin-mediated, caveolin-mediated, or raft-mediated) and the engagement of immune cells. To examine these effects in detail, we studied how the protein coronas influenced interactions with peripheral blood mononuclear cells (PBMCs) using single-cell mass cytometry by time-of-flight (CyTOF) [6]. The CyTOF analysis revealed that the protein corona significantly altered MXene-immune cell interactions in a cell-type-specific manner, modulating both uptake frequency and intracellular accumulation.
Our findings highlight that the surface chemistry of MXenes not only determines the types of proteins that bind to nanomaterials but also plays a critical role in shaping immune cell responses. By understanding and controlling these processes, we can optimize the design of nanomaterials for biomedical applications such as drug delivery, imaging, and immune modulation.

References

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