

## Immunological Responses Induced by Coroneted 2D MoS<sub>2</sub> Nanosheets

The rapid development of nanotechnology brings us to the new era of nanomaterials and their applications. With the increasing amount of the engineered nanoparticles in the environment, their penetration into the organisms may be purposely or accidentally. Thus, understanding the interaction of nanomaterials with biomolecules, cells, and the whole organism and investigations of underlying mechanisms are becoming increasingly important. The initial “synthetic identity” of nanoparticles will transfer to the “biological identity” after administration into the protein-enriched environments which determines what “cell see” .[1] Specifically, the composition of the protein corona “fingerprint” alters we upon contact with various bio-fluids, which predict the corresponding biological fate (e.g., inflammatory responses, biodistribution, and toxicity) of nanoparticles in vivo.[2] Moreover, the formation of protein corona is a complex process and there no “identical” protein corona on the surface of nanoparticles due to variable physicochemical parameters of nanomaterials (e.g., size, nature, charge, shape, etc.) and physiological conditions of the host (e.g., health state, age, temperature, pressure, blood coagulation, etc.). Therefore, developing the stable and specific protein corona formation for targeted delivery with the suppressed immune response and “shielding” effect, to block the adsorption of the external proteins is necessary for the safe and effective nanomedicine fabrication. Therefore, we studied how 2D MoS<sub>2</sub> nanosheets with large surface area may affect the adsorption of proteins, their structures, physiological functions and mediates inflammatory effects. Moreover, we investigated the biological effects of individual coroneted nanosheets. Interestingly, human serum pre-coated nanosheets showed increased inflammatory effect by macrophages. In details, immunoglobulin G and fibrinogen pre-coated nanosheets induced stronger inflammation compared to serum albumin and transferrin proteins. Additionally, we observed that 2D nanosheets variously altered proteins’ conformations and further immune response. Noticeably, IgG pre-coated nanosheets showed higher opsonization and strong secretion of pro-inflammatory cytokines by macrophages due to FcγR and TLR receptors cross talk. The findings highlighting the contribution of blood protein components to inflammatory effects of nanosheets may provide important insights in nanosafety evaluation and rational design of biomedical nanostructures in the future.

[1]. Walczyk, D.; Bombelli, F. B.; Monopoli, M. P.; Lynch, I.; Dawson, K. A., What the cell “sees” in bio-nanoscience. *J. Am. Chem. Soc.* 2010, 132: 5761-5768.

[2]. Walkey, C. D.; Olsen, J. B.; Song, F.; Liu, R.; Guo, H.; Olsen, D. W. H.; Cohen, Y.; Emili, A.; Chan, W. C. W., Protein corona fingerprinting predicts the cellular interaction of gold and silver nanoparticles. *ACS Nano* 2014, 8: 2439-2455.

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