Impact of Person-Specific Biomolecular Coronas on Nanoparticle–Immune Cell Interactions

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It is well known that particles interact with a multitude of plasma components, forming a biomolecular corona. This corona is the primary determinant of downstream biological responses of particles, including recognition by and association with human immune cells. The formation of a biomolecular corona is person-specific, given the variation in the blood proteome as a result of genetic background, lifestyle, and underlying health conditions of an individual. Research on person-specific coronas of nanoparticles has focused on diseased-derived plasma variance, whereas variance among healthy donors has been overlooked. However, in clinical trials, healthy volunteers are commonly involved to provide important baseline information about new therapeutics. Therefore, unravelling the effect of blood variance among healthy donors on corona composition and particle–immune cell association should help to rationally improve the success of nanomedicines.

In this project, we investigated the formation of personalized biomolecular coronas on particles using plasma from a cohort of healthy donors and their impact on particle–immune cell interactions using an *ex vivo* human blood assay.[1] A matrix of mesoporous silica (MS), poly(ethylene glycol) (PEG)-coated MS particles, and PEG particles (where the MS template is removed) with different sizes (800, 450, 100 nm) were examined and compared with clinically relevant PEGylated doxorubicin-encapsulated liposomes (Doxil). We then performed an in-depth proteomics characterization of the biomolecular protein coronas that was correlated to the nanoparticle–blood cell association results. Our results show that the personalized coronas formed on the MS, PEG-coated MS, and Doxil nanoparticles from plasma of each donor significantly influence the interactions of the nanoparticles with monocytes and B cells (up to a 60-fold difference) regardless of the particle size, dosage, or donors of immune cells. Distinct proteomic fingerprints were observed on the donor-specific coronas, with individual variance in the proteome driving differential association with specific immune cell types. We identify key immunoglobulin and complement proteins that are explicitly enriched or depleted within the corona and that significantly correlate with the cell association pattern observed across the healthy donors. This study demonstrates how plasma variance in healthy individuals significantly influences the blood immune cell interactions of nanoparticles.

References

[1] Ju, Y.; Kelly, H. G.; Dagley, L. F.; Reynaldi, A.; Schlub, T. E.; Spall, S. K.; Bell, C. A.; Cui, J.; Mitchell, A. J.; Lin, Z.; Wheatley, A. K.; Thurecht, K. J.; Davenport, M. P.; Webb, A. I.; Caruso, F.; Kent, S. J., Person-Specific Biomolecular Coronas Modulate Nanoparticle Interactions with Immune Cells in Human Blood. *ACS Nano* **2020,** *14*, 15723-15737.