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Review Article

Impact of Vroman's Effect on Pharmacodynamics and Pharmacokinetics on Nanoparticulate Drug Delivery Systems

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ABSTRACT
Nanoparticle drug delivery can produce a unique pharmacokinetic and pharmacodynamic effect and unveiled better safety *in vivo* and *in vitro* toxicity profiles when compared with conventional drugs. In 1960, Vroman revealed that competitive protein exchange is a general phenomenon that occurs when a protein mixture adsorbs to a surface is called 'Vroman's effect' which is responsible for the fate of the nanoparticles. The development and formation of protein corona on nanoparticles is due to the adsorption of proteins on the surface. It is vital in specific targeting and alter the size and composition of the nanoparticle. The entropy-driven binding manages this adsorption of protein on the surface. Binding of polyethylene glycol to the nanoparticles decreases the non-specific binding and increases the targeting of tissue via enhanced permeability and retention effect. An individual disease state and components in biofluids can modify the structure and shape of protein corona on nanoparticles. By label-free transducers, we can detect targets using Vroman's effect. The biological identification of nanoparticles can lead to deleterious consequences, such as immunotoxicity, due to the formation of the protein corona.

Keywords: Vromans effect, Nanoparticles, Protein corona, Disease state, Biofluids.

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INTRODUCTION

Nano-drug delivery shows long-term effectiveness in the blood and produces therapeutic action up to a specific period. Nano-drug delivery can deliver the drug to the mutated cells by carrying the diversified cargos, including the hydrophobic and amphiphilic drugs and genes.[1] Nanoparticle drug delivery can produce a unique pharmacokinetic and pharmacodynamic effect. After entering the nanoparticles (NP) into the body, they interact with proteins present in the blood. By giving drugs in low doses, it minimizes the chances of drug toxicity.[2-6] Nano-drug delivery systems decrease dosage frequency, improve patient compliance, safety and biocompatibility, minimize toxic effect and maintain therapeutic effect (Figure 1). Physicists have studied the Vroman effect, in which proteins bound on a surface are displaced by later entering proteins. Competitive protein exchange is a general phenomenon that occurs when a protein mixture adsorbs to a surface.[7]

The Fate of Nanoparticles in the Biological Milieu - Vromans Effect

The outcome of nanoparticles is mostly determined by their fundamental features. For example, upon entering the body, they interact with proteins in the blood.

Effect of protein corona on nanoparticles

The serum is the non-cellular component in the blood consisting of 3000-3700 various types of proteins. Fibrinogen in the circulation plays a significant role in drug delivery by designing negatively charged nanoparticles. By the modification of proteins on a surface immunological response of the body can be triggered.

Hard and soft coronas

The hard, soft, and interfacial protein coronas make up the protein corona on the Nanoparticle surface. The Corona consists of a strongly bonded monolayer, whereas the soft part is bounded and present on the top, and rapid exchange of proteins occurs.[8-10] The Vromans effect involves the exchange of proteins competitively on the surface of a protein mixture. Small molecular proteins were initially coated and adsorbed onto the surface, followed by larger molecular weight proteins. This protein interchange was depending on the molecular weight of the proteins - ranging from low to high.[11]

Development of the protein corona - molecular aspects

The fate of nanoparticles is determined by the coat of protein corona that surrounds their surface. The type of corona formation on the nanoparticles could depend upon the binding strength, dissociation rate, surface area and charge. Blood contains different types of proteins like a soft and hard corona.[12]

Impact of the np-biomolecule corona on the biological system

Polyethylene glycol-modified the surface of the nanoparticles decreases the degradation of immune-mediated Nanoparticle or folic acid, over expresses folate receptors, and enhances the intended site drug delivery. The uneven development of blood vessels in the tumor setting has resulted in leaky vasculature.[13-16] The ideal parameters of the surface ligand of the nanoparticles are modified for effective targeting. Other variables, such as tumour kind, level, height, and systolic blood pressure, among others, have a significant impact.[17-19] In this domain, PEGylation has become the global standard. According to several studies, binding of

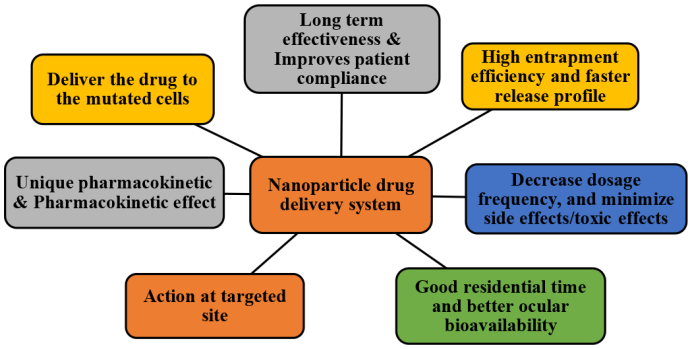

Figure 1: Unique properties of Nanoparticle drug delivery.

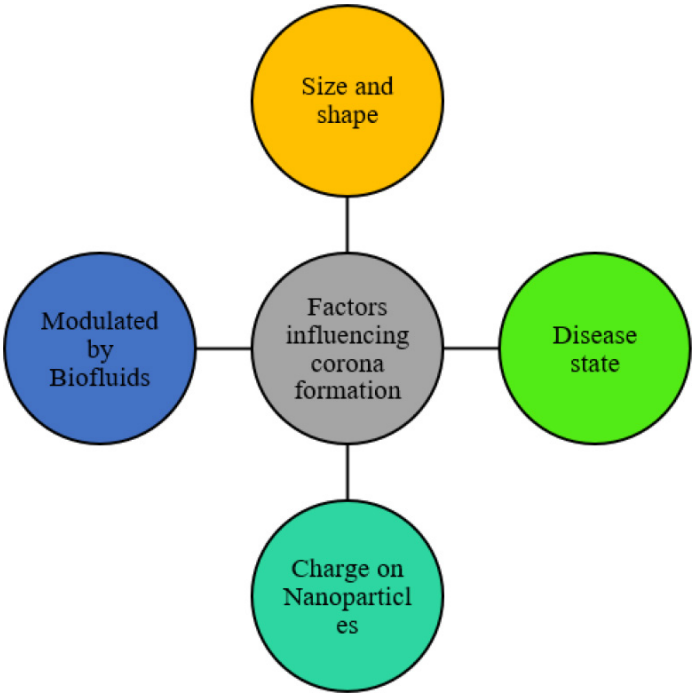

Figure 2: Factors that influence corona formation.

PEG to NPs reduces non-specific serum protein binding, improving the targeting of passive tumor tissue via the EPR effect.[20]

Choosing the optimal surface density and PEG length for the NP delivery procedure is crucial. In certain situations, various preparations of PEG-liposome generated unique coronas on NPs, inhibiting cellular absorption. Increased PEG length lowered liposome protein adsorption, apolipoprotein affinities, and even the absolute amount of opsonins collected.[21] On the other hand, Papi *et al.*[22] PEGylation of Onivyde, a liposomal FDA-approved medicine, was revealed to be somewhat vital than particulate chemistry for stealth effects. Whereas prolonged circulation times are necessary for active targeting, effective absorption of NP cargo by target cells is essential for therapeutic efficacy.

Factors Influencing Corona Formation

The nanoparticle nature of the protein corona is modified by the volume, shape, and polarity of the particles (Figure 2). *In vivo* studies of nanoparticles have shown the effect of particle shape on protein corona formation. Gold nanoparticles incubated in mouse blood form nano star, nanorods and nanostars. The total amount of protein composition altered their size and form.[23] The size of the nanoparticles is vital for protein corona formation. The binding strength of 30nm particles with platelet factor 4 was double that of massive particles. Binding 200nm particles to apolipoprotein A-I and serum albumin was twice that of other ranges.[24] The particle charge influence on corona formation is examined by incubating negatively charged polystyrene and positively charged amino-conjugated nanoparticles in human plasma. Complement C1r, Apolipoprotein F, and mannose-binding protein are responsible for the development of corona on positively charged nanoparticles.[25] These differences produced by the nanoparticles a zeta potential at -10mV to -20mV range, independent of the physiochemistry of nanoparticles.[26] Vroman dynamic effect is observed by complement c3 binding to iron oxide nano-worms by the *in vivo* study. Human plasma incubated c3 particles were recovered and administered into a c3-deficient animal, which recovered 5 min later. After injection on non-precoated particles, natural murine c3 was preserved, and protein adsorption and de-adsorption of nanoparticles in complex dynamics were observed.[27] The unique manner of corona formed on the particles based on their environment is determined by fingerprinting.[28] Most of the dynamic process is seen in the soft corona over 30nm thick, turned a protein cloud. It consists of protein stacks supported by plasma proteins ranging from 3-15nm in diameter. The layer of soft Corona is thicker than the hard corona layer.[29-31]

By incubating gold nanorods in immunoglobulin G(IgG), Human Serum Albumin at specific concentrations protein concentration was analyzed. Soft corona contains a high concentration when compared with hard corona.[32] Protein corona has a different dynamic effect on abundant proteins in the circulation and proteins that inhabit the corona. Serum albumin was the highest concentration present in the blood. In comparison, the protein alpha 1 antitrypsin exhibited high concentrations in the protein corona compared to blood. A study by Bovin *et al.*[33] assessed the twenty most abundant proteins by focusing on biological functioning. Coagulation factor and lipoproteins classes increased the protein corona, whereas molecular transport-related proteins decreased. These studies suggest that evaluating the protein Corona formation in *in vitro* and *in-vivo* samples is necessary because it impacts biological activity.

DISEASE STATE ON CORONA FORMATION

The Vroman effect can be explained without using any bioreceptors. Surface plasmon resonance (SPR) may be a label-free technique. The adsorption of proteins is examined by angle shift SPR, i.e., high molecular proteins displace low relative molecular mass proteins.[34] An individual's disease state or lifestyle may alter plasma proteome and also the shape of a PC. For instance, protein glycation improves the anaerobic metabolism of low-density lipoproteins (LDLs) in diabetic patients, allowing soluble albumin to decrease.[35] Liver diseases can also alter the detected amount of albumin in the blood. Therefore, as therapeutic biomarkers, some plasma proteins, including albumin, help to diagnose medical conditions.[36] Smoking contributes to increases in nitro tyrosine plasma protein alterations, decreasing fibrinogen (coagulation factor) and surfactant protein (SP)-A.[37] The cancer secretome refers to the huge amount of proteins released into physiological secretions by cancer cells and organs. Hundreds of tumor-derived proteins, such as autoantibodies, have been discovered. Plasma proteomes from disease states such as cancer can contribute to the production of coronas on NPs.[37-40] Muller *et al.*[41] Research focused on how polymeric NPs infuse lipids into the PC, Physicochemical properties of two oppositely charged lipid nanoparticles treated with plasma from patients with pancreatic cancer or stable have been studied. The zeta potential of simple, ionised NPs incubated in plasma from pancreatic and healthy people differed only little, hinting that NPs with differing charges might attract distinct

proteins.[42-43] NPs function as a nano-concentrator by generating a corona peculiar to the liquid sample and isolating rare plasma proteins with therapeutic value.[44] A study of the properties of carbon nanotubes (CNTs) generated underlying flaws, which was not detected with stable mouse serum. Protein corona (PC) may be generated by an overabundance of cholesterol binding to NPs in other proteins. Lipids play a key role in PC proliferation.[45-46]

Research by Shannahan *et al.*[47] shows the capacity for the inflammatory response aortic endothelial cells of sera-treated iron oxide NPs from hyperlipidemic individuals show capacity for an inflammatory response. Intermediates such as glucose or cholesterol impact the immunogenicity of fibrinogen-NP complexes. Modifying plasma components and influencing the development of NP coronas are also conceivable. NPs travel through the lining of the Respiratory tract fluid (RTLF) and produce a corona that depicts the RTLF composition, which may include inborn immunity proteins like SP-A.[48] Surprisingly, the RTLF elicited a PC in asthma patients that decreased surfactant proteins and metal-handling proteins while boosting alpha-1-antitrypsin on NPs.[49] When inhaled NPs interact with the pulmonary surfactant substrate, they can form a PC that differs from that produced in the blood. The PCs produced on NPs comprised core proteins, like as SP-A, SP-B, and SP-D, and lipids, which appeared to be devoid of molecule properties.[50-51]

BIO-FLUIDS MODULATE THE STRUCTURE OF CORONA

The structure of the corona is modulated by the biofluids present in the body. Corona protein's long-term development is influenced by the physical and chemical features of nanoparticles. The underlying biological environment is the most effective tool for encouraging the PC structure.[52-53] Protein absorbent in the surrounding atmosphere was depending on protein content, according to an early investigation of NPs in plasma utilising silica and sulfonated polystyrene NPs. This was one of several studies to indicate that because of environment-influenced variations in the PC, the same NPs can behave differently.[54] Another study found that minor discrepancies in the PC generated on NPs can occur due to factors such as blood selection, whether whole using EDTA or RPMI and PBS media to counteract coagulation.[55] The detection and behavior of NPs have vital implications for the design of nanomaterials as diagnosis and treatment plan, affected by changes in the physiological system. NPs were developed for human PCs containing immunoglobulins, supplements, and apolipoproteins, while different proteins, such as fibrinogen, were absorbed by the same NPs in the mouse serum.[56]

NANOTOXICITY AND THE BIOMOLECULE CORONA

The formation of the Precursor polycyclic plate (PC) by macrophages can alter the identification of non-potentiated Phagocytic Phosphates (NP) in response to Bovin Serum Albumin. By potentiating NPs holding titanium dioxide (TiO_2) in the PC, enhanced release of inflammatory cytokines IL-1ß and IL-6 from human macrophage was seen.[57] PC was made with disulfide-stabilized poly(methacyl) acid nonporous polymeric NPs, which inhibited the NPs' ability to be internalised by human monocytes (THP-1) in a way similar to how BSA defined FBS-containing media for PC development.[58]

CONCLUSION

Vroman has observed competitive exchange of proteins on the surface of nanoparticles. Nanoparticles interact with body fluids like blood and forms corona on the nanoparticles surface. Corona size and composition are altered by the generated corona, which varies depending on the protein present in the surroundings. The creation of hard corona around nanoparticles is primarily due to apolipoprotein A-1, whereas Human serum albumin is responsible for forming soft corona in the biological environment. Disease state can be detected by label free transducers by using Vromans effect.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Edgar JYC, Wang H. Introduction for design of nanoparticle-based drug delivery systems. Curr Pharm Des. 2017;23(14):2108-12. doi: 10.2174/1381612822666161025154003, PMID 27784242.
2. Rawal T, Patel S, Butani S. Chitosan nanoparticles as a promising approach for pulmonary delivery of bedaquiline. Eur J Pharm Sci. 2018;124:273-87. doi: 10.1016/j.ejps.2018.08.038, PMID 30176365.
3. Angioletti-Uberti S, Ballauff M, Dzubiella J. Competitive adsorption of multiple proteins to nanoparticles: The Vroman effect revisited. Mol Phys. 2018;116(21-22):3154-63. doi: 10.1080/00268976.2018.1467056.
4. Karmali PP, Simberg D. Interactions of nanoparticles with plasma proteins: Implication on clearance and toxicity of drug delivery systems. Expert Opin Drug Deliv. 2011;8(3):343-57. doi: 10.1517/17425247.2011.554818, PMID 21291354.
5. Kumar L, Verma S, Bhardwaj A, Vaidya S, Vaidya B. Eradication of superficial fungal infections by conventional and novel approaches: A comprehensive review. Artif Cells Nanomed Biotechnol. 2014;42(1):32-46. doi: 10.3109/21691401.2013.769446, PMID 23452349.
6. De Jong WH, Borm PJ. Drug delivery and nanoparticles: Applications and hazards. Int J Nanomedicine. 2008;3(2):133-49. doi: 10.2147/ijn.s596, PMID 18686775.
7. Hirsh SL, McKenzie DR, Nosworthy NJ, Denman JA, Sezerman OU, Bilek MM. The Vroman effect: Competitive protein exchange with dynamic multilayer protein aggregates. Colloids Surf B Biointerfaces. 2013;103:395-404. doi: 10.1016/j.colsurfb.2012.10.039, PMID 23261559.
8. Liu N, Tang M, Ding J. The interaction between nanoparticles-protein corona complex and cells and its toxic effect on cells. Chemosphere. 2020;245:125624. doi: 10.1016/j.chemosphere.2019.125624, PMID 31864050.
9. Winzen S, Schoettler S, Baier G, Rosenauer C, Mailaender V, Landfester K, *et al.* Complementary analysis of the hard and soft protein corona: Sample preparation critically effects corona composition. Nanoscale. 2015;7(7):2992-3001. doi: 10.1039/c4nr05982d, PMID 25599336.
10. Kharazian B, Hadipour NL, Ejtehadi MR. Understanding the nanoparticle–protein corona complexes using computational and experimental methods. Int J Biochem Cell Biol. 2016;75:162-74. doi: 10.1016/j.biocel.2016.02.008, PMID 26873405.
11. Choi S, Yang Y, Chae J. Surface plasmon resonance protein sensor using Vroman effect. Biosens Bioelectron. 2008;24(4):899-905. doi: 10.1016/j.bios.2008.07.036, PMID 18768307.
12. Lundqvist M, Augustsson C, Lilja M, Lundkvist K, Dahlbäck B, Linse S, *et al.* The nanoparticle protein corona formed in human blood or human blood fractions. PLOS ONE. 2017;12(4):e0175871. doi: 10.1371/journal.pone.0175871, PMID 28414772.
13. Bonvin D, Bastiaansen JAM, Stuber M, Hofmann H, Mionic Ebersold MM. Folic acid on iron oxide nanoparticles: Platform with high potential for simultaneous targeting, MRI detection and hyperthermia treatment of lymph node metastases of prostate cancer. Dalton Trans. 2017;46(37):12692-704. doi: 10.1039/c7dt02139a, PMID 28914298.
14. Flores O, Santra S, Kaittanis C, Bassiouni R, Khaled AS, Khaled AR, *et al.* PSMA-targeted theranostic nanocarrier for prostate cancer. Theranostics. 2017;7(9):2477-94. doi: 10.7150/thno.18879, PMID 28744329.
15. Zhang Z, Wang H, Tan T, Li J, Wang Z, Li Y. Rational design of nanoparticles with deep tumor penetration for effective treatment of tumor metastasis. Adv Funct Mater. 2018 Oct;28(40):1801840. doi: 10.1002/adfm.201801840.
16. Matsumura Y, Maeda H. A new concept for macromolecular therapeutics in cancer chemotherapy: Mechanism of tumoritropic accumulation of proteins and the antitumor agent smancs. Cancer Res. 1986;46(12 Pt 1):6387-92. PMID 2946403.
17. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an emerging platform for cancer therapy. Nat Nanotechnol. 2007;2(12):751-60. doi: 10.1038/nnano.2007.387, PMID 18654426.
18. Nichols JW, Bae YH. EPR: Evidence and fallacy. J Control Release. 2014;190:451-64. doi: 10.1016/j.jconrel.2014.03.057, PMID 24794900.
19. Salvati A, Pitek AS, Monopoli MP, Prapainop K, Bombelli FB, Hristov DR, *et al.* Transferrin-functionalized nanoparticles lose their targeting capabilities when a

biomolecule corona adsorbs on the surface. Nat Nanotechnol. 2013;8(2):137-43. doi: 10.1038/nnano.2012.237, PMID 23334168.

20. Suk JS, Xu Q, Kim N, Hanes J, Ensign LM. PEG ylation as a strategy for improving nanoparticle-based drug and gene delivery. Adv Drug Deliv Rev. 2016;99(A):28-51. doi: 10.1016/j.addr.2015.09.012, PMID 26456916.
21. Pozzi D, Colapicchioni V, Caracciolo G, Piovesana S, Capriotti AL, Palchetti S, *et al.* Effect of polyethyleneglycol (PEG) chain length on the bio–nano-interactions between pegylated lipid nanoparticles and biological fluids: From nanostructure to uptake in cancer cells. Nanoscale. 2014;6(5):2782-92. doi: 10.1039/c3nr05559k, PMID 24463404.
22. Papi M, Caputo D, Palmieri V, Coppola R, Palchetti S, Bugli F, *et al.* Clinically approved pegylated nanoparticles are covered by a protein corona that boosts the uptake by cancer cells. Nanoscale. 2017;9(29):10327-34. doi: 10.1039/c7nr03042h, PMID 28702661.
23. García-Álvarez R, Hadjidemetriou M, Sánchez-Iglesias A, Liz-Marzán LM, Kostarelos K. *In vivo* formation of protein corona on gold nanoparticles. The effect of their size and shape. Nanoscale. 2018;10(3):1256-64. doi: 10.1039/c7nr08322j, PMID 29292433.
24. Hu Z, Zhang H, Zhang Y, Wu R, Zou H. Nanoparticle size matters in the formation of plasma protein coronas on Fe_3O_4 nanoparticles. Colloids Surf B Biointerfaces. 2014;121:354-61. doi: 10.1016/j.colsurfb.2014.06.016, PMID 24974013.
25. Lundqvist M, Stigler J, Elia G, Lynch I, Cedervall T, Dawson KA. Nanoparticle size and surface properties determine the protein corona with possible implications for biological impacts. Proc Natl Acad Sci U S A. 2008;105(38):14265-70. doi: 10.1073/pnas.0805135105, PMID 18809927.
26. Alkilany AM, Nagaria PK, Hexel CR, Shaw TJ, Murphy CJ, Wyatt MD. Cellular uptake and cytotoxicity of gold nanorods: Molecular origin of cytotoxicity and surface effects. Small. 2009;5(6):701-8. doi: 10.1002/smll.200801546, PMID 19226599.
27. Chen F, Wang G, Griffin JI, Brenneman B, Banda NK, Holers VM, *et al.* Complement proteins bind to nanoparticle protein corona and undergo dynamic exchange *in vivo*. Nat Nanotechnol. 2017;12(4):387-93. doi: 10.1038/nnano.2016.269, PMID 27992410.
28. Lundqvist M, Stigler J, Cedervall T, Berggård T, Flanagan MB, Lynch I, *et al.* The evolution of the protein corona around nanoparticles: A test study. ACS Nano. 2011;5(9):7503-9. doi: 10.1021/nn202458g, PMID 21861491.
29. Docter D, Westmeier D, Markiewicz M, Stolte S, Knauer SK, Stauber RH. The nanoparticle biomolecule corona: Lessons learned – challenge accepted? Chem Soc Rev. 2015;44(17):6094-121. doi: 10.1039/c5cs00217f. PMID 26065524.
30. Choi HS, Liu W, Misra P, Tanaka E, Zimmer JP, Itty Ipe BI, *et al.* Renal clearance of quantum dots. Nat Biotechnol. 2007;25(10):1165-70. doi: 10.1038/nbt1340, PMID 17891134.
31. Monopoli MP, Walczyk D, Campbell A, Elia G, Lynch I, Bombelli FB, *et al.* Physical– chemical aspects of protein corona: Relevance to *in vitro* and *in vivo* biological impacts of nanoparticles. J Am Chem Soc. 2011;133(8):2525-34. doi: 10.1021/ja107583h, PMID 21288025.
32. Alex SA, Chandrasekaran N, Mukherjee A. Impact of gold nanorod functionalization on biocorona formation and their biological implication. J Mol Liq. 2017;248:703-12. doi: 10.1016/j.molliq.2017.10.119.
33. Bonvin D, Aschauer U, Alexander DTL, Chiappe D, Moniatte M, Hofmann H, *et al.* Protein corona: Impact of lymph versus blood in a complex *in vitro* environment. Small. 2017;13(29):1700409. doi: 10.1002/smll.201700409, PMID 28582610.
34. Schaaij-Visser TB, De Wit M, Lam SW, Jiménez CR. The cancer secretome, current status and opportunities in the lung, breast and colorectal cancer context. Biochim Biophys Acta. 2013;1834(11):2242-58. doi: 10.1016/j.bbapap.2013.01.029, PMID 23376433.
35. Pradeep T, Haranath C. A review on diabetes mellitus Type II. Int J Pharm Res Rev. 2014 Sep;3(9):23-9.
36. Anderson NL, Anderson NG. The human plasma proteome: History, character, and diagnostic prospects. Mol Cell Proteomics. 2002;1(11):845-67. doi: 10.1074/mcp.r200007-mcp200, PMID 12488461.
37. Jin H, Webb-Robertson BJ, Peterson ES, Tan R, Bigelow DJ, Scholand MB, *et al.* Smoking, COPD, and 3-nitrotyrosine levels of plasma proteins. Environ Health Perspect. 2011;119(9):1314-20. doi: 10.1289/ehp.1103745, PMID 21652289.
38. Loke SY, Lee ASG. The future of blood-based biomarkers for the early detection of breast cancer. Eur J Cancer. 2018;92:54-68. doi: 10.1016/j.ejca.2017.12.025, PMID 29413690.
39. Hajipour MJ, Laurent S, Aghaie A, Rezaee F, Mahmoudi M. Personalized protein coronas: A "key" factor at the nanobiointerface. Biomater Sci. 2014;2(9):1210-21. doi: 10.1039/c4bm00131a, PMID 32481892.
40. Hajipour MJ, Raheb J, Akhavan O, Arjmand S, Mashinchian O, Rahman M, *et al.* Personalized disease-specific protein corona influences the therapeutic impact of graphene oxide. Nanoscale. 2015;7(19):8978-94. doi: 10.1039/c5nr00520e, PMID 25920546.
41. Müller J, Prozeller D, Ghazaryan A, Kokkinopoulou M, Mailänder V, Morsbach S, *et al.* Beyond the protein corona – lipids matter for biological response of nanocarriers. Acta Biomater. 2018;71:420-31. doi: 10.1016/j.actbio.2018.02.036, PMID 29524674.
42. Colapicchioni V, Tilio M, Digiacomo L, Gambini V, Palchetti S, Marchini C, *et al.* Personalized liposome–protein corona in the blood of breast, gastric and pancreatic cancer patients. Int J Biochem Cell Biol. 2016;75:180-7. doi: 10.1016/j.biocel.2015.09.002, PMID 26369869.
43. Caputo D, Papi M, Coppola R, Palchetti S, Digiacomo L, Caracciolo G, *et al.* A protein corona-enabled blood test for early cancer detection. Nanoscale. 2017;9(1):349-54. doi: 10.1039/c6nr05609a, PMID 27924334.
44. Zheng T, Pierre-Pierre N, Yan X, Huo Q, Almodovar AJ, Valerio F, *et al.* Gold nanoparticle-enabled blood test for early-stage cancer detection and risk assessment. ACS Appl Mater Interfaces. 2015;7(12):6819-27. doi: 10.1021/acsami.5b00371, PMID 25757512.
45. Tavakol M, Montazeri A, Naghdabadi R, Hajipour MJ, Zanganeh S, Caracciolo G, *et al.* Disease-related metabolites affect protein–nanoparticle interactions. Nanoscale. 2018;10(15):7108-15. doi: 10.1039/c7nr09502c, PMID 29616243.
46. Raghavendra AJ, Fritz K, Fu S, Brown JM, Podila R, Shannahan JH. Variations in biocorona formation related to defects in the structure of single walled carbon nanotubes and the hyperlipidemic disease state. Sci Rep. 2017;7(1):8382. doi: 10.1038/s41598-017-08896-w, PMID 28814800.
47. Shannahan JH, Fritz KS, Raghavendra AJ, Podila R, Persaud I, Brown JM. From the cover: Disease-induced disparities in formation of the nanoparticle-biocorona and the toxicological consequences. Toxicol Sci. 2016;152(2):406-16. doi: 10.1093/toxsci/kfw097, PMID 27255384.
48. Kumar A, Bicer EM, Morgan AB, Pfeffer PE, Monopoli M, Dawson KA, *et al.* Enrichment of immunoregulatory proteins in the biomolecular corona of nanoparticles within human respiratory tract lining fluid. Nanomedicine. 2016;12(4):1033-43. doi: 10.1016/j.nano.2015.12.369, PMID 26767511.
49. Kumar A, Bicer EM, Pfeffer P, Monopoli MP, Dawson KA, Eriksson J, *et al.* Differences in the coronal proteome acquired by particles depositing in the lungs of asthmatic versus healthy humans. Nanomedicine. 2017;13(8):2517-21. doi: 10.1016/j.nano.2017.06.008, PMID 28647590.
50. Raesch SS, Tenzer S, Storck W, Rurainski A, Selzer D, Ruge CA, *et al.* Proteomic and lipidomic analysis of nanoparticle corona upon contact with lung surfactant reveals differences in protein, but not lipid composition. ACS Nano. 2015;9(12):11872-85. doi: 10.1021/acsnano.5b04215, PMID 26575243.
51. Whitwell H, Mackay RM, Elgy C, Morgan C, Griffiths M, Clark H, *et al.* Nanoparticles in the lung and their protein corona: The few proteins that count. Nanotoxicology. 2016;10(9):1385-94. doi: 10.1080/17435390.2016.1218080, PMID 27465202.
52. Pieper R, Gatlin CL, Makusky AJ, Russo PS, Schatz CR, Miller SS, *et al.* The human serum proteome: Display of nearly 3700 chromatographically separated protein spots on two-dimensional electrophoresis gels and identification of 325 distinct proteins. Proteomics. 2003;3(7):1345-64. doi: 10.1002/pmic.200300449, PMID 12872236.
53. Shannahan J. The biocorona: A challenge for the biomedical application of nanoparticles. Nanotechnol Rev. 2017;6(4):345-53. doi: 10.1515/ntrev-2016-0098, PMID 29607287.
54. Walkey CD, Chan WC. Understanding and controlling the interaction of nanomaterials with proteins in a physiological environment. Chem Soc Rev. 2012;41(7):2780-99. doi: 10.1039/c1cs15233e, PMID 22086677.
55. Strojan K, Leonardi A, Bregar VB, Križaj I, Svete J, Pavlin M. Dispersion of nanoparticles in different media importantly determines the composition of their protein corona. PLOS ONE. 2017;12(1):e0169552. doi: 10.1371/journal.pone.0169552, PMID 28052135.
56. Solorio-Rodríguez A, Escamilla-Rivera V, Uribe-Ramírez M, Chagolla A, Winkler R, García-Cuellar CM, *et al.* A comparison of the human and mouse protein corona profiles of functionalized SiO 2 nanocarriers. Nanoscale. 2017;9(36):13651-60. doi: 10.1039/c7nr04685e, PMID 28875999.
57. Borgognoni CF, Mormann M, Qu Y, Schäfer M, Langer K, Öztürk C, *et al.* Reaction of human macrophages on protein corona covered TiO_2 nanoparticles.

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