Nanoparticles are structures characterized by very small sizes that are used in medicine, among others, as carriers of drug molecules in order to increase the effectiveness of treatment and prevention of certain diseases. Recently, the most famous example of the use of nanoparticles is the lipid carriers used in mRNA vaccines against the SARS-Cov-2 virus by Pfizer / BioNTech and Moderna. Similar lipid carriers are also used in some anti-cancer, anti-fungal drugs and ointments.
Lipid nanoparticles when contact with body fluids, e.g. blood, plasma, etc., adsorb on their surface proteins which are called the protein corona (from Latin “crown”) of the nanoparticles. Such a protein corona may change the properties of the nanoparticle, e.g. by influencing the interaction with cells, and consequently increase or decrease the effectiveness of the drug substance transported. The protein composition and the physiological role of the protein biocorona are not fully understood. However, the above issues are necessary for a better understanding of the efficacy of drug molecules transported in nanoparticles such as liposomes or lipid nanoparticles. The above types of nanoparticles are most commonly used in medicinal products available on the market.

An important step in the study of the protein corona is its separation from unbound proteins to ensure the integrity of the protein corona and a high degree of separation from other, free proteins.

In our project, we have proposed the use of asymmetric flow field-flow fractionation (AF4) as a method of separating nanoparticle-corona complexes formed in the laboratory during incubation in serum or whole blood.
The aim of our research is to adapt the AF4 method for isolation of lipid nanoparticles-corona complexes from unbound proteins, after incubation in plasma and whole blood. As a reference method, we will use the magnetic separation method, which is described in the literature as the most effective method of isolation nanoparticle-corona complexes. However, magnetic separation method can only be used to separate nanoparticles with specific properties, i.e. magnetic nanoparticles. Therefore, in our project, for comparative purposes, we will obtain also magnetic liposomes and lipid nanoparticles by incorporating magnetic iron(III) oxide nanoparticles into their structure.
Then, in order to better understand the functioning of the protein corona, we will examine the influence of the corona on the interaction of liposomes and lipid nanoparticles with selected cells (macrophages, epithelial cells and cancer cells), which are potential "recipients" of nanoparticles used in medicine and their cargos, i.e. drug molecules or a nucleic acid (e.g., mRNA). In the final stage, we will examine the influence of the corona on the efficiency of nucleic acid delivery (model mRNA) in lipid nanoparticles (analogous to those used in mRNA vaccines against the SARS-Cov-2 virus) in cell culture and in an animal model.

Why are the results of our project important? The outcomes of our project will enhance understanding of (i) the composition of protein corona formed in different fluids on the surface of the most commonly used types of drug delivery system (liposomes, lipid nanoparticles), and (ii) nanoparticle-corona complexes uptake mechanism in cells that are physiological targets for those nanoparticles. Thus, we may further be able to design lipid nanoparticles and liposomes with better properties and improved efficacy. Importantly, the presented project contributes to understanding the corona effect on the mRNA delivery by lipid nanoparticles. The above aspect is important while facing the increasing role of mRNA therapeutics and delivery systems nowadays. In addition, project results could initiate further research that will increase the effectiveness of drugs that use nanoparticles as drug carriers and will allow the use of the properties of the protein corona in new applications, e.g. as markers, diagnostics and other purposes.
Above all, the results of the project may have great potential to significantly impact the drug delivery field and improve the research methodology and understanding of the role of the biomolecular corona of lipid-based nanoparticles.
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