Trends in Analytical Chemistry 65 (2015) 30–46

Contents lists available at ScienceDirect

Trends in Analytical Chemistry

journal homepage: www.elsevier.com/locate/trac

Proteomics analysis of the mode of antibacterial action of nanoparticles and their interactions with proteins

Hani Nasser Abdelhamid [a,b,*], Hui-Fen Wu [b,c,d,e,f,**]

[a] Department of Chemistry, Assuit University, Assuit 71515, Egypt
[b] Department of Chemistry, National Sun Yat-Sen University, Kaohsiung, Taiwan 804
[c] School of Pharmacy, College of Pharmacy, Kaohsiung Medical University, Kaohsiung, Taiwan 807
[d] Institute of Medical Science and Technology, National Sun Yat-Sen University, Taiwan 80424
[e] Center for Nanoscience and Nanotechnology, National Sun Yat-Sen University, Kaohsiung, Taiwan 804
[f] Doctoral Degree Program in Marine Biotechnology, National Sun Yat-Sen University, Kaohsiung, Taiwan 804

ARTICLE INFO

Keywords:
Antibacterial action
Bionanoscience
Biocomptability
Cytotoxicity
Living cell
Mineralo-protein nanoparticle
Nanoparticle
Protein corona
Proteomics
Toxicity

ABSTRACT

The interactions of nanoparticles (NPs) with "protein corona" and live cells are likely to become important in bionanoscience. These interactions play the central role in nanomedicine and nanosafety issues. The protein-adsorption layers located on the surface of colloidal NPs play an important role in their interaction with living cells, so characterization of the protein corona is of the utmost importance for understanding how exposure to NPs affects the biological responses of cells and organisms. This review deals with the interaction of NPs with proteins, live cells and organelles, and considers the proteomics analysis by which these interactions affect cytotoxicity. We offer an overview of the cytotoxicity of different NPs using proteomics analysis. We also review proteomics analysis of natural mineralo-protein NPs. Among the different approaches, proteomics analysis is simple, informative and cheap.

Contents

* Corresponding author. Tel.: +00201279744643.
E-mail address: hany.abdelhameed@science.au.edu.eg (H.N. Abdelhamid).
** Corresponding author. Tel.: +886 7 5252000 3955; Fax: +886 7 525 3908.
E-mail address: hwu@faculty.nsysu.edu.tw (H-F. Wu).

http://dx.doi.org/10.1016/j.trac.2014.09.010
0165-9936/

1. Introduction

Nowadays, the synthesis and application of nanomaterials or nanoparticles (NPs) and exploration of their properties have attracted attention from many branches of science, such as physics, chemistry, biology, and engineering. Nanotechnology includes materials and particles with dimensions in the range 1–100 nm. This overview covers recent advances in NP interactions with proteins and living cells. The second part covers the cytotoxicity of NPs using proteomics analysis. We do not cover or evaluate any other methodology used to probe cytotoxicity and biocompatibility.

Applications of nanotechniques in proteomics have been growing steadily over the years [1–8]. Application of NPs in proteomics opened the way to exploration of the proteome that may provide the platform for discovery of next-generation biomarkers and this leads to the identification of large numbers of proteins in complex biological samples. It was defined as nanoproteomics [9]. Our main goals are to highlight protein-NP interactions and the proteomics analysis that reveals the toxicity of different NPs and to review the specific experimental considerations while drawing some general conclusions about current knowledge in the field of nanotoxicity or nanocytotoxicity. We cover proteomics analysis of cells, tissues and the human body. We also summarize proteomics analysis of natural mineralo-protein NPs.

2. Protein-nanoparticle interactions

There is growing appreciation of the basic interactions of nanoscale objects with proteins and living systems [10–14]. These interactions play a central role in nanomedicine and in concerns about nanosafety. For this reason, we believe that a clear view of these interactions is necessary and is becoming a key objective in bionanoscience. The interaction of nanoscale objects with proteins is defined as “protein corona”, which implies a long-lived equilibrium state [15]. In contrast, some particles will have only a “weak” corona, meaning that most of the biological macromolecules will have a weak association to the surface.

It is important to bear in mind that, due to the large surface area and the tiny size of NPs, their surfaces are energetic. Understanding the protein corona and its underlying dynamics of change may reveal the biological activity, the biodistribution, and the bioactivities of NPs [15–18]. By understanding NP-protein interactions, we can potentially define and predict NP-cell interactions and elucidate the bioactivity aspects for biomedical applications.

In general, NPs have a very active surface chemistry due to their extremely large surface area-to-volume ratio. They tend to reduce their large surface energy by interacting with the surrounding components that contain donating or accepting sites. For example, the dispersion of NPs in a biological entity (e.g., cells, tissues, and organs) results in their surfaces being covered by a complex layer of biomolecules (e.g., proteins and lipoproteins), and that may change the activities of the exogenic materials. This new biological identity (i.e., NP@protein) creates a new interface between the NPs and the rest of the biological entity. These new interactions depend on the stability of the new entity. Thus, some NPs form a stable hard core with the biological macromolecules (hard corona) and the others form a weak core (weak corona) [12,18–24]. The strength of these interactions will affect the nature and the strength of the interaction of the NP@protein with the surrounding biomolecules.

It was reported that, in some cases, the protein in the protein corona does not undergo any significant changes. For example, iron-oxide NPs (IONPs) selectively capture the pediocin protein to generate IONP@protein. The authors claimed that the protein in the new nanocomposites did not induce any significant perturbation of the native structure of pediocin and could therefore ensure a high retention of typical pediocin activity [19,25]. The same behavior was reported for nisin-interacted gold-NP-capped citrate (AuNP@citrate) [25]. This good feature enabled us to generate robust antimicrobial agents [24,25].

The protein corona is a significant indicator of particle biodistribution [26,27]. Thus, deep understanding of the biological effects triggered by NPs requires detailed knowledge of how protein coronas are involved in nanobiology, nanomedicine and nanotoxicology [28–30]. The toxicity and the uptake of NPs by cells may change after the formation of protein corona [31–33].

2.1. Forces governing protein-nanoparticle interactions

The biological responses to NPs are greatly affected by the main forces available in the nanobiology system (e.g., electrostatic, hydrophobicity, hydrophilicity, Van der Waals, and hydrogen bonds) and the intrinsic characteristics of the NPs and the proteins that drive the formation of the protein corona (Table 1) [21,32,33]. The primary interaction of the protein corona is thought to be electrostatic [32–41].

In a study of the interaction between quantum dots and human serum albumin (QD-HAS), the thermodynamic parameters of the system indicated that electrostatic interactions played a major role in the binding reaction because negative enthalpy and positive entropy values were obtained [39]. Also, QD-capped chitosan (CdS@CTS) interacts with whole cells by electrostatic forces [41]. The same capping materials can provide other forces, such as hydrogen bonds [42,43]. The interaction of bovine serum albumin (BSA) with Au colloids and surfaces was studied using zeta (ζ)-potential and quartz-crystal microbalance (QCM) measurements. Data revealed that BSA interacts with AuNPs and Au surfaces by an electrostatic mechanism when citrate is present on the NP surface [44]. Hydrophobic interactions were also reported around copolymer NPs (contain -CH_3 groups with apolipoproteins), which have the highest affinity for the most hydrophobic NPs [15].

2.2. Factors affecting protein-nanoparticle interactions

The blood plasma corona is highly complex and protein binding did not simply correlate with the relative abundance of proteins in the plasma. The formation of the protein corona

Table 1
Types of the interaction pathway between proteins and nanoparticles

Interaction	Type	Comments
Non-covalent	1. Hydrogen bond 2. Electrostatic forces 3. Hydrophobic 4. Van der Waals forces 5. π-π	Weak, affected by pH, T and time of the interaction
Covalent	Crosslinking chemistry between the nanoparticle surface molecules and the protein function groups (NH_2 and COOH)	Strong, require chemical reagent, such as EDC, not affected by pH, T and time

EDC, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide.