Biotechnology Advances 35 (2017) 889–904

Contents lists available at ScienceDirect

Biotechnology Advances

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

Research review paper

In-vitro in-vivo correlation (IVIVC) in nanomedicine: Is protein corona the missing link?

Priyanka Jain[a], R.S. Pawar[a], R.S. Pandey[b], Jitender Madan[c], Sulakshna Pawar[d], P.K. Lakshmi[a], M.S. Sudheesh[a,*]

[a] Faculty of Pharmacy, VNS Group of Institutions, Nathu Barkheda, Neelbud, Bhopal 462044, India
[b] SLT Institute of Pharmaceutical Sciences, Guru Ghasidas Vishwavidyalaya, Bilaspur, C.G. 495009, India
[c] Department of Pharmaceutics, Chandigarh College of Pharmacy, Mohali, Panjab, India
[d] Sagar Institute of Research and Technology-Pharmacy, Bhopal, India

ARTICLE INFO

Keywords:
Nanoparticles
Protein corona
Targeting
Bio-nano interface
IVIVC
Physicochemical property
Inflammation
Cell uptake

ABSTRACT

One of the unmet challenges in nanotechnology is to understand and establish the relationship between physicochemical properties of nanoparticles (NPs) and its biological interactions (bio-nano interactions). However, we are still far from assessing the biofate of NPs in a clear and unquestionable manner. Recent developments in the area of bio-nano interface and the understanding of protein corona (PC) has brought new insight in predicting biological interactions of NPs. PC refers to the spontaneous formation of an adsorbed layer of biomolecules on the surface of NPs in a biological environment. PC formation involves the spatiotemporal interplay of an intricate network of biological, environmental and particle characteristics. NPs with its PC can be viewed as a biological entity, which interacts with cells and barriers in a biological system. Recent studies on the bio-nano interface have revealed biological signatures that participate in cellular and physiological bioprocesses and control the biofate and toxicity of NPs. The ability of in-vitro derived parameters to forecast in-vivo consequences by developing a mathematical model forms the basis of in-vitro in-vivo correlation (IVIVC). Understanding the effect of bio-nano interactions on the biological consequences of NPs at the cellular and physiological level can have a direct impact on the translation of future nanomedicines and can lead to the ultimate goal of developing a mathematical IVIVC model. The review summarizes the emerging paradigms in the field of bio-nano-interface which clearly suggests an urgent need to revisit existing protocols in nanotechnology for defining the physicochemical correlates of bio-nano interactions.

1. Introduction

The study on protein corona (PC) has led to a paradigm shift in the field of nanomedicine which has opened new avenues for the translation and safe usage of nanoparticles (NPs). The spontaneous formation of a PC on the NP surface in body fluids is now believed to be a critical determinant of the biofate of NPs (Lundqvist et al., 2008). Several years of research on NPs has failed to determine specific conclusions regarding the physicochemical correlates of their biological activity. Current in-vitro data of NPs poorly translate into in-vivo predictions (Shcharbin et al., 2014). Toxic effects of NPs have also raised some concerns and the cause for these effects is still largely unknown. The growing interest in the study of PC is due to its possible correlation with several important phenomena in biological systems (Albanese et al., 2014). Several challenges encountered in nanotechnology research are due to poorly designed experimental protocols. In order to obtain reliable and realistic data, existing protocols in nanotechnology must be carried under physiologically relevant in-vitro conditions taking into account the interactions occurring at the bio-nano interface. Therefore, gaps in knowledge still remain.

The basic aim of this review is to provide researchers working on basic and translational nanomedicine with a mechanistic understanding of the bio-nano interface and its role in developing an in-vitro in-vivo correlation (IVIVC) model. We also focus on the lacunae in the experimental designs, now used in nanotechnology which may be responsible for a poor IVIVC. The review is divided into two sections. The first part deals with the effect of physicochemical property of NPs on the PC formation and the second part deals with the impact of NP-PC complex on its biological activity. An in-depth analysis of the intermolecular forces between biomolecules and NPs at the bio-nano interface is beyond the scope of the current discussion. For a comprehensive review on the biophysical aspects of PC formation, readers may refer to

* Corresponding author.
E-mail address: mssudheesh78@gmail.com (M.S. Sudheesh).

http://dx.doi.org/10.1016/j.biotechadv.2017.08.003
Received 1 June 2017; Received in revised form 4 August 2017; Accepted 19 August 2017
Available online 26 August 2017
0734-9750/ © 2017 Elsevier Inc. All rights reserved.

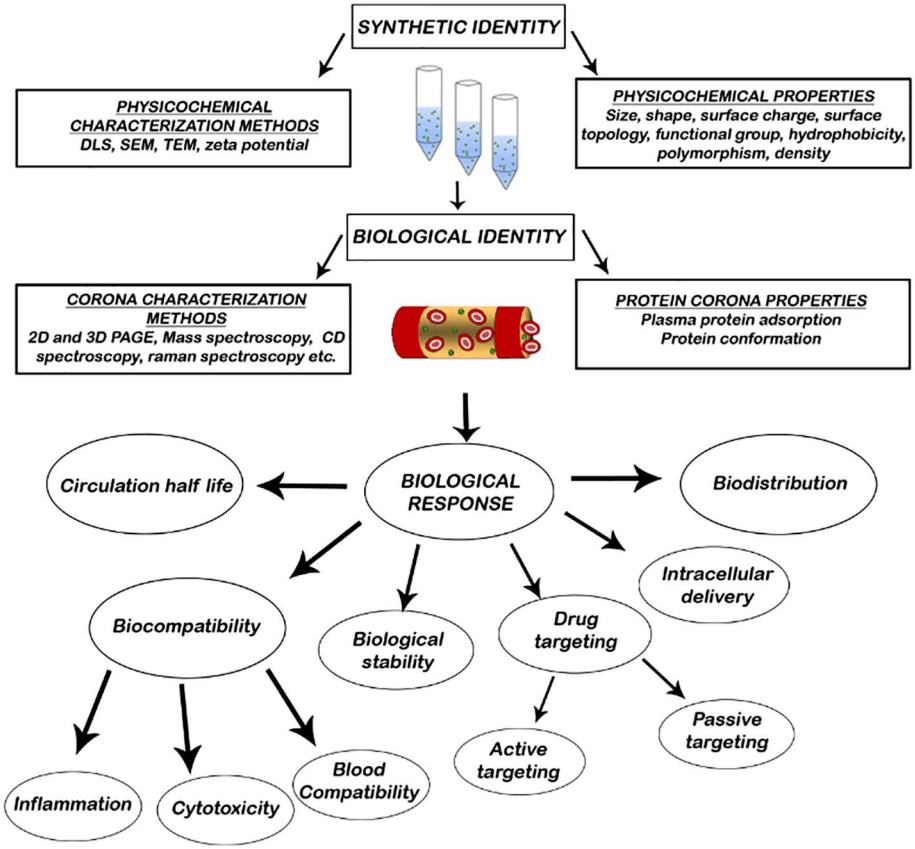

Fig. 1. Possible relationship between synthetic identity, biological identity and biological response of nanoparticles.

Nel et al., 2009. The main focus of the current discussion is on the biological consequences of bio-nano interactions and its implications on IVIVC.

2. Synthetic identity versus biological identity of NPs

The adsorbed layer of biomolecules defines the biological identity of NPs whereas physicochemical properties of NPs define its synthetic identity. The delineation of the synthetic identity and biological identity of NPs might seal the existing gap in knowledge and bring about predictability in nanomedicine research (Fadeel et al., 2013) (Fig. 1). The interest in the study of bio-nano interface gained significance by the seminal works initiated by Dawson and co-workers (Cedervall et al., 2007a,b; Lundqvist et al., 2008). Biological identity is a derived property of a NP and depends on the environment, which in the case of nanomedicines comprises of a myriad of physiological biomolecules. The PC formation shows a “memory” effect depending on the sequence of biomolecules, the NP encounters. The protein which interacts with the NP first has the largest abundance in the PC. It is hypothesized that the “memory” effect may be a consequence of initial NP-protein interaction (e.g. a conformational change in the adsorbed protein), which influences the subsequent protein-protein interaction during PC formation (Vilanova et al., 2016). The NPs with its PC can get access to otherwise inaccessible areas by biomimicking endogenous and exogenous substances and can have unanticipated consequences (Lara et al., 2017). As a matter of fact, the phenomenon of biomimicry has been used as a strategy for selective drug targeting by cloaking NPs with platelet membrane which provides a shielding effect against immune response (Hu et al., 2013b).

The characterization of the PC and its correlation with observed biological effects of NPs is currently the biggest challenge in bionanoscience. The accessibility of NPs to cells and organs throughout the body and its environmental impact makes the study of PC relevant to biological systems. A lack of a rational understanding of the biological identity may well be the “missing-link” in the development of a predictive in-vitro model. The bio-nano interface has ushered a totally new field of study less known to the scientific community and we believe that this could be a possible turning point for the safe translation of NPs. However, understanding the bio-nano interface is extremely challenging, given the complexity to replicate a dynamic physiological environment and the difficulty to adapt currently available analytical methods to these situations. Here, we systematically analyze current gap in knowledge and provide a comprehensive overview of the possible future challenges in decoding the bio-nano interface.

3. Effect of physicochemical properties of NP on protein adsorption

The surface characteristic of engineered NPs is regarded as the principle determinant of bioactivity in a targeted drug delivery. A slight change in physicochemical properties alters the biological effect of NPs for unknown reasons. This brings unpredictability in terms of the toxicity and biofate of NPs and results in poor in-vitro in-vivo correlation. The study of PC may help us in underpinning the unpredictable behavior of NPs.

3.1. Size, shape, curvature and charge effect

In the early research, the principle determinant of NP delivery and toxicity was particle size (Park et al., 2013; Xiong et al., 2013). However, now it is realized that not only size but curvature, surface chemistry, hydrophobicity, charge etc. of NPs also appear to affect protein binding and it is quite clear that size alone cannot explain the unpredictable and heterogeneous outcomes of NPs. However, size is one of the most important determinants of PC composition and therefore its biological effect. The highly curved surface and small size of NPs

Download English Version:

https://daneshyari.com/en/article/6451144

Download Persian Version:

https://daneshyari.com/article/6451144

Daneshyari.com