DIRNANO

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Production and molecular design of recombinant proteins for functional modulation of biomolecular corona effects

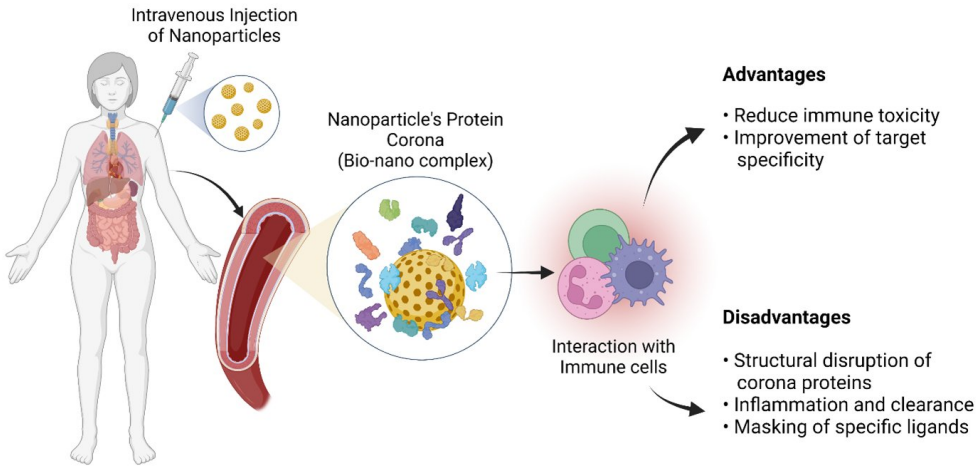
Nanomedicine has become an attractive field of research. According to PubMed, the number of published scientific articles on “nanomedicine” was slightly over 700 by the year 2007, but in the last 15 years that number has reached nearly 40,000 (www.pubmed.org). Despite this rise in popularity, nanosized agents have historically been used in medicine and in particular they have long been applied for the modulation of the immune response (Duschl, 2016). For example, colloidal gold is used to treat the autoimmune condition rheumatoid arthritis (Dreaden et al., 2012) and preparations of aluminum hydroxide (alum) are used as vaccine adjuvants (Powell et al., 2015).

Nanomedicine and the Immune Defenses

Nanomedicines are in the range of 1 to 100 nanometers (nm) and in this small size lay their advantages. In the context of the immune system, nanoparticles (NPs) overlap in size with most viruses (10-200 nm)(Lipscomb & Masten, 2002) and are therefore within the immune cell’s target size range. Toxic NPs, as well as polymeric NPs with repetitive patterns, are expected to be identified as nonself by the immune system and activate different pathways of the immune response. Research has exploited this immune activating characteristic of nanoparticles and some NP formulations have already reached the market: several vaccines, one immunosuppressant, and two drugs for autoimmune conditions (Duschl, 2016). Most of the approved nanopharmaceuticals are designed for cancer treatment. Cancer can be treated as a immunological disease. That is, the modulation of certain immune functions can aid the recovery of cancer patients such as the inhibition of immune cells that maintain tumor tolerance (Dauer et al., 2005) or the activation of immunity against the tumor (cancer vaccines).

The Nanoparticle's Biomolecular Corona

A general consideration for pharmaceutical treatments is the question of how the agent is seen by the body. In the case of NPs, this issue is especially complex. When NPs are inserted in a liquid medium that contains biological substances – such as the blood – a layer of this substances binds the nanoparticles (Duschl, 2016). This layer is commonly known as corona and is usually dominated by proteins, but can also contain other compounds (lipids, amino acids, nucleic acids,…)(Monopoli et al., 2012). The characteristics of the particular NP surface, as well as the availability of proteins, defines the specific proteins that form the corona. This biological shell changes the properties of the NPs and may have direct effects on immunity – for example, through the association and activation of immune proteins. Therefore, once the NP formulation has entered the body we are actually dealing with a bio-nano complex, whose composition and behavior is not easy to predict. In some cases the protein corona can be beneficial by reducing potential toxicity. Mainly due to the fact that immune cells will interact with the self-proteins of the corona and will not detect the NPs as nonself (Duschl, 2016). However, often the protein corona triggers inflammation and the eventual clearance of NPs from the organism. As the NPs are expelled from the body, they can no longer exert their therapeutic function.



Nanomedicine and DIRNANO Project

In DIRNANO we believe it is important to understand the mechanisms and consequences of the NP's corona formation. Thus, some of our research efforts are focused on the identification of the corona proteins and the study of the protein-NPs interface. We are expecting this knowledge will allow us to fine-tune the interactions between NPs and immune system, which in turn will aid in the development and commercialization of novel nanopharmaceuticals.

The DIRNANO members are working hard on their respective projects.

Collaborations and mobility between the different host organizations are now blooming. Upcoming events that will benefit from the participation/organization of DIRNANO ESRs are included in a list below.

For regular information on the Network's activities visit our Linkedin page!

- *1 st International Supramolecular Chemistry Summer School*
  Cagliari, Sardinia (Italy)
- *School of Nanomedicine* Rome, 8 th -10 th June 2022
- *DIRNANO Ambassadors.* Our ESRs in Padua (Italy) will prepare a workshop for high school students. This divulgation activity is aimed at increasing the public's knowledge on nanomedicne and maybe light the spark of curiosity for science in the future generations.
  Padova, 23rd and 30th June 2022.

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