NANODEVICES FOR THE SPECIFIC DELIVERY OF BIOLOGICALLY ACTIVE MOLECULES: UP-TO DATE CHALLENGES AND PERSPECTIVES

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Polymer-based nanotechnologies were developed and are now proposed as an alternative to classical formulations for drug administration, delivery and targeting. A better fundamental knowledge of the in vivo interaction of nanoparticles with biological fluids has led, in the past, to the tailoring of systems efficient, after intravenous administration, in targeting the macrophages of the reticuloendothelial system (the Kupffer cells of the liver or the macrophages of the spleen and of the bone marrow). This specific tissue and cells distribution is explainable by the opsonization processes which occur at the surface of these carriers. Therapeutic applications of these systems include the treatment of cancer liver diseases. On the contrary, avoiding the recognition by the liver and the spleen is also possible by developing long circulating polymeric colloidal carriers ("stealth" systems) able to avoid the opsonization process and the recognition by the macrophages. The design of such carriers is based on the physico-chemical concept of the “steric repulsion”: by grafting polyethyleneglycol chains at the surface of nanoparticles, the adsorption of seric proteins may be dramatically reduced due to steric hindrance. Such an approach allows maintaining the drug carrier for a longer time into the circulation and the resulting extravasation towards non reticuloendothelial-located cancers may become possible. Now, new applications and exciting perspectives are proposed for the delivery of drugs to previously non accessible diseased sanctuaries, like the brain (treatment of glioma and autoimmune diseases of the brain) or the ocular tissues (treatment of the autoimmune uveitis). In these specific diseases, the production of cytokines makes the vascular endothelium dramatically permeable to certain types of nanoparticles, which open options for new medicines. It is not questionable if new research programs are needed to better understand the role of cytokines on the endothelium permeability as well as the influence of the molecular coverage of the nanoparticles on their extravasation ability. From those researches, more rationale strategies for the targeting of inflamed tissues should emerge.

Crucial is also the need to find intelligent nanomedicines to overcome resistances to chemotherapies both in the field of cancer diseases and viral infections (AIDS). In this view, it is out of question that the regulation of the cellular drug influx/efflux as well as the control of the intracellular drug trafficking is a key point of the success.

New generation of polymer based nanotechnologies allow also the efficient targeting of cells expressing certain receptors, markers and/or antigenic determinants. As an illustration of this approach, folate decorated nanoparticles were found to recognize in a highly specific manner cancer cells with hyper expression of the folic acid binding protein.

During these last decades and as discussed above, all the efforts done have concentrated to design efficient nanotechnologies for the targeting of chemical entities towards the diseased areas; the 21st century could turn into the development of nanotechnologies for the targeted delivery of physical treatments (ie.of tumors). This approach will need to perform original chemistry with metallic-core based nanoparticles but also to improve our knowledge on the interaction of electromagnetic waves with living tissues.

This lecture is an overview of what could be the research on nanotechnologies in the near future. The message is that to be efficient, it should have a strong Pharmaceutical flavour at the frontier of the Physics, the Chemistry and the Biology.