Abstract Title

Design and Development of Nano-Vectors for Biomedical Applications

Symposium Track

Authors' names

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Abstract body

Many effective anticancer drugs have been developed with spectacular in vitro performance on a variety of cancer cell lines. However, a drug dose systemically administered generally does not reclaim the same promise that it fulfills in vitro. It is well accepted that only between 1 and 10 parts per 100,000 of intravenously administered therapeutic molecules reach their parenchymal targets in vivo, and similar limitations have been observed in the transport and diffusion of medical imaging agents, such as radiolabeled antibodies and paramagnetic tracers. This is mostly related to the variety of biological and biophysical barriers, along the circulatory system, that prevent the systemically administered molecules from reaching their biological target in the desired mass fractions. Nanoscale Devices, as Nano-Vectors (NVs), offer the potential to avoid these limitations because of their multifunctional capabilities and engineerability. A nanovector for drug delivery or medical imaging comprises a central "cargo" where the therapeutic and/or contrast agents (pay-loads) are localized; and a surface coating which is functionalized so that polymeric spacers, antibodies or ligands can be grafted (Fig.1). As free drug molecules or contrast agents, NVs are injected intravascularly and to execute their diagnostic or therapeutic missions have to make their way into the circulatory system and eventually bind to the biological target. Two different strategies are currently under investigation [Ferrari, 2005]: (i) passive targeting of the tumor microenvironment through the endothelial fenestrations; (ii) active targeting of the endothelial cells lining the tumor microvasculature. Case (ii), however, is the strategy holding the largest opportunities and promises for the development of optimal drug delivery and imaging systems. In this case the NVs have to firmly adhere to the endothelial cells lining the vessels of the tumor microvasculature and from there release their therapeutic load to the surrounding tumor tissue without crossing the capillary walls.

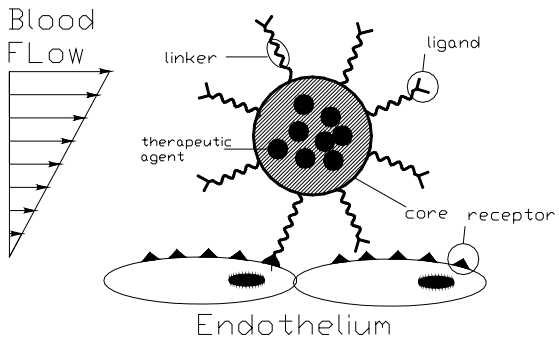

Fig.1: A NanoVector interacting with an endothelial substrate

The strength of the NV/target cell adhesion is of fundamental importance in this case. Such an adhesion is mediated by non-covalent bonds forming among ligand molecules on the NV surface and counter molecules (receptors) at the cell surface [Decuzzi et al., 2004], and by non-specific interactions at the NV/cell interface [Decuzzi et al., 2005].
In this work the effect of the size of spherical particles on the strength of adhesion under flow will be addressed both theoretically and experimentally. An extended DLVO theory will be employed to describe the non-specific adhesive interaction, whereas a stochastic based approach will be used for describing the ligand-receptor specific interaction. By doing so, the critical conditions for adhesion will be estimated in terms of (i) the maximum dislodging hemodynamic force above which no adhesion could be likely; (ii) the minimum number of ligands grafted over the NV below which no adhesion could be likely; and (iii) the maximum size of the NV above which no adhesion could be likely. The theoretical predictions will be qualitatively and quantitatively compared with the results of adhesion experiments in a flow chamber system. The results stemming from this analysis will guide the fabrication of NVs with superior and controlled adhesive properties.

Keywords

Drug Delivery; Imaging; NanoParticles;

References

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