C Advanced Delivery of Therapeutics:
New Challenges for Materials

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Symposium C

Advanced Delivery of Therapeutics: New Challenges for Materials

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Scope of Symposium

This symposium will highlight current challenges and new concepts in the delivery of therapeutics including small molecular drugs, peptides, proteins, nucleic acids and cells, and mainly focus on cancer therapy. Topics will address biological barriers for delivery of therapeutics, and novel materials that are designed and developed to overcome these barriers. In addition, strategies for combinatorial drug delivery will be discussed to combat multidrug-resistant problems.

Symposium Topics

- Nano-structured materials including polymers and organic/inorganic hybrids
- Novel materials based on synthetic peptides, nucleic acids and polymer constructions
- Novel delivery approaches for therapeutic drugs, peptides, proteins and genes
- Delivery of cell-based therapies and immunotherapy
- Nanotoxicology

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A00808-01415

Cell-Surface Interactions: Examining the Biological-Physical Interface

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Cell-based research is a booming sector in life science. Stem cell therapy and tissue engineering are upcoming techniques in modern medicine and will soon bring therapeutic benefits for a broad range of diseases. The recent progress at the beginning era of Nanomedicine include specific targeting of cells with drug-loaded particles, and therefore the cell and its interaction with extrinsic material is right in the focus of interest. Although there is constantly increasing knowledge of how living cells behave in their natural environment and chemically correspond with their surroundings, little is known about the mechanical-physical interplay of a cell and a solid surface.

Such artificial substrates, serving as a growth support for cells ex vivo, are required for most cell cultural standard applications and can nowadays accurately be modified down to the nanometer range for optimum conditions. By modulating the interaction of cell and surface, a highly valuable tool for various other medical applications can be obtained, and a considerable amount of effort has been put in this issue in the recent years. However, most of the strategies currently available concern chemical modifications of the material used, and only few research groups have examined the physical-topological influence of surface features.

There is clear evidence that the topologic and viscoelastic properties of the contacting material affect a cells behavior as much as the chemical environment, and that the response to these physical parameters can be an important trigger regarding lifespan and disease. Nanopatterned surfaces distinctively regulate cell growth, and matrix elasticity corresponding to the in vivo conditions directs stem cell differentiation to a specialized tissue. Cells are able to adapt the uptake of particles depending on their mechanical properties, and the development of "stealth particles" that are not recognized by the immune system can enhance the bioavailability of problematic drugs.

All this requires further studies of the physical-biological interface, and the mechanics that allow a cell to "feel" its surroundings. This will provide a challenging task to biophysical research in the future, and a close network of nanotechnologists, physicists and biologists will be needed to succeed.

The first results of an interdisciplinary collaboration in this context are presented here, covering the characterization of living cells and their substrates by atomic force microscopy and other techniques, applied to biocompatible nanoparticles and cell-culture models that are in use for preclinical medical research.

A00887-01555

Synthesis of Functionalized Dendrons for Surface Modifications of Biodegradable Nanoparticles

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The surface modifications of biodegradable nanoparticles targeting restenosis following vascular intervention have been extensively studied for sustained delivery of therapeutic agents. These modifications aim to provide and enhance efficient delivery of therapeutics, to maintain therapeutic effect in target vascular site, and to improve the stability of therapeutic agents against factors leading to early degradation. The synthesis of functionalized dendrons bearing multiple active terminal end groups and a single reactive function at the focal point as a method of nanoparticle modification is the primary focus of this article. Multiple active amine terminals on the dendrons allow the attachment of PEG (polyethylene glycol) shielding ligands, which would be evaluated for their targeting and attachment efficiency respectively. Dendron 3,4-bis(4-aminocyclohexyl)-2,5-dicyclohexylcyclopentanone was successfully synthesized bearing active amine terminal end groups. Experimental results were characterized via NMR (nuclear magnetic resonance) spectroscopy, MALDI-TOF (matrix-assisted laser desorption/ ionization – time of flight) spectrometry, and FTIR (fourier transform infrared) spectroscopy. The potential utility derived from the coupling of dendrons and antibodies to nanoparticles could be explored as an effective drug delivery system to achieve localized and sustained restenosis prevention therapy.

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