NOVEL MATERIALS FOR NANOSIZED DRUG DELIVERY SYSTEMS

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Ideally, nanosized drug-loaded pharmaceutical carrier should: (a) accumulate in required organ or tissue, and (b) penetrate inside target cells delivering there its load. Organ or tissue (tumor, infarct) accumulation could be achieved by the passive targeting via the enhanced permeability and retention effect or by the specific ligand(antibody)-mediated active targeting, while the intracellular delivery could be mediated by certain internalizable ligands or by cell-penetrating peptides. To be able to behave this way, drug carrier should simultaneously carry on its surface various moieties capable of functioning in a certain orchestrated order.

Within the frame of this concept, multifunctional stimuli-responsive materials for nanocarriers are developed, i.e. nanocarriers are prepared that, depending on the particular requirements, can circulate long; target the site of the disease via non-specific and/or specific mechanisms; respond local stimuli characteristic of the pathological site by, for example, releasing an entrapped drug or deleting a protective coating facilitating thus the contact between drug-loaded nanocarriers and target cells; and even provide an enhanced intracellular delivery of an entrapped drug with its subsequent delivery to specific intracellular organelles. Such carriers can be additionally supplemented with reporter moieties to follow their real-time biodistribution and target accumulation. Among new developments to be considered are: drug- or/and RNA-loaded delivery systems additionally decorated with cell-penetrating peptides for the enhanced intracellular delivery; “smart” multifunctional drug delivery systems, which can reveal/expose temporarily hidden functions under the action of certain local stimuli characteristic for the pathological zone (such as lowered pH, redox-conditions, hypoxia, or locally increased expression of certain enzymes); new means for controlled delivery and release of siRNA; approaches for intracellular drug delivery and organelle targeting; and application of nanocarriers co-loaded with siRNA and drugs to treat multidrug resistant tumors.