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Nanomedicines: A new way for Drug Delivery

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Even if new molecules are discovered to treat severe diseases like cancers, the clinical use and efficacy of conventional chemotherapeutics is hampered by the following limitations: (i) drug resistance at the tissue level due to physiological barriers (non-cellular based mechanisms), (ii) drug resistance at the cellular level (cellular mechanisms), and (iii) non-specific distribution, biotransformation and rapid clearance of the drugs in the body. Advanced nanodevices may overcome some of these limitations.

This will be illustrated by several nanomedicine platforms developed in the laboratory:

- The design of biodegradable doxorubicin-loaded polyalkylcyanoacrylate nanoparticles for the treatment of the multidrug resistant hepatocarcinoma (a nanomedicine with phase III clinical trials ended) [1].
- The construction of nanoparticles made of metal oxide frameworks (NanoMOFs) [2,10], a highly hyperporous material obtained by the complexation of iron oxide clusters with diacids. The nanopores of this material may be designed according to the molecular dimension of the drug molecule to be encapsulated.
- The “squalenoylation” [3,4], a technology that takes advantage of the squalene's dynamically folded molecular conformation, to link this natural and biocompatible lipid with anticancer drug molecules [5, 11] to achieve the spontaneous formation of nanoassemblies (100–300 nm) in water, without the aid of surfactants. Surprisingly, these squalene-based nanoparticles are using the circulating LDL as “indirect” carriers for targeting cancer cells with high expression of LDL receptors [6]. The application of the “squalenoylation” concept for the treatment of brain ischemia and spinal cord injury will be discussed too [4]. And very recently,we discovered that the linkage of squalene to leu-enkephalin (a neuropeptide) (i) prevented rapid plasma degradation of the peptide, (ii) allowed to target the peptide into the body painful area, (iii) conferred to the targeted neuropeptide a significant anti-hyperalgesic effect, (iv) without the morphine side effects (ie. Addiction, tolerance and resiratory depression) [12]. The possibility to use other terpenes (natural or synthetic) than squalene to design nanoparticles for the treatment of cancer will be discussed, too [9].

The design of “multidrug” nanoparticles combining in the same nanodevice chemotherapy and imaging (ie., “nanotheranostics”) or various drugs with complementary biological targets was also examined [7]. Finally, it will be shown that the construction of nanodevices sensitive to endogenous (ie. pH, ionic strenght, enzymes etc.) or exogenous (ie., magnetic or electric field, light, ultrasounds etc.) stimuli may allow the spatio-temporal controlled delivery of drugs and overcome resistance to current treatments [8].

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