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Funtionalized Lipid and Polymer Nanoparticles for BioMedical Application and Cancer Radiotherapy: Synthesis, SANS and DLS

Modular targeting materials bearing a specific ligand head can supply a cell or tumor receptor recognition to radiotherapy enhancers, hydrophobic drugs (BCS classes 2, 4) or mRNA, entrapped in nanoscaled drug carriers, e.g. liposomes, micelles and polymer particles. This drug / co-drug complex concept requires the synthesis of special modular targeting materials.
We synthesized targeting modifiers of oral drug nano-intermediates and parenteral drug loaded nanoparticles which consist of four structure domains (fig.1) with lipid or hydrophobic polymer anchors (Fig.1, left). The components are varied and optimized in a case specific manner. The nanoparticles, e.g. intestinal lipid-bile nanoparticles, biodegradable polymer (PLGA), lipid particles as well as the anchor domain are hydrophobic, while iron oxide can be included for bio-medical manipulation. With proteins as ligands, e.g. transferrin or albumin, the surface bound protein is transformed to an artificial membrane protein. The linker binds the ligand in two steps: adsorption and a fast covalent bond formation as terminal step. The hydrophilic spacer is essential for keeping the distance from the nanoparticles surface.
The nanoparticle anchor groups were amino-lipids (DMPE, Stearylamine), Cholesterol, and PLA derivatives with amino or carboxy headgroups. A thiol-linker was attached as S-S-dimer through diamino- and peptide spacers with DCCD catalysis. The synthesis strategy avoided expensive protective groups by two-side block synthesis, with late coupling of the halfes. Finally the S-S-dimer was cleaved before activation of the thiol-group for protein coupling by a sulfur bridge.
The structure of modified nanoparticles bearing 2% activated anchor was analyzed by dynamic light scattering DLS, neutron small angle scattering SANS with D2O-contrast variation and metal specific X-ray scattering ASAXS. The biomedical effect of the drug is proven in cell culture tests. The multi-targeting modification is applied to lanthanide loaded polymer nanoparticles (PLGA, patent of the Gutenberg-University) for indirect radiation therapy IRT and liposomes as fast development system.

Primary authors: Mrs KREBS, Lidija (Gutenberg University, Pharmaceutical Technology); Mr WILHELMY, Christoph (Gutenberg University, Pharmaceutical Technology); Prof. LANGGUTH, Peter (Gutenberg University); Prof. SCHMIDBERGER, Heinz (Gutenberg University Clinics, Radiooncology); Dr SÄNGER, Markus (Gutenberg University Clinics, Radiooncology); Dr JOHNSON, Raphael (KNUST University); MATSARSKAIA, Olga; SCHWEINS, Ralf; Dr NAWROTH, Thomas (Gutenberg University Mainz)

Presenter: Dr NAWROTH, Thomas (Gutenberg University Mainz)