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Pharmaceutical development of injectable nanomedicine targeting breast cancer

Anti-cancer theranosis (therapy and diagnosis) using nanomedicine is a promising perspective, related to a possibility to combine several diagnostic and therapeutic functions in order to potentiate them. Superparamagnetic iron oxides (SPIONs) are often used as nanomedicine platforms due to the possibility to stimulate their intratumoral staining and drug delivery with help of a magnetic field as well as to contrast tumors on Magnetic Resonance Imaging (MRI). In order to inject SPIONs intravenously, their biocompatibility and efficiency has to be improved by surface coating with neutral biocompatible polymers like Polethylene Glycol (PEG) functionalized with molecular cancer targeting ligands like peptides and antibody fragments. We are developing PEGylated and bio-functionnalized injectable nanovectors based on PEGylated SPIONs. Their polymeric shell is covalently coupled with membranotropic cell-penetrating peptides gH625 and/or with scFv fragments of antibody trastuzumab which binds specifically to membranes of HER2 positive breast cancers. The nanosystems can thus act as vectors of chemotherapeutic drugs of anticancer-active siRNA. The pharmaceutical development strategy we apply includes not only a rational design of the nanosystems but also step-by-step optimization of their structure in order to reach the better biocompatibility/bioactivity. For each nanoform, tens of independent batches were generated and their physico-chemical characteristics (size and zeta potential, chemical composition and structure) were established. Prior to *in vivo* essay on breast cancer xenografts in mice, the nanoforms interaction with cancer cells has been studied *in vitro*, on various cancer cell lines, overexpressing or not cancer-specific receptors. Comparison of biological behavior of the ligand free vs. ligand carrying PEGylated nanovectors allowed us to demonstrate that the moderate presence of ligands was not able to affect the nanomedicine forms size and zeta potential. Nevertheless, the bio-ligands enhanced the nanomedicine-cell interactions, both quantitatively (intracellular accumulation) and qualitatively (internalization, subcellular distribution and cargo delivery/transfection).

Biography

Igor Chourpa is Director of Analytical Chemistry Department at the Faculty of Pharmacy of the University François Rabelais of Tours, France, and Head of the research group "Nanomedicine & Nanoprobes" EA6295. This group develops nanomedicines for anticancer theranosis, i.e. diagnosis by medical imaging and therapy by delivery of chemotherapy or siRNA. His particular expertise domain is optical microspectroscopy (Raman, surface-enhanced Raman and fluorescence) and spectral imaging. He has authored 62 publications in peer-reviewed journals. He is member of Editorial Boards of *J. Anal. Meth. Chem.* (Hindawi) and Int. *J. of Nanopart. Nanotechnol.* (Helics).

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