amino acid side chain or in between two amino acids. Cellular uptake of the new bioconjugates was investigated with different methods like fluorescence microscopy, atom absorption spectroscopy or flow cytometry. High accumulation could be observed in different tumour cells. Furthermore, cell viability assays showed that those organometallic peptide conjugates are very potent and possess promising cytotoxic properties.

See references below for additional reading
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A48
Polyelectrolite complex based microspheres for colon specific anticancer drug delivery

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Localized delivery of chemotherapeutic agents has long been the aim of clinical colon cancer therapy in order to limit the indiscriminate activity of many anti-cancer drugs on rapidly dividing cells, including normal tissues. The ideal drug delivery system (DDS) is envisioned to selectively and efficiently transport the anticancer drug to the target cells. It will not only minimize side effects associated with inappropriate drug distribution, but will also enhance therapeutic efficacy by increasing local drug concentration. The goal of our study was to develop wheat-germ aglutinin (WGA) functionalized chitosan-Ca-alginate microspheres (MS) loaded with acid-resistant nanoparticles (NP) of 5-FU, as colon targeting DDS and evaluate its *in vitro* efficacy and *in vivo* biodistribution. The rationale behind the design of the formulation is the presence of high level of polysaccharides of microbial origin in the human colon and the possibility of direct binding of MS to the mucosal surface by nonspecific or specific ligand–receptor interactions using biological molecules (WGA), thus enabling active uptake of 5-FU in the target cancer cells. A simple one-step spray drying procedure was used to produce polyanion/polycation MS loaded with acid-resistant NP of 5-FU with mean diameter of ~14.74 μm, high production yield (~50%) and encapsulation efficiency (~72%). Using 1,1′-Carbonyl-diimidazol as a surface group activation agent, successful conjugation of WGA to MS surface was achieved (~50%). Haemagglutination test confirmed that WGA, treated by covalent coupling procedure, still retained its specific carbohydrate binding activity on the surface of MS. *In vitro* efficiacy was evaluated by investigating 5-FU permeability and [methyl-3H]thimidine uptake in Caco-2 cells. The cumulative amount of transported 5-FU through Caco-2 cells was 15.1% and 6.5% for 5-FU solution and WGA conjugated MS, respectively. Cell culture studies also indicated a marked decrease in [methyl-3H]thimidine uptake for WGA decorated MS compared to 5-FU solution, suggesting that immobilization of WGA onto MS surface, due to the improved interaction and enhanced tissue accumulation of 5-FU could led to improved efficacy in targeted anticancer colon therapy. *In vivo* biodistribution studies were conducted with oral administration of ^{99m}Tc labeled MS on fasted male Wistar rats. The imaging was performed at different time intervals post administration. The results showed that MS traversed fairly quickly through upper part of GI tract and resided in the colon for relatively longer period of time, probably due to the particle size, pH dependent swelling and surface properties of the MS. Overall, the results of this work showed that cross-linked polycation/polyanion MS loaded with 5-FU and decorated with WGA, were able to effectively deliver 5-FU to colon region, thus affecting the transport of 5-FU into the cells and consequently improving the efficacy.

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Engineering macrophages to synthesize recombinant adenoviruses in hypoxic areas of human prostate tumours

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Background: Like many other forms of human malignancy, prostate carcinomas contain multiple regions of transient and chronic hypoxia. New therapies targeting the hypoxic areas of tumours need to be designed as these sites are highly resistant to conventional cancer therapies. We have recently shown that macrophages accumulate in these hypoxic areas of prostate tumours, so we investigated the possibility of using these cells to deliver therapeutic genes to these otherwise inaccessible sites. *Materials and methods*: We designed a novel system in which macrophages are used to deliver hypoxia-regulated therapeutic adenovirus. In this approach, macrophages are co-transduced with a hypoxically activated E1A/B plasmid and an a hypoxia-regulated E1A/B construct and an E1A-dependent oncolytic adenovirus, whose proliferation is restricted to prostate tumor cells using prostate-specific promoter elements from the TARP, PSA and PMSA genes. *Results*: When co-cultured with prostate tumour spheroids, these 'armed' macrophages migrated into the hypoxic centres of the 3D tumour masses where E1A/B protein expression was upregulated, resulting in replication of the latent E1A/B-deficient adenovirus. Multiple copies of the virus (~5000/macrophage) were released and infected neighbouring prostate tumour cells, resulting in widespread gene expression. Systemic administration of co-transduced macrophages into mice bearing human prostate xenografts resulted in their subsequent trafficking into the hypoxic areas of tumours leading to viral replication and widespread infection of neighboring tumour cells, resulting in the marked inhibition of tumor growth and reduction of pulmonary metastases. *Conclusions*: We show for the first time that macrophages can be engineered to express high titres of a therapeutic adenovirus