specifically in hypoxic areas of human prostate tumours and that expression of the gene being delivered in the adenovirus can be restricted to prostate tumour cells by placing it under the control of a prostate-specific promoter (PSA). This novel approach employs three distinct levels of tumour-specific targeting; the homing of the macrophages to tumours, the synthesis and release of therapeutic adenovirus only in hypoxia tumour areas, and the targeting of therapeutic gene expression to prostate tumour cells.

doi:10.1016/j.drudis.2010.09.398

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Targeted nanodrug delivery systems for the treatment of tuberculosis

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South Africa currently has the highest incidence of TB in the world at 358 per 100,000 people. In 2007 alone 112,000 people died of TB in South Africa, of which 94,000 (72%) were co-infected with HIV [1]. Although TB treatments exist, poor patient compliance and drug resistance pose a great challenge to programs worldwide. To improve the current inadequate therapeutic management of TB, a polymeric anti-TB nanodrug delivery system, for anti-TB drugs, was developed that could enable entry, targeting, sustained release for longer periods and uptake of the antibiotics in the cells, hence reducing the dose frequency and simultaneously improve patient compliance. The aim was to prepare functionalised polymeric nanodrug delivery vehicles to target TB infected macrophage cells. Successful nanoencapsulation of anti-TB drugs and a targeting agent, mycolic acids (MA) was achieved. MA (a lipid molecule on the cell wall of M.tb) was explored due to its cholesteroid properties [2] that could attract it to the infected macrophages/foam cells. The nanoparticles were characterized and subjected to *in vitro* analyses in THP-1 and U937 cells in order to determine their uptake and localization. Cytotoxicity in different cell lines was also analysed. In another approach targeting was achieved via attaching nucleic acid aptamers [3], onto the surface of drug-carrying PLGA nano-particles. The aptamers were prepared via the SELEX process [4], specifically against the mannose receptor (MR), which is significantly over-expressed during the activation of the macrophages in the presence of M.tb. Uptake of the MA PLGA nanoparticles was achieved where little co localization was observed with endocytic markers, indicating that they could be localized in the cytosol. Vesicles bearing these particles were also observed in the cell membrane of these cells. We will report the uptake of the aptamers to THP-1 cells illustrating the feasibility of using the nucleic acid species for active targeted drug delivery. The success of these two approaches of anti-TB drug targeting will greatly address the challenges of poor bioavailability, reduced efficacy and adverse side effects for diseases such as TB.

See references below for additional reading

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doi:10.1016/j.drudis.2010.09.399

A52
Targeted SAINT-O-Somes, a novel type of liposomes for improved delivery of siRNA

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Gene silencing by siRNA has become a powerful technique with a great potential for therapeutic application. Increased insight in the role of endothelial cells in the pathology of cancer and inflammatory diseases has shifted the interest in the development of siRNA drug delivery devices for pharmacological intervention towards these cells. Additionally, endothelial cells are readily accessible for substances transported by the blood and their heterogeneity allows for specific drug targeting approaches. Liposomes represent a drug-carrier system for the delivery of siRNA that can be tailored on demand to introduce cell specificity. However, unlike in macrophages or in many tumor cells, in endothelial cells the processing of liposomes and subsequent release of drug content is inefficient due to the absence of adequate intracellular processing machinery which limits pharmacological efficiency. Therefore, we developed a lipid based drug delivery system with a superior intracellular release characteristic which is suitable for the *in vivo* delivery of siRNA. The design of the carrier is based on long circulating conventional liposomes that were formulated with a cationic amphiphile, 1-methyl-4-(cis-9-dioleyl)methyl-pyridinium-chloride (SAINT-18). These so-called SAINT-O-Somes have a diameter of 100 nm and showed a 10-fold higher encapsulation efficiency for siRNA compared to liposomes without SAINT and protect the siRNA from degradation for at least 6 weeks. Moreover, SAINT-O-Somes are fully stable in a biological relevant milieu (i.e. presence of serum), but are destabilized in the lower pH in endosomes of endothelial cells, enabling release of siRNA into the cytoplasm of the cell. In order to efficiently target activated endothelial cells, SAINT-O-Somes were equipped with antibodies against E-selectin or VCAM-1 adhesion molecules that are (over)expressed at sites of inflammation.