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Multifunctional locked nucleic acid modified chimeric survivin targeted nano-bullets against cancer stem cells

Theranostics, the combination of diagnostics and therapies is a new concept in cancer management. Our published work strongly suggests that orally administered multifunctional targeted "nano-bullets" (nanocarriers; NCs) with iron saturated bovine lactoferrin (Fe-bLf) were able to kill tumours. Here for the first time, we are developed multifunctional-targeted nanocapsules conjugated with stably modified aptamers to target and kill cancer as well as cancer stem cells. These nanocapsules labeled with biosensors, will deliver anti-cancer molecules to colon tumours and help to monitor the therapy in real-time imaging. A cell permeable dominant negative mutant form of survivin (dNSurR9C84A), dNSurR9C84A has shown promising anticancer properties by inhibition of survivin and reduces the chance of side effects since survivin is not expressed in normal cells in an adult. However due to short half-life of dNSurR9C84A a drug delivery system based on low molecular weight chitosan was used which could prolong the bioavailability of dNSurR9C84A. These chitosan nanoparticles were well characterized before examining effects on colon cancer cells (Caco-2). The nanoparticle transport studies were carried out both in vitro and ex vivo in order to understand the mechanism of low molecular weight chitosan nanoparticles with intestinal cells. The in vivo Biodistribution studies showed a highly selective and specific patter of uptake of the targeted nanocarriers or "nanobullets" (CHNP-dNSurR9C84A-LNA-Nu+Ep) in the tumour. The targeted nanocarriers were also able to significantly inhibit the tumour volume up to a period of 95 days. These nanobullets showed specific internalization in cancer stem cells and led to cancer stem cells specific apoptosis, thus proved to be appropriate for oral administration in colon cancer.

Biography

Associate Professor Jagat R Kanwar is the Head of Nanomedicine-Laboratory of Immunology and Molecular Biomedical Research (LIMBR). Dr. Jagat R Kanwar has received his Master's degree in Medical Biochemistry and PhD in Molecular Immunology from PGIMER, Chandigarh, India in 1992. He has an international reputation and expertise in investigating fundamental and applied molecular signaling aspects of pathogenesis of cancer, chronic inflammation and neurodegenerative diseases, thereby, leading to the development of treatment strategies from bench to bedside. He has more than 100 publications in high impact factor and peer reviewed international journals, 27 book chapters and 3 edited books. Assoc Prof Kanwar's research has generated several patents/PCTs with more than five licensed patents for commercialization to BioPharma industry. His group is currently working on drug discovery and nanomedicine for oral and systemic drug delivery of a range of biomacromolecules (proteins/peptides, siRNAs and aptamers) for targeting survivin, HIF-1α and other apoptotic and inflammatory cell signaling molecules in cancer, chronic inflammation and neurodegenerative disorders.

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