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Nanoformulated nanocarriers with modified lactoferrin for cancer and bio-distribution through MRI

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Background: At nano scale, the fundamental and vital properties of matter can be changed, which can be used for daunting task such as oral administration of bio-macromolecules to be able to achieve sustained delivery, controlled release, target specific delivery and combinatorial therapy.

Objectives: Main objective of the study was to develop, characterize and see the bio-distribution of iron saturated lactoferrin protein loaded novel ceramic nanocarriers to deliver orally and monitor these tumours MRI imaging in xenograft colon cancer.

Methods and Results: In our study, we demonstrate the formulation of a novel alginate enclosed, chitosan coated ceramic anti cancer nano carriers (ACSC NC). These NC were loaded with multi-functional anti cancer bovine lactoferrin (bLf), a natural milk based protein, for improvement of intestinal absorption, in order to develop a novel platform to carry anti cancer protein and/or peptides for oral therapy. Size, morphology, internalization and release profiles of the ACSC NC under varying pH were determined. Furthermore, uptake of these NC *in vitro* in colon cancer cell lines was analyzed, by measuring the endocytosis and transcytosis. NCs were characterised through various physical and biological assays. Transcytosis studies indicate the transcytosis of the NC, with minimal damage to the Caco-2 cell monolayer. In conclusion, these NC can be used for future targeted protein/peptide or nucleic acid based drug delivery to treat fiddly diseases such as cancer and neurodegenerative disorders. Lf+ loaded ACSC NC significantly reduced tumour vascularity and blood flow, and increased anti-tumour cytotoxicity, tumour apoptosis and the infiltration of tumours by leukocytes. Lf+ increased the average weight of the spleens of tumourbearing mice by ~20%, accompanied by a major increase in the numbers of particular leukocyte subsets in the spleen. CD4+, CD8+, NK, IFN-γ+-expressing and dendritic cell numbers in the spleen were significantly ($P<0.001$) increased compared to corresponding cell numbers for mice maintained on the control diet. Lf+ bound to the intestinal epithelium and was preferentially taken up within Peyer's patches. It increased the production of Th1 and Th2 cytokines within the intestine and tumour, including TNF, IFN-γ, as well as nitric oxide that have been reported to sensitize tumours to doxorubicin chemotherapy. Importantly, it restored both red and white peripheral blood cell numbers depleted by doxorubicin chemotherapy, potentially fortifying the mice against cancer. In summary, bLf is a potent natural adjuvant and fortifying agent for augmenting cancer chemotherapy, but needs to be saturated with iron and administered orally in Lf+ loaded ACSC NC to be effective. Bio-distribution of iron saturated lactoferrin was determined my MRI and confirmed by other imaging techniques. We also compared our results with the doxorubicin and taxol loaded ACNC-NPs.

Conclusion: Taken together, our results are highly encouraging for the development of combination nano-therapeutic strategies that combine gene silencing and drug delivery to provide more potent and targeted therapeutic, especially in late and metastatic breast cancer.

Biography

Dr Kanwar is an immunologist and molecular biochemist with an international reputation in investigating fundamental and applied molecular aspects of cancer and chronic inflammation. He did his PhD from Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India. Before joining Deakin University in 2006, he was a Senior Scientist/Senior Research Fellow in the University of Auckland, Auckland, New Zealand. During the past decade his research both academic and commercial has centered on understanding the pathophysiological mechanisms and/or finding treatments for a variety of chronic inflammatory diseases and different types of cancer. Dr Kanwar has published 55 research articles, 12 invited reviews and 5 book chapters, in highly ranked, international, peer-reviewed journals. These publications have added to the body of knowledge in the fields of immunology, cancer gene therapy, nanomedicine, cell biology and biotechnology, and have extended these disciplines. He is a key inventor on 9 international patents and has provided consultancy to 5 Biotechnology based companies. He is a member of editorial board for 7 international journals and a nominated member of more than 12 national and international societies including American Society of Nanomedicine. He has extensive and close collaborations with colleagues from New Zealand, Australia, Singapore, India, China and USA.