Nano-theranostics for real-time imaging and on-chip microfluidic assays: Promises of precision nanomedicine

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Oral administration of bio-macromolecules is an uphill task, and the challenges presented in the gut milieu, from varying pH and enzymatic activity, are difficult to overcome. In this regard, nanotechnology promises new hope and offers advantages such as controlled release, target-specific delivery, combinatorial therapy with lower doses, and abolished toxicities. We found that survivin, a member of the family of inhibitors of apoptosis proteins is overexpressed in several human tumours. Lactoferrin is also known to over-express in inflammatory diseases such as inflammatory bowel and Crohn's. **Aim:** This study aims to develop polymeric-ceramic nanocarriers in order to achieve oral delivery of the anti-cancer nano-nutraceutical protein iron saturated bovine lactoferrin (Fe-bLf) and dominant negative mutant of survivin (SurR9-C84A). We assessed the differential expression of survivin, other apoptotic biomarkers and lactoferrin in stool and serum samples of colorectal cancer (CRC) patients. We compared serum and stool samples from CRC patients and samples from healthy volunteers using an in vitro enzyme-linked immunosorbent assay to evaluate the survivin and lactoferrin response in patients. Three different detection systems were compared and Microfluidics-Device Based system was found to be most sensitive and specific for diagnosis. Our findings also suggest that the reduction in the serum survivin and copro-lactoferrin levels of advanced CRC patients after chemotherapy can be used as a predictor of response to the chemotherapy. In conclusion a positive association between survivin and lactoferrin concentrations in sera and stool samples of patients with CRCs was established. Our results suggest that analysis of both parameters would assist in screening patients with CRC. In addition, we developed dominant negative mutant of survivin (SurR9-C84A) and loaded into Alginate enclosed chitosan- calcium phosphate nano carriers (ACSC-NCs), in order to improve the oral bioavailability and to protect the peptide from the harsh environment in the gastrointestinal tract. These CSC-NCs loaded with SurR9-C84A were tested in a xenograft mice model of human colon cancer. We found that all tumor-bearing mice regressed tumors significantly. Anti-tumour activity was mediated by inducing apoptosis and necrosis in tumours. Thus, these CSC-NCs can be exploited for oral administration to protect from variable pH in the intestinal tract and resistance to gastric enzymes, which otherwise digest proteins in the gastrointestinal tract. These NCs can thus be used for future targeted protein/peptide or nucleic acid-based drug delivery to treat complex diseases, including cancer. Fe-bLf-loaded NCs were found to help in the absorption of iron. They thus may have the utility of enhancing iron uptake during iron deficiency without interfering with the absorption of calcium. **Conclusion:** With the promising results of our study, the future potentials of the NCs loaded Fe-bLf and dominant negative mutant of survivin (SurR9-C84A) in chemoprevention, and the treatment of human colon cancer deserve further investigations for translational research and preclinical studies of other malignancies.