Cancer Theranostics with Nano-enabled Bacterial Bots

Abstract

The contemporary cancer therapeutics are being strategically designed to obtain improved outcomes as compared to the conventional methods. The primary challenges faced by the conventional mode of therapies such as surgeries, radiation therapies, and later chemotherapy are difficulty in tumor accessibility, undesirable impact on normal cells, ineffectiveness towards cancer stem cells, missing the targets, rapid drug release prior to reaching the targets, poor pharmacokinetics of drugs, and resistance development to the therapy. In order to focus on the improvements, target specificity through small molecules, aptamers, antibodies, nucleic acid, stimuli sensitive polymers have been developed. Coating of the drug with polymers and loading the drugs on nano-carriers for enhanced bioavailability, slower release and safety from immune attacks have also been introduced. Developing methods for immunotherapy are also being practiced. Gradually the newer methods such as gene therapy, immunotherapy, and combined therapies have overtaken the conventional methods. Although these methods have shown improved results in comparison to the previous methods but the threat imposed by the cancer stem cells and drug resistance are still continuing. The advent of bacteria-mediated therapy has shown some light towards a path of developing a resistance – free cancer therapy. Since, the anaerobic bacteria preferably colonize in the hypoxic areas of the tumor and act on the core of the tumor, hence, there is a better opportunity for the bacteria to eradicate the stem cells and prevent relapse of cancer. The attenuated strains achieved through genetic engineering and over-expression of endotoxins and therapeutic genes have generated hopes for a better future of cancer therapeutics. The commonly used strains are *Salmonella, Bifidobacterium, Clostridium, E. coli* and Lactic acid bacteria (LAB). The bacteria-based therapy can have two usages, first as a therapeutic entity and second as a delivery vehicle. The anti-cancer effects of the bacteria can be inherent or can be inculcated through genetic modifications of endotoxin gene, pro-drug activating enzymes, siRNA, shRNA based silencing, and immune system evoking via over-expression of cytokines specifically activating T-cells and macrophages. The anti-biotic susceptibility, suitability for genetic manipulation, and low immunogenicity are required criteria for bacteria to be a therapeutic agent. The risk factor associated with the bacteria-mediated therapy is controlling the growth and number of bacteria after the therapeutic regimen is over. A few studies have been reported on these aspects and a lot more is yet to be explored. In order to avoid the adversities of using a pathogenic strain, the shift can be made towards opting for safer strains that do not require genetic manipulation and have inherent anticancer effects. The safest option is to use human gut friendly bacteria. The gut bacteria play a pivotal role in drug actions, resistance and overall health of an individual. The gut microbes, which have inherent anti-cancer properties are *Streptococcus pyrogenes, Mycobacterium bovis*, *Serratia marcescens*, *Lactobacillus plantarum*, *Lactobacillus rhamnosus* GG*, Lactobacillus acidophilus, Salmonella, Clostritidium, Bifidobacterium and E. coli*. Out of this vast range of bacterial strains the, *Lactobacillus* are among the safest strains as they are non-pathogenic. This could solve the safety issues of using attenuated pathogenic strains. The *Lactobacillus* strains are anti-tumorigenic naturally and are antibiotic susceptible, making them suitable as an anti-cancer agent and also as a carrier. The current dissertation work was up-taken to explore the potential of wild type *Lactobacillus rhamnosus* as a living bacbot that could function as a theranostic agent having anti-cancer effects mediated by an anti-cancer drug methotrexate and their inherent abilities in annihilating cancer tumours.