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Mini Review

Nanobiosensors for the Detection of Cell Free micro-RNA in Carcinogenesis – A Mini Review

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Abstract

MicroRNAs (miRNAs) are small non-coding RNAs with small number of nucleotides and control gene expression primarily at post-transcriptional and transcriptional phases [1]. The target gene expression is regulated by these miRNAs by degrading or inhibiting translation of the respective messenger RNA. The primary functions of miRNAs include regulating immune system, differentiation and development, cell proliferation, cancer and cell cycle by as hitherto unknown mechanism. MiRNAs have significant contribution to malignancy by releasing tumour suppressors and oncogenes. Different miRNA profiles are responsible for various types of tumours, hence, could serve as phenotype signature for different cancers. This unique identification can be used in cancer diagnostics, prognostics and therapeutics. Hence, discovery of new miRNAs will pave novel path in understanding the cancer genetics. However, smaller size, low concentration, sequence homology and stability are some of the major challenges involved in classification and specific recognition of miRNAs. To overcome these problems, synthesis of a nano-biosensor might assist in detection of differentially regulated miRNAs with high sensitivity, specificity and cost-effective manner. A major complication for integrating nanoformulation into clinical application is the additional toxicity. This can be circumvented by using non-toxic shells along with surface modification which can also increases the ability of NPs to detect circulating cell free miRNAs in a non-invasive manner. This ultra-short review provides comprehensive information on nanoformulations suitable for detecting these miRNAs and their biogenesis, effects in disease and treatment condition especially in cancer.

Introduction

In cancer cells, miRNAs were heavily deregulated. MiRNA regulating lin-14 protein expression was discovered in Caenorhabditis elegans by Ambros et al. [2] and let-7 (developmental timing) [2,3] are few examples. There are several cascades of regulatory genes that are leading to controlling the expression pathways by deregulated miRNAs. At present there are about 1872 human miRNA precursor genes that are processed into approximately 2578 mature miRNA sequences that have been documented (http://www.mirbase.org). Many studies have reported the presence of free flowing (extracellular) miRNAs in plasma, serum, saliva, breast milk and cerebrospinal fluid [4-6], urine, tears, seminal fluid [7], and ovarian follicular fluid [8]. In contrast to cellular RNA, these free flowing miRNAs are highly stable, will not degrade at room temperature even for 80 hours and boiling or freezing and high or low pH conditions [9,10].

Need of Nanoparticles in miRNA Detection

Laboratory based sensing by utilizing novel microRNA biosensors for disease diagnosis has shown to have great promise. There are numerous studies which have been reported on the use of nanomaterials in sensor development [11] including for the detection of microRNA sequences [12]. Among these nanotechnology approaches have presented to overcome some limitations of conventional microRNA detection and quantification strategies such as qPCR, northern blotting, in situ hybridization microarray, next generation sequencing, isothermal exponential amplification [13]. These approaches have well known limitations such as poor reproducibility, cross-hybridization, low selectivity, poor sensitivity, time-consuming procedures, the requirement of large quantity of sample, expensive infrastructure equipments, or specific skills to apply the procedures. Micro RNAs were found to be up/down regulated in various disease conditions [14], specific miRNAs are known to be found in the blood stream as a result of in cancerous tumour present in different organ such as colorectal, breast, ovarian, and prostate cancers [1,15-19]. RNA interference (RNAi) technology or RNA technology facilitated therapeutic approach for various deadly diseases like cancer [20]. In this technology, the gene expression is regulated using a short 21–23 nucleotide double stranded RNA sequence. RNA nanoparticles harbouring EGFR aptamer when injected in animal model induced with breast cancer shown to effectively target tumour cells through receptor mediated endocytosis [21]. The anti-miRNA-21 after entering the tumour cell, binds to the target region and blocks the tumorigenic properties of the miRNA-21 [22] and thus inhibit tumour growth [23].

RNA nanotechnology is versatile and can be used to construct 2D, 3D, and 4D structures for use in biosensing. Its applications are not limiting to pharmaceutical development but also to controlled release of functional agents by using their thermodynamic properties. RNA structure and chemistry negative charge disallows nonspecific cell entry and thus minimizes toxicity. Furthermore, it can harbor multiple functionalities while retaining their accurate folding. Applying RNA Aptamers for targeted therapeutic drug delivery or as potent inhibitors, immunotherapy and chemotherapeutic drug delivery proved to have greater clinical solution [24].

Future Perspective and Conclusion

Considering the advantage of these nanomaterials, multi-target enabled nanosensor devices which can sense quickly with high sensitivity can be developed with reduced costs. Diagnosing cancer onset and metastasis and to monitor the treatment response from blood derived factors can help the clinicians to prognosticate the disease conditions. Early stage cancer detection and more specific outcome is the need of this current scenario. Nanomaterials revolutionize the goals of cancer therapy and diagnosis overcoming the limitations and side-effects caused by chemotherapy. It also helps shaping the future development of treatments. Nanotechnology based molecular diagnostic and therapeutic methods are progressing rapidly in the recent times, it will further grow into a vital opportunity for cancer diagnosis and treatment in future. The major challenges to be met in nanoformulation are controlling batch wise variability and hence preventing the hampered reproducibility and stability in biological fluids and also, the small molecule drug loading capacity.

In conclusion, the increasing range of study dedicated to the understanding of nanotechnology based devises is having a remarkable power in the progress of nanosensors for the prompt diagnosis of malignancy and for the therapeutic dose monitoring. Thus, nano technology has the prospective to contribute confidently to retard, resist and remedy cancer.

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