

Multifunctional Nanotherapeutics: “The Engines of Healing”

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The occurrence of cancer is well parameterized in a more systemic fashion due to abalative derailing of numerous cell signalling paradigms ultimately triggering explosive chaotization in cellular growth patterns [1,2]. The ingenious complexity in a bunch of intricate cancer signalling mechanisms along with prominent tumour survival mechanisms including anti apoptotic proteins (survivin, livin, hypoxia, heat shock proteins etc), oncogenic signalling, tumour suppressor mechanisms have imposed a major cessation for the therapeutic success of current chemo and radiological treatment regimes thereby promoting drug resistant cancers [3-7]. To address these concerns, nanotechnological based strategies had recently conquered therapeutic ground. Nanoscale entities tagged with functional tumour specific molecules such as receptor-mediated tumour ligands, aptamers, locked nucleic acid conjugates (LNA), RNA interference technology, microRNA, siRNA, peptidomimetics, antibodies, combinationatorial therapeutic formulations, drug encapsulation and imaging probes are deemed to be relatively smaller than the cancer cell itself and hence, targeted drug delivery with enhanced selectivity, therapeutic synergism can be achieved [8-10]. The dramatic outreach of multifunctional nanotherapeutic approaches have been exploited in the area of cancer diagnostics by utilisation of economically viable nanomicrofluidic lab on chip devices promoting personalised cancer nanomedicine and in the area of therapeutic imaging by utilisation of state of art imaging technologies including fluorescent imaging strategies, magnetic resonance imaging (MRI), positron emission tomography (PET), single photon emission computed tomography (SPECT), photodynamic laser therapy (PDT) [11]. The major concerns arising due to prominent side effects associated with conventional therapeutics had forced the scientific community to explore natural product derived therapeutics including medicinal herbs, curcumin, lactoferrin, neem etc for the anticancer ability [5]. Surprisingly, these natural therapeutic entities revealed their promising capability in bursting out the nodal cancer signalling mechanisms causing remarkable inhibition in cancer progression [12].

Multifunctional nanodrug delivery systems were fabricated with natural product derived therapeutics. Polymer based formulations with drug encapsulated in alginate coated nanocarriers (ACNC) and alginate gel encapsulated chitosan ceramic nanocore nanocarriers caused enhanced mitochondrial tumour apoptosis leading to survivin down regulation [1]. Another set of completely variable natural product based super paramagnetic iron oxide nanoparticle (SPIONS) nanotherapeutic formulations were devised in a combinatorial strategy coupling with tumour targeting entities including epithelial cell adhesion molecule (EPCAM), aptamer variants in combination with locked nucleic acid conjugates including LNA - nucleolin aptamer, LNA – EPCAM aptamer [10]. These multifunctional nanotherapeutics exhibited predominant anticancer activity both *in vitro* and *in vivo* [8,10]. Furthermore, advanced near infrared fluorescence *in vivo* imaging studies were conducted to delineate effective localisation patterns and anti tumour activity of drug coupled SPIONS [1]. Studies

to extrapolate the theranostic abilities of nano drug delivery system utilising MRI, SPECT, PDT and SPECT imaging modalities are under progression [1].

In conclusion, multifunctional nanotherapeutic approaches can offer lucrative advantages in the realms of cancer diagnosis, targeted therapy and advanced therapeutic imaging capabilities [2,13]. However, there is an inherent necessity to further channelize the developments in the era of nanomedicine along with unison of upcoming technologies including computational biology, systems biological engineering approach in order to reap maximum benefits from so called nanotherapeutics - “the engines of healing” as phrased and speculated by Erix Drexel in his notable work “the engines of creation” [2,14].

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Received October 04, 2012; Accepted October 10, 2012; Published October 12, 2012

Citation: Kanwar JR (2012) Multifunctional Nanotherapeutics: “The Engines of Healing”. *J Cancer Sci Ther* 4: xxiii-xxiv. doi:10.4172/1948-5956.1000e115

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