NuBCP-9 for Cancer Therapy: A Nanotechnological Approach

Sumeet Kapoor\textsuperscript{1,*}, Swati Ojha\textsuperscript{2}, Aji Alex\textsuperscript{3}, and Amit K. Gupta\textsuperscript{4}

\textsuperscript{1,3}Centre for Biomedical Engineering, Indian Institute of Technology Delhi, India
\textsuperscript{2}Department of Biochemical Engineering and Biotechnology, Indian Institute of Technology Delhi, India
\textsuperscript{4}Department of Mechanical Engineering, Indian Institute of Technology Delhi, India

Editorial

Chemotherapeutics are antineoplastic agents that are widely used for number of malignancies but they cause toxicity and development of multidrug resistance [1]. Therapeutics peptides (TP’s) represent a new wave of anticancer agents which have shown promising results [2]. They inhibit or mimic protein–protein interactions in a specific manner that may lead to induction of apoptosis or cell death. Although TP’s are biocompatible and target specific but they suffer from drawbacks of degradation by serum proteases and generation immune response. Modification of amino acid skeleton like addition of unnatural D-amino acids in peptide sequence [3] or glycosylation can protect TP’s from degradation by proteases but systemic circulation is difficult to attain [4].

NuBCP-9 is a small therapeutic peptide (short amino acid consisting of nine amino acids) that selectively kills cancer cells [5]. The mechanistic pathway of NuBCP-9 is shown in figure 1. Binding of NuBCP-9 to BH4 domain of BCL-2 protein in the outer mitochondrial membrane protein induces conformation change in such a way that it become apoptotic from its anti-apoptotic function that evenly leads to apoptosis by induction of caspases [6]. However, NuBCP-9 alone undergoes proteolytic cleavage and evoke immune response thus cannot enter the target cell.

In some reports delivery of NuBCP-9 conjugated to cell penetrating peptides (CPP) [7] and super paramagnetic iron oxide nanoparticles (SPIONs) have been reported [8]. Merck KGaA, Darmstadt, Germany is supplying CPP conjugated NuBCP-9 for various research studies. However, CPP causes membrane blebbing and necrosis in the target cells and SPIONs are still under clinical trials for various cancer therapy applications.

Myriad number of nanocarriers prepared from biodegradable polymers like polylactic acid, polycaprolactone, polyglycolic acid and polyhydroxybutyrate has been successfully employed for delivery of number of anticancer agents [9]. These polymers are approved by FDA as they produce nontoxic metabolites in the body after metabolism.

Nanotechnological approach for delivery of NuBCP-9 using polylactic acid [10] and polyhydroxybutyrate [9] were reported and confirmed the superiority of this approach over other previously opted approaches. The approach precludes all drawbacks faced by CPP and SPIONs.

Monaj et al. have reported 74% tumor regression with NuBCP-9 peptide conjugated superoxide iron oxide nanoparticles whereas a complete regression was observed with NuBCP-9 peptide encapsulated polylactic acid copolymeric nanoformulations in BALB/c mice bearing Ehrlich syngeneic tumors. NuBCP-9 encapsulated polyhydroxybutyrate based nanoformulation showed 90% tumor regression under in vivo conditions [9].

Figure 1: Mode of action of NuBCP-9 peptide.
NuBCP-9 has great potential as anticancer agents and polymeric nanocarriers can increase their scope to a level where they can completely replace existing chemotherapeutic agent and drugs.

Conflict of Interest

Authors declared that they have no conflict of interest.

References


*Corresponding author: Sumeet Kapoor, Centre for Biomedical Engineering, Indian Institute of Technology Delhi, India; E-mail: s.kapooriitd@gmail.com

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