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Breast cancer-targeted delivery of BRCA1 and BRCA2 tumor suppressor genes using carbonate apatite inorganic nanoparticles

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Breast cancer is the second leading cause of cancer death among women all over the world which entails loss of function mutation in certain important tumor suppressor genes like BRCA1 and BRCA2. Among sporadic breast tumors, 50-70% has lost an allele of BRCA1 and 30-50% has lost an allele of BRCA2. By implying the idea of gene therapy this research explores administration of tumor suppressor gene BRCA1 and BRCA2 in the form of plasmids using inorganic nanoparticle (NP) of carbonate apatite (CaAp) as carrier vector. Unlike viral or non-viral (liposome, organic polymer) vectors, inorganic nanoparticle of carbonate apatite mediated plasmid gene delivery has enhanced efficiency and biocompatibility with limited side effects. Cytotoxicity study carried out in human MCF-7 breast cancer cell line showed that compared to untreated cells, treatment of MCF-7 cells with the NP bound pDNA/BRCA1 and NP bound pDNA/BRCA2 could reduce cell viability to 78% and 87%, respectively. Also, in 4T1 cell line delivery of pDNA/BRCA1 and pDNA/BRCA2 in presence of carbonate apatite carrier showed reduction in cellular viability by 85% and 84%, respectively. Effects of BRCA1 and BRCA2 plasmid gene delivery on the expression of MAPK signaling pathway proteins were observed in both of the cell lines treated through Western blotting. CaAp nanoparticles with electrostatically associated BRCA1 and BRCA2 plasmid genes were also intravenously delivered to breast tumor in a syngeneic mouse model. Results obtained from the tumor regression study showed 46% and 44% tumor inhibition rate in mice treated with BRCA1 and BRCA2 plasmid genes compared to untreated group of mice.

Biography

Nabilah Ibnat has completed her Masters from University of Dhaka, Bangladesh and presently she is pursuing her Doctorate from School of Medicine and Health Sciences, Monash University, Malaysia. She has been working as a Research Officer at International Centre for Diarrheal Disease Research, Bangladesh for more than five years. She has also published one review paper as a first author and 6 research papers as a co-author.

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