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Regime of gene silencing: Efficient siRNA delivery into cancer cells using nanocapsules

Archana Raichur
IIT-Delhi, India

RNA interference and the therapeutic applications using small interfering RNA was discovered more than 10 years ago and currently is used in various applications including cancer theragnostic. However, the research in this field is still in its infancy. Many challenges like safe delivery of targeted siRNA to nucleus and cytosol of cancerous cells without compromising the activity of siRNA needs to be addressed. We have overcome this hurdle with the help of nanotechnology using PLGA hollow NPs (PLGAHNPs) and suppressing the oncogene of MYC transcription factors by using anti myc-siRNAs in human cancer cell lines. siRNA was encapsulated in PLGAHNPs. PLGAHNPs of size 70 nm had high efficiency of gene release at pH 4.2 under in vitro conditions. Cell penetrating peptide (CPP)- Tat peptide (TAT) and peptide nucleic acid nucleolus localizing signal (PNA-NLS) was used for siRNA delivery without interrupting the therapeutic activity of siRNA. Incubation of the siRNA encapsulated PLGAHNPs functionalized with TAT and PNA-NLS (TAT-siRNA-PNA-PLGAHNPs-siRNA) with cancer cells resulted in reduced cell proliferation. A downregulation of gene expression by 90% was observed even with low concentration of siRNA. We found complete arrest of cell division which was mediated by downregulation of MYC expression. Further we used the combination of gold nanoparticles with PNANLS and siRNA encapsulated in PLGAHNPs around the mean size diameter of 100nm. The encapsulation efficiency of siRNA with AuNPs is increased by 20% when compared to siRNA alone in PLGAHNPs. The gene expression of MYC in cancer cells was down regulated by 92%.

e: araichur5@gmail.com