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Mechanistic insights related to *myc* downregulation and *myc* signaling pathway by hollow PLGA NPs in cancer cells

Archana Raichur Joshi
Indian Institute of Technology, India

RNAi (RNA interference) therapeutics is a powerful gene therapy technique for suppressing specific genes in the cells and cellular pathways. It has great potential in biomedical applications including in the treatment of genetic disorders, cancer, viral infections and autoimmune diseases. Many challenges like safe delivery of targeted siRNA to nucleus and cytosol of cancerous cells without compromising the activity of siRNA need to be addressed. One of the novel ways to overcome the barriers is using non-viral, that is gene delivery using nano-composites. Polymer nanoparticles (NPs) are widely used and studied for drug and gene delivery. One of the advantages of using biocompatible polymer NPs is that, compared to non-biocompatible NPs, they tend to accumulate at a faster rate inside the cancer cells. This rapid accumulation is favorable for site-targeted drug and gene delivery. In our study, we synthesized a nanocomposite by encapsulating sequence-specific siRNA and pRNA into PLGA Hollow NPs (HNPs, monodispersed and of uniform diameter of 70nm-yet to report). Further, these Hollow NPs were loaded with sequence-specific PNA and were used to target *myc*- mRNA and the nucleus of IMR-32 and T84 cancer cell lines, *in vitro*. To the best of my knowledge, this is the first time anybody has successfully produced hollow PLGA NPs. It is observed that after six hours of incubation, a majority (approximately 85%) of the cells start to peel off the substratum and float in the media. The remainder continues to adhere to the substratum and changes morphology. The cells floating in the media are found to undergo apoptosis within a day. When the cells adhered to the substratum are incubated further overnight, they show dendritic outgrowth and gastrular formation. It is also observed that genes *KM20* and *Zyxin* express in these cells. Interestingly, the extent of gene expression is nearly equal to that in normal cells, suggesting that the TOR signaling pathway, which is observed in normal cells, is also activated in the incubated cells.

Biography

Archana Raichur Joshi with PhD in BioNano and Biomedical Engineering. She is an International MEXT scholar, Japan. She did her doctoral course at age of 28 years and currently working as Research Scientist at Indian Institute of Technology, Kanpur in Mechanical Engineering Department, India. Earlier she worked as Vice President in Educational Trust, Biomedical Engineering Department, Orchids International Techno Services. Recently she is focusing on gene delivery nanotherapeutics and protein sorting mechanisms in cancer cells.

araichur5@gmail.com

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