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Study of mTOR gene expression in plasma based microRNA-7 / Chitosan Complexes in Hepatocellular carcinoma cell lines

Melek Evirgen
Department of Pharmaceutical Biotechnology, Turkey

MikroRNAs are small, endogenous and non-coding RNA molecules which regulate gene expression. Recent studies show that deregulation of miRNAs have been associated with different diseases including cancer. Therefore, miRNAs are important therapeutic target in cancer. However, major obstacles of usage miRNAs in therapy are stability, rapid clearance and internalization. For this reason, it is important in terms of therapy with appropriate carrier system to the cells. Aim of this study is to investigate efficacy (invasion, apoptosis and cell proliferation) and usability in hepatocellular carcinoma (HCC) cancer cell lines (Hep3B and HepG2) of polyplexes forms of chitosan and miR-7 mimic. miR-7 mimic and chitosan complex was prepared. In vitro characterisation of these complex was done. With these dosage have used to investigate mTOR protein levels by using ELISA assays and invasion, apoptosis and cell proliferation assays have done. Our studies show that chitosan/miR-7 complex was internalized stably to cancer cells, thus deregulated miRNA levels repaired. Invasiveness of cancer cells was reduced. Chitosan complexes were shown to be safe and efficient delivery system for miRNA.

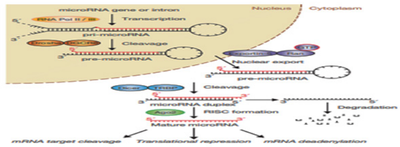

Figure 1 The 'linear' canonical pathway of microRNA processing. The miRNA processing pathway has long been viewed as linear and universal to all mammalian miRNAs. This canonical maturation includes the production of the primary miRNA transcript (pri-miRNA) by RNA polymerase II or III and cleavage of the pri-miRNA by the microprocessor complex Drosha–DGCR8 (Pasha) in the nucleus. The resulting precursor hairpin, the pre-miRNA, is exported from the nucleus by Exportin-5–Ran-GTP. In the cytoplasm, the RNase Dicer in complex with the double-stranded RNA-binding protein TRBP cleaves the pre-miRNA hairpin to its mature length. The functional strand of the mature miRNA is loaded together with Argonaute (Ago2) proteins into the RNA-induced silencing complex (RISC), where it guides RISC to silence target mRNAs through mRNA cleavage, translational repression or deadenylation, whereas the passenger strand (black) is degraded. In this review we discuss the many branches, crossroads and detours in miRNA processing that lead to the conclusion that many different ways exist to generate a mature miRNA.

melekevirgen@gmail.com