Gelatin and Hyaluronic Acid Nanoparticle Based Delivery of miR-34a for Treatment of Pancreatic Cancer

Pancreatic cancer is poorly responsive to available chemotherapy. miR-34a has been suggested as a potential therapy for pancreatic cancer, however it needs to be specifically targeted to the intracellular environment of pancreatic cancer cells before it can be explored for use in the clinic. Without an effective delivery system, miR-34a will degrade inside the human body. In this study, two types of nanoparticles, hyaluronic acid-polyethyleneimine (HA-PEI) combined with hyaluronic acid-polyethylene glycol (HA-PEG) and gelatin nanoparticles, were evaluated as means of delivering miR-34a plasmid into a pancreatic carcinoma cell line. HA-PEI/PEG and gelatin nanoparticles containing a plasmid encoding miR-34a or scrambled null vector were synthesized. The miR-34a- and null plasmid DNA-complexed gelatin nanovectors were 125+/-19 and 134+/-27 nm in diameter, respectively; the encapsulation percentage of the miR-34a plasmid in gelatin nanoparticles was 84%. HA-PEI/PEG- and gelatin-encapsulated miR-34a plasmid and control nanoparticles were added to a Panc-1 cell line with results assessed after 24, 48, 72, and 96hours. Plasmid-encoded gene transcription in Panc-1 cells was confirmed by confocal microscopy by demonstrating GFP production with both HA-PEI/PEG- and gelatin-encapsulated miR-34a plasmid. Quantitative reverse transcriptase PCR targeting Notch1, CASP3, BCL2, BIRC5, APAF1, and BAX revealed decreased expression, compared to the control, of the antiapoptotic genes Notch1 and BCL2 at 48, 72, and 96hours with HA-PEI/PEG- and at 72hours with gelatin-encapsulated miR-34a plasmid. Hyaluronic acid-based and gelatin nanoparticles are promising delivery strategies for miR-34a-based therapy of pancreatic cancer, and generally for delivering systemic microRNAs to cancer cells.

Awards Won:

Fourth Award of $500