Therapeutic intervention using autologous exosomes for treatment of early-stage pancreatic cancer

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Background: Pancreatic cancer (PanCa) is the third deadliest cancer in United States with a poor survival rate. Despite extensive research efforts, there is not any substantial progress in cancer therapeutics; major challenges lie with inherent drug toxicity, ineffectiveness, and resistance due to impediments against intracellular drug delivery. From a therapeutic delivery standpoint, novel delivery vehicles are required that are both biocompatible and non-immunogenic for a patient in order to maximize the chances of cure. This is possible by utilizing an autologous biological material, which can be applied as a personalized medicine to match the individual circumstances and molecular profile of the patient. One such approach has been optimized in our lab, which utilizes exosomes from the matched tumor adjacent normal (NAT) area following surgical resection. Using exosomes as a scaffold, our objective is to deliver therapeutics safely and effectively to the patient tumor site.

Results: NAT derived exosomes showed effective size and zeta potential (size: 44.12 ± 0.89; Zeta potential: -14.9 mV), which is ideal for drug delivery purposes. The purification of exosomes was confirmed using proteins isolated from exosomes through Western blotting for expression of exosomal markers, such as CD63 expression. Immunofluorescence for CD63 expression confirmed the efficient delivery of exosomes in PanCa cells. Our results indicated high drug loading capacity of NAT derived exosomes as demonstrated using drug, Ormeloxifene (ORM) though UPLC. Exo-ORM treatment efficiently delivered ORM into the cancer cells and inhibited the cancer cell characteristics, such as, proliferation compared with ORM alone. Additionally, NAT derived exosomes showed enhanced expression of tumor suppressor microRNA, miR-145, suggestive of their therapeutic importance. We observed restoration of lost miR-145 levels in PanCa cells on incubation with NAT derived exosomes for 48hrs. This further indicates their relevance for their utilization in the development of an anti-cancer therapy.

Conclusion: Our observations offer importance of the utilization of NAT derived exosomes for personalized medicine as a therapeutic delivery vehicle in PanCa.