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A novel therapeutic approach for metastatic Breast Cancer: Glucose deprivation of tumor cells

Abstract:

Background: Metastatic breast cancer remains a critical challenge due to the tumor cells' metabolic adaptability and resistance to current therapies. We propose a novel therapeutic strategy focused on depriving tumor cells of glucose while selectively delivering nutrients to normal cells.

Methods: The approach involves depleting glycogen stores in normal tissues via a crash diet and prolonged fasting, followed by the administration of Total Parenteral Nutrition (TPN) supplemented with essential ingredients encapsulated in liposomes for 30 days. These liposomes are designed to selectively target normal cells by leveraging their unique metabolic environment.

Results: The liposomes are coated with a pH-sensitive copolymer, Polyethylene glycol-Poly-L-histidine (PEG-PLH), designed to bind with glucose transporters (GLUTs) on all cells to release the nutrient material. The Poly-L-histidine (PLH) component is engineered to undergo conformational changes in the acidic microenvironment of tumor cells, which prevents the copolymer from binding to the GLUTs on tumor cells while maintaining its functional structure in a normal tissue environment. This selectivity is further enhanced by using superhydrophobic fluorinated compounds conjugated with trastuzumab, which specifically binds to HER2+ tumor cells. The superhydrophobic structure creates a repulsive surface in response to the hydrophilic PEG coating on the liposomes, effectively deterring the liposomes from accumulating in metastatic sites. Additionally, zwitterionic modifications of the liposome surfaces in the low-pH microenvironment of tumor cells create a hydration layer around the liposomes. This prevents their passage through the capillary walls and accumulation in tumor tissues. Consequently, this strategy facilitates the targeted delivery of nutrients to healthy tissues.

Conclusion: These three strategies effectively reduce glucose availability to tumor cells while maintaining normal cellular metabolism in normal tissues. The reviewed scientific evidence suggests that this method has the potential to improve therapeutic outcomes and decrease the likelihood of metastasis in HER2+ breast cancer especially in combination with the conventional methods. Further in vitro and in vivo studies, followed by clinical trials, are essential to validate this approach and explore its applicability to other solid tumors.

Biography

Kamran Shirbache has dedicated his medical career to pioneering research in cancer treatment, consistently seeking innovative approaches to eradicate the disease. His current model is the culmination of years of studying various metabolic strategies and developing targeted drug delivery systems to effectively treat cancer.