Engineering Bifidobacterium infantis–Melittin–Nanoparticle Biohybrids for Targeted Deep Tumor Penetration, Enhanced Payload Localization, and Potent Spheroid Disruption in a 3D Cancer Model

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Breast cancer, the most common cancer in US women, accounts for approximately 32% of new diagnoses annually. Approximately 42,170 women will die from breast cancer in 2025. Current treatments are limited in their ability to deliver potent therapeutics deep into tumors without harming healthy tissue. This project aims to explore the efficacy of engineering biohybrid carriers that combine melittin-loaded nanoparticles with Bifidobacterium infantis to enhance targeted delivery and improve the therapeutic impact of MCF-7 spheroids. Spheroids were grown on a low-attachment plate. Melittin was dissolved at concentrations ranging from 50µg/ml to 1500µg/ml. Melittin-loaded BSA nanoparticles were conjugated using desolvation. Particles were coated with chitosan, allowing them to bind to Bifidobacterium infantis when incubated. Results of the ANOVA indicated significant differences among treatment groups ($p=7.4 \times 10^{-37}$). A Post-hoc Tukey HSD analysis indicated that the biohybrid treatments at 50, 100, 500, 750, 1000, and 1500 µg/m significantly reduced cell viability compared with the controls. Biohybrids outperform free melittin and nonparticle-only formulations, likely due to enhanced tumor penetration and localized melittin release. Fluorescent imaging reveals core collapse and structural disintegration consistent with melittin's pore-forming mechanism. Dose-dependent cytotoxicity of biohybrid treatments at 50,100, 500, 750, 1000, and 1500 µg/ml showed the most significant results. Findings support bacteria-mediated delivery as a promising strategy to overcome diffusion barriers in solid tumor models. Melittin penetrates deeply into spheroids and induces rapid structural collapse and cell death as a membrane-disruptive peptide.

Awards Won: