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MetroHealth Medical Center

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Abstract Submission Form

Poster Title: **A Novel Solid Lipid Nanoparticles (SLN) platform for Targeted Silencing of WAVE3 and Enhanced Sensitization of Triple-Negative Breast Cancer Tumors to Chemotherapy**

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Location of Laboratory: **Rammelkamp building R455**

Category: **Cancer Biology**

Chemoresistance is a significant challenge in breast cancer treatment, particularly in triple-negative breast cancer (TNBC), which comprises six genetically distinct subtypes. The mesenchymal (M) and mesenchymal stem-like (MS-L) TNBC subtypes exhibit reduced response rates to conventional chemotherapies, often linked to the activation of metastatic processes driven by WAVE3, that our group has established as a major driver of this process.

Our published studies have identified WAVE3 is a pivotal contributor to the invasion-metastasis cascade of TNBC tumors through the regulation of several hallmarks of cancer, including the cancer stem cell phenotype that tightly linked to the resistance to standard-of-care therapies. This study explores the use potential utility of a novel nanoparticle platform to target WAVE3, in order to enhance chemosensitivity, and therefore mitigate TNBC metastasis.

We have developed three Solid Lipid Nanoparticle (SLN) formulations: non-pegylated, pegylated, and RGD peptide-modified SLNs, which we are assessing for direct targeting of WAVE3, through the precise delivery anti-WAVE3 siRNAs.

SLNs, synthesized meticulously, exhibit diameters of 20-100 nm. Characterization confirms composition, while in vitro studies demonstrate SLN safety and reduced cytotoxicity. Controlled release experiments suggest potential for optimizing siRNA loading and SLN surface modifications for effective WAVE3 gene silencing.

Our ongoing studies are investigating the effect of SLN loaded with anti-WAVE3 siRNAs on the expression levels of WAVE3 in several TNBC cell lines, and its subsequent effect of the oncogenic behavior of these cancer cells, both in vitro and in vivo mouse models for TNBC tumor progression and metastasis.

This research underscores SLNs' versatility as a promising gene delivery system. Ongoing experiments will yield valuable insights into WAVE3 silencing via SLNs and its impact on TNBC treatment, advancing innovative strategies to combat chemoresistance and metastasis in TNBC.