

# A Novel Nanoparticle-microRNA Treatment to Overcome Drug Resistance and Tumor Metastasis in Lung Cancer

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The development of drug resistance and tumor metastasis in cancer cells severely limits chemotherapy effectiveness. This study used a novel approach of combining gene therapy with nanotechnology-based delivery mechanism to overcome tumor metastasis and combat drug resistance to cisplatin (chemotherapeutic) in an in vitro lung cancer model. The study isolated four anti-apoptotic genes (Survivin, c-Myc, Bcl-2, KRAS) correlated with drug resistance, and two cell migration genes (PAK1, DIAPH2) correlated with tumor metastasis. A bioinformatics program identified let-7a as the optimal microRNA effective at silencing the target genes. The research created a core-shell nanoparticle system composed of hyaluronic acid modified with polyethylene glycol, and conjugated with polyethylenimine, to encapsulate let-7a microRNA. The study analyzed the cellular uptake and gene knockdown efficiency of the nanoparticle-microRNA treatment. The nanoparticles successfully targeted the CD44 receptor, delivered let-7a miRNA into cisplatin-resistant cells, and efficiently downregulated expression of drug resistance and tumor metastasis genes by over 200%. An MTT assay demonstrated that the nanoparticle-microRNA treatment lowered the IC50 value of cisplatin by 41% indicating its ability to overcome drug resistance in lung cancer cells in conjugation with cisplatin. An isobologram and a combination index value of less than 0.1 established strong synergy between cisplatin and nanoparticle-microRNA treatment. The treatment also inhibited cell migration in both drug sensitive and drug resistant cells by over 60% indicating an anti-tumor metastasis mechanism. Therefore, the nanoparticle-microRNA system has potential to be a viable therapeutic solution to prevent drug resistance and tumor metastasis.

## Awards Won:

Patent and Trademark Office Society: First Award of \$3,000