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

Jain, Anirudh

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