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Opinion Article

Novel Gold Nanoparticle-Based Platform for Enhanced Targeted Drug Delivery in Triple-Negative Breast Cancer

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DESCRIPTION

Triple-Negative Breast Cancer (TNBC) remains one of the most challenging subtypes to treat due to the absence of targetable receptors and its aggressive nature. Conventional chemotherapeutic approaches often result in significant systemic toxicity while delivering suboptimal concentrations to tumor sites. Our research group has developed a novel Gold Nanoparticle (AuNP) platform functionalized with tumor-homing peptides that demonstrates remarkable specificity for TNBC microenvironments. The AuNPs, measuring approximately 50 nm in diameter, were synthesized using a modified citrate reduction method and subsequently conjugated with both doxorubicin and a targeting peptide identified through phage display screening. This dual-functional approach enables both active targeting and therapeutic payload delivery in a single nanostructure.

Triple-Negative Breast Cancer (TNBC) is an aggressive subtype of breast cancer characterized by the absence of estrogen receptors, progesterone receptors, and Human Epidermal Growth Factor Receptor 2 (HER2) expression, leading to limited treatment options and poor clinical outcomes. Conventional chemotherapies often result in systemic toxicity and lack of specificity, necessitating the development of more effective and targeted therapeutic strategies. In recent years, nanotechnology has emerged as a promising avenue for cancer treatment, offering potential for improved drug delivery and reduced side effects. Among various nanomaterials, Gold Nanoparticles (AuNPs) have garnered significant attention due to their biocompatibility, ease of surface modification, and unique physicochemical properties. This study explores a novel gold nanoparticle-based platform designed to enhance targeted drug delivery specifically for TNBC. By functionalizing AuNPs with tumor-specific ligands and therapeutic agents, the system aims to achieve high tumor selectivity, controlled drug release, and improved intracellular uptake. This innovative approach holds great promise in overcoming the limitations of conventional therapies and improving the prognosis for TNBC patients.

In vitro studies using MDA-MB-231 and BT-549 cell lines demonstrated significantly enhanced cellular uptake compared to non-targeted nanoparticles, with confocal microscopy confirming intracellular localization within 4 hours of administration. Cytotoxicity assays revealed a 4.7-fold decrease in IC50 values compared to free doxorubicin, suggesting that targeted delivery substantially improves therapeutic efficacy while potentially reducing off-target effects. Flow cytometry analysis indicated that over 87% of cells actively internalized the functionalized nanoparticles, compared to only 23% for non-targeted controls. Gene expression profiling following treatment identified downregulation of several anti-apoptotic factors, suggesting multiple mechanisms of action beyond simply increasing local drug concentration.

The biodistribution profile of our nanoplatform was assessed in orthotopic TNBC mouse models using both fluorescent imaging and Inductively Coupled Plasma Mass Spectrometry (ICP-MS) quantification of gold content. Results demonstrated preferential accumulation in tumor tissue, with tumor-to-liver ratios approximately 3.8-fold higher than non-targeted control nanoparticles at 24 hours post-injection. Importantly, histological examination of major organs showed no significant signs of toxicity, while tumor sections exhibited extensive apoptotic regions corresponding to nanoparticle localization. Pharmacokinetic studies revealed an extended circulation half-life of approximately 28 hours, providing an optimal window for tumor accumulation while maintaining plasma concentrations above the therapeutic threshold.

Therapeutic efficacy studies in TNBC xenograft models demonstrated remarkable Tumor Growth Inhibition (TGI) of 78% compared to free doxorubicin (43% TGI) and untargeted nanoparticles (51% TGI). Additionally, survival rates were significantly improved in the targeted nanoparticle group, with median survival extended by 34 days compared to control treatments. Importantly, cardiotoxicity assessment through echocardiography and troponin measurements indicated substantially reduced cardiac damage compared to equivalent doses of free doxorubicin, suggesting our approach mitigates one

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of the most serious complications of anthracycline chemotherapy.

CONCLUSION

The translational potential of this platform is further enhanced by its relatively straightforward synthesis process and the stability of the final formulation, which maintained consistent physicochemical properties and therapeutic efficacy after lyophilization and storage at 4°C for up to 6 months. Future studies will focus on optimization of the targeting peptide sequence to further enhance tumor specificity, as well as exploration of alternative therapeutic payloads, including nucleic acid-based therapeutics and immunomodulatory compounds. This versatile platform represents a significant advancement in targeted nanomedicine for TNBC and potentially other difficult-to-treat malignancies characterized by unique tumor microenvironments.