MiR126-targeted-nanoparticles combined with PI3K-AKT inhibitor as a new strategy to overcome melanoma resistance

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Metastatic melanoma is a highly lethal cancer if not diagnosed in time and presents significant treatment challenges, particularly due to the early recurrence of the disease despite advancements in therapies like $BRAF^{V600E}$ inhibitors and immunotherapy. This study explores innovative therapeutic strategies, focusing on the targeted delivery of the oncosuppressor microRNA 126 (miR126) using chitosan nanoparticles. These nanoparticles are designed to encapsulate miR126 and are functionalized with an antibody that specifically binds to the melanoma-associated chondroitin sulfate proteoglycan (CSPG4), enhancing the selective delivery to tumor cells. *In vitro* and *in vivo* experiments demonstrated that co-administering miR126 with a PI3K/AKT inhibitor significantly reduced tumor growth and metastasis in mice with BRAF inhibitor-resistant melanoma. The findings suggest a promising approach to enhance treatment efficacy for resistant metastatic melanoma by protecting the therapeutic agent from degradation while ensuring targeted delivery to cancer cells.