Combined Exosome Release Inhibitory & Fibroblast Phenotype Reversal Nanomedicines Normalize CAFs & Potentiate Cancer Immunotherapy

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Background & Methodology

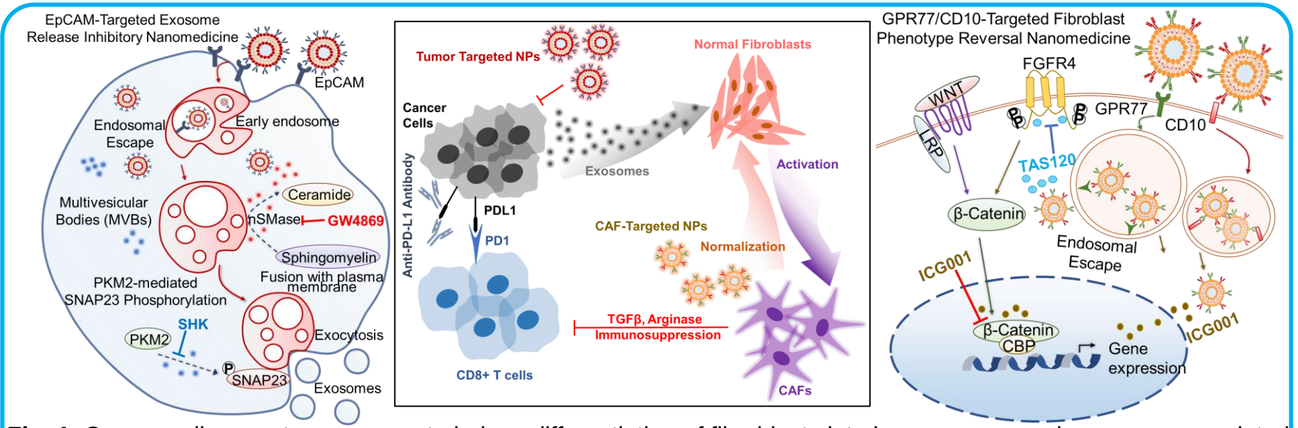

Fig. 1. Cancer cells secrete exosomes to induce differentiation of fibroblasts into immunosuppressive cancer associated fibroblasts (CAFs). Then, cancer cells maintain the CAFs phenotype via activating FGFR & Wnt/β-catenin signaling pathways. Therefore, normalization of CAFs is a major goal to enhance the efficacy of cancer immunotherapy.

Results (In vitro Cell Study)

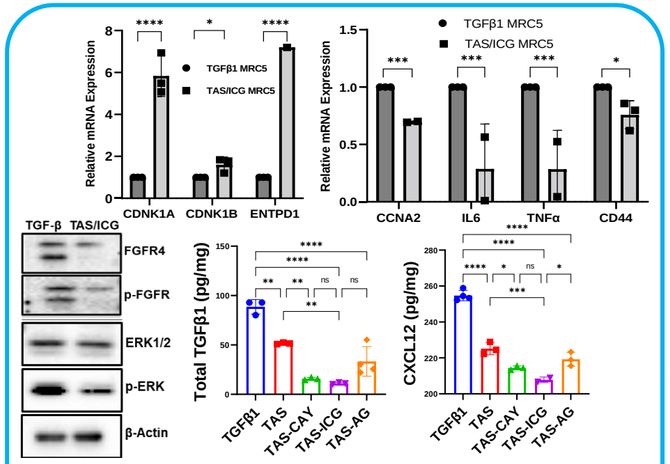

Fig. 4. Mechanistic analysis including qRT-PCR, Western Blot & ELISA of TAS/ICG Nano-treated MRC5 CAFs.

Results (In vivo Study)

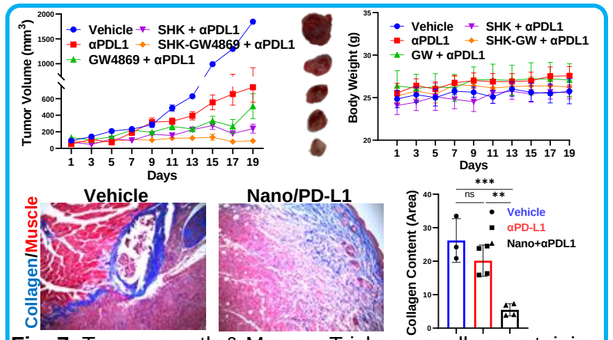

Fig. 7. Tumor growth & Masson Trichrome collagen staining of LLC syngeneic mice treated with SHK/GW Nano.

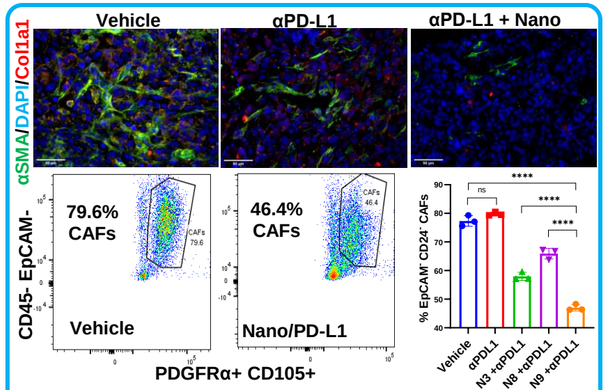

Fig.8. Immunofluorescence imaging & flow cytometry of CAFs in treated tumor tissues (Scale bar: 50 µm).

Results (Exosome Characterization)

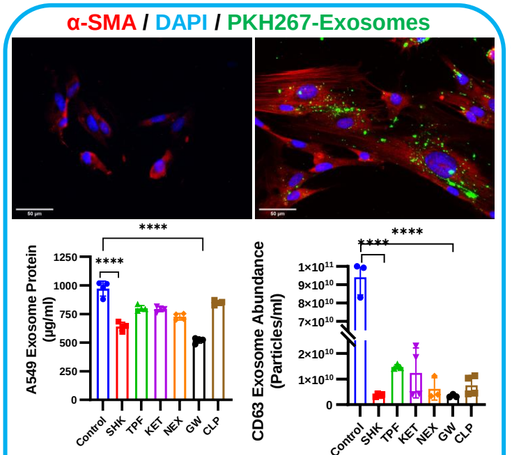

Fig. 2. internalization & Quantitation of A549 exosomes into MRC5 fibroblasts (Bar:50 µm).

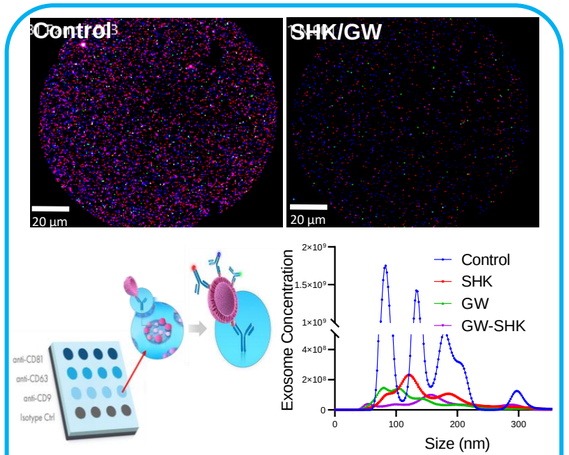

Fig. 3. Interferometric imaging & Nanoparticle Tracking Analysis of A549 exosomes.

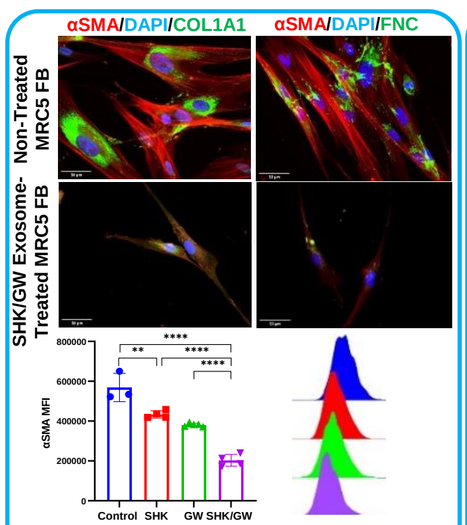

Fig.5. Immunofluorescence imaging & flow cytometry of MRC5 fibroblasts

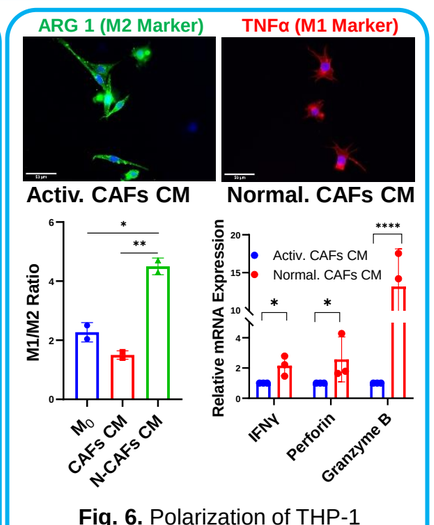

Fig. 6. Polarization of THP-1 macrophages & qRT-PCR of CD8+ T cells treated by active. vs normal. CAFs CM.

Conclusion

Simultaneous Inhibition of tumoral exosome-mediated activation of fibroblasts and blocking FGFR-Wnt/β-catenin signaling reversed the immunosuppressive CAFs phenotype to quiescent one which enhanced the antitumor efficacy of αPD-L1 antibody.