MMP9 gene silencing by siRNA delivery using hybrid nanoparticles reduced the migration of TNBC cells

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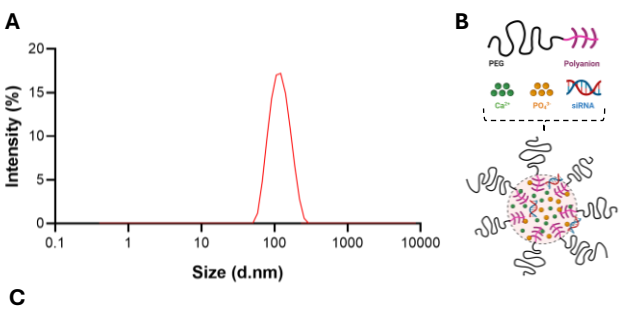
Introduction

Triple negative breast cancer (TNBC) is the most aggressive subtype and breast cancer metastasis is the main cause of mortality (1, 2). Enzymes such as matrix metalloproteinases (MMP) that possess proteolytic activity increase cell mobility due to extracellular matrix degradation, which plays a crucial role in metastasis. Authors associated MMP overexpression to a malignant phenotype (3, 4), and previous report showed overexpression of MMP9 in TNBC (5). Therefore, we used hybrid nanoparticles (NP) to deliver MMP9 siRNA to evaluate the RNAi effects in TNBC cells.

Results



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Z-average (nm)	PdI	ZP (mV)	EE%
111.7 ± 0.03	0.091 ± 0.004	0.088 ± 0.1	80

Figure 1. (A) Size distribution histogram weighted by intensity, (B) representative scheme of the NP, and (C) summary of physicochemical characterization

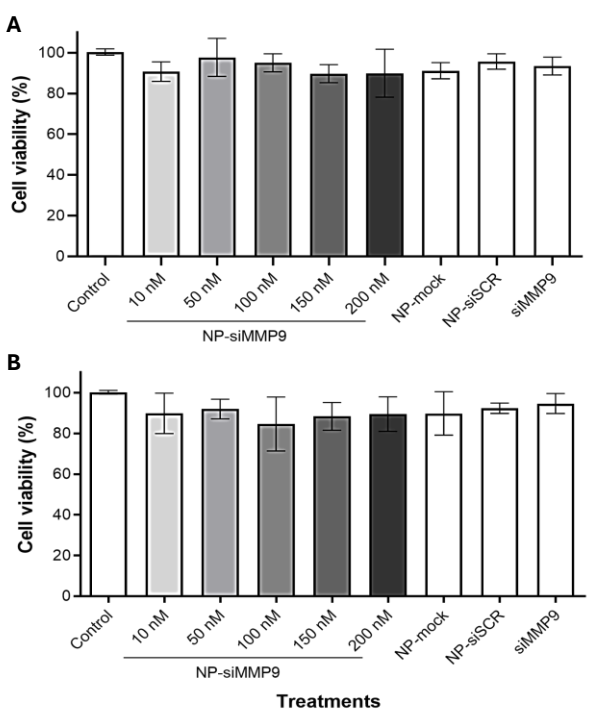

Figure 2. Cell viability of TNBC (MDA-MB-231) at (A) 24 h and (B) 48 h after NP-siMMP9 treatment and controls. Results are expressed as mean ± standard error of the mean (SEM). *p < 0.05 (ANOVA followed by Tukey.

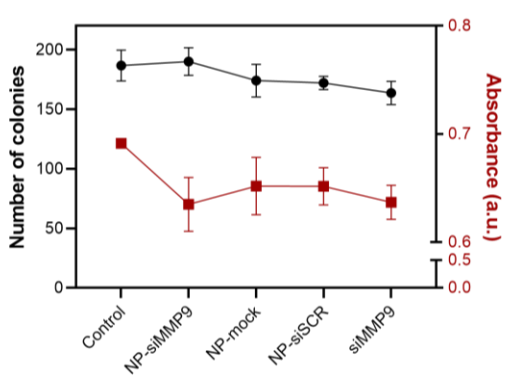

Figure 3. Colony formation in TNBC (MDA-MB-231) after the treatment with NP-siMMP9 and controls. Results are expressed as mean ± standard error of the mean (SEM). *p < 0.05 (ANOVA followed by Tukey.

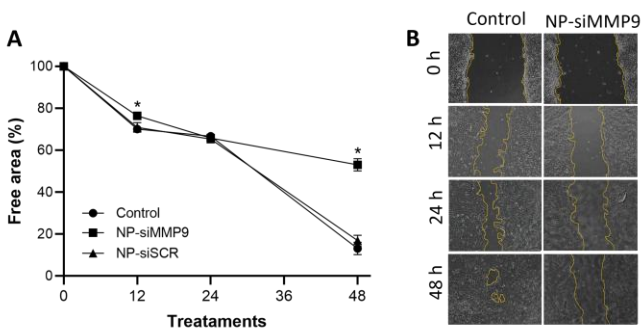

Figure 4. Wound healing assay in TNBC MDA-MB-231 cells after NP-siMMP9 treatment and control. (A) Microscopical images and (B) free area of the scratched area

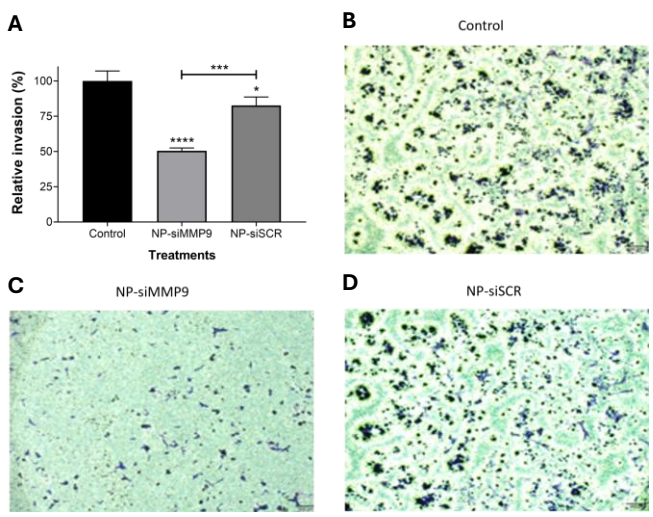

Figure 5. Cell invasion assay. (A) Relative invasion (%) and (B) Representative images of non-treated cells (control), (C) NP-siMMP9 and (D) NP-siSCR. Results are expressed as mean ± standard error of the mean (SEM). *p < 0.05 (ANOVA followed by Tukey.

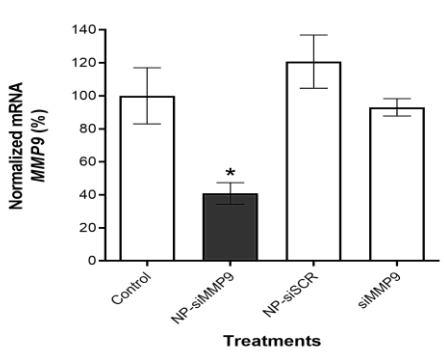

Figure 6. MMP9 gene expression in TNBC MBA-MB-231 cells after NP-siMMP9 and free siMMP9 (150 nM) treatment and controls at incubation time of 24 h. Results are expressed as mean ± standard error of the mean (SEM). *p < 0.05 (ANOVA followed by Tukey.

Conclusion

Our findings suggest that the MMP9 gene could be an interesting molecular target for TNBC, as an adjuvant therapy aiming to achieve antimigratory effects. Furthermore, we can infer that the hybrid nanosystem successfully delivered genetic material into the cytoplasm of the cells, making it a promising option for gene delivery.

References
(1) Li et al. Journal of Hematology & Oncology 2022. (2) Garrido-Castro et al. Cancer Discovery 2019:176-198. (3) Jiang et al. Oncogene. 2007:2245-2252. (4) Hey & Linder. Journal of Cell Science. 2024: jcs261898. (5) Joseph et al. Breast Cancer Research and Treatment. 2020:267-282.

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