Sargassum fusiforme–Derived Exosome-Like NVs Enhance Osteogenesis, Suppress Osteoclastogenesis in OVX Mice

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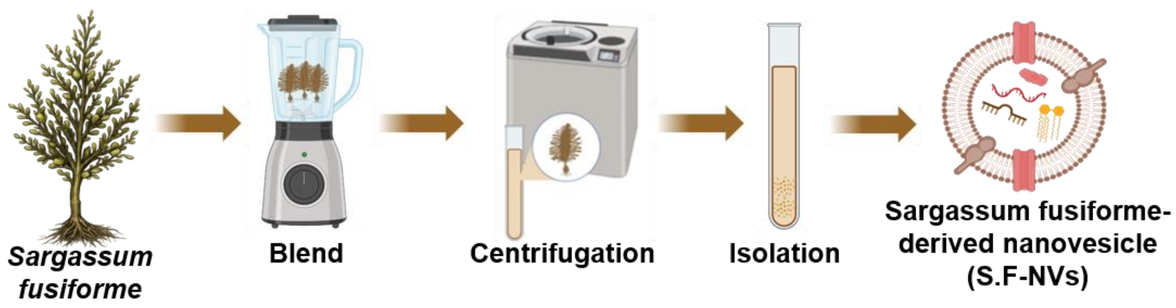
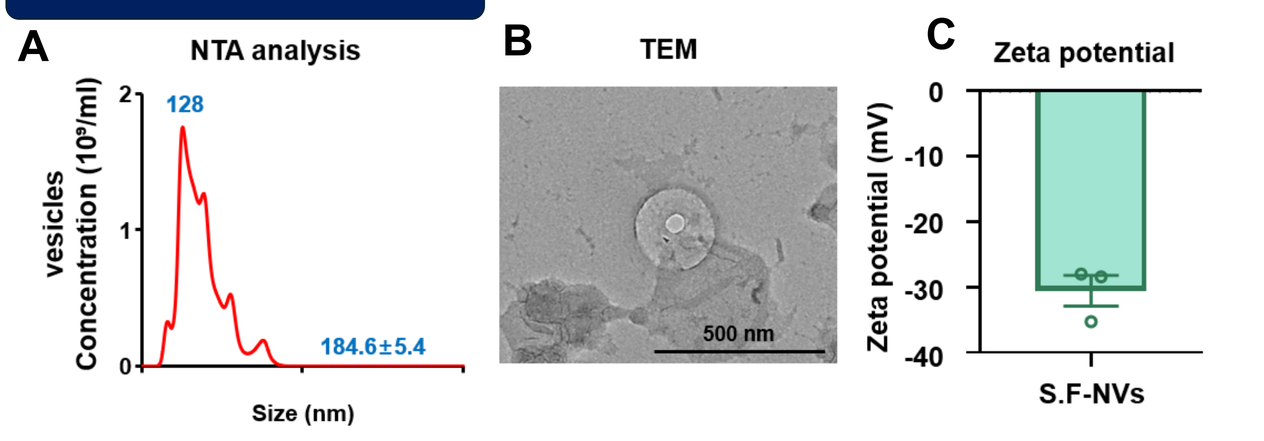
Introduction

Osteoporosis is driven by uncoupled bone remodeling, causing bone loss and fragility after estrogen decline. Long-term antiresorptive may raise safety concerns, motivating safer, naturally derived approaches. We evaluated *Sargassum fusiforme*–derived exosome-like nanovesicles (S.F-NVs) as an orally deliverable marine nanotherapeutic to restore remodeling balance by enhancing osteoblast activity and limiting osteoclast formation, with focus on BMP–Smad1/5/8 and mitogen-activated protein kinase signaling.

Method



Results



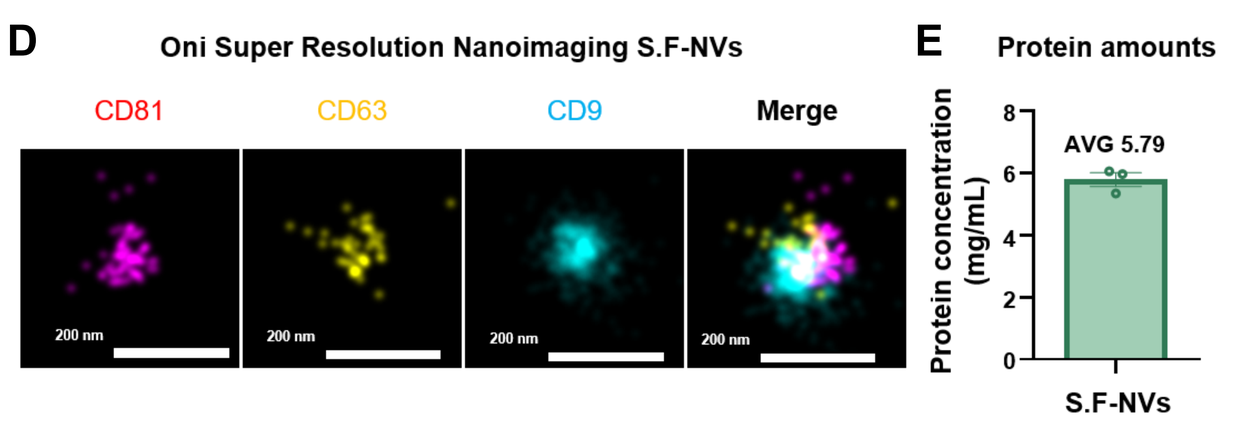


Fig 1. Characterization and cellular uptake of S.F-NVs. (A) Particle size distribution of S.F-NVs measured by NTA. (B) Representative TEM image. (C) Zeta potential. (D) Super-resolution nanoimaging of EV markers CD81, CD63, and CD9. (E) Protein concentration of S.F-NVs.

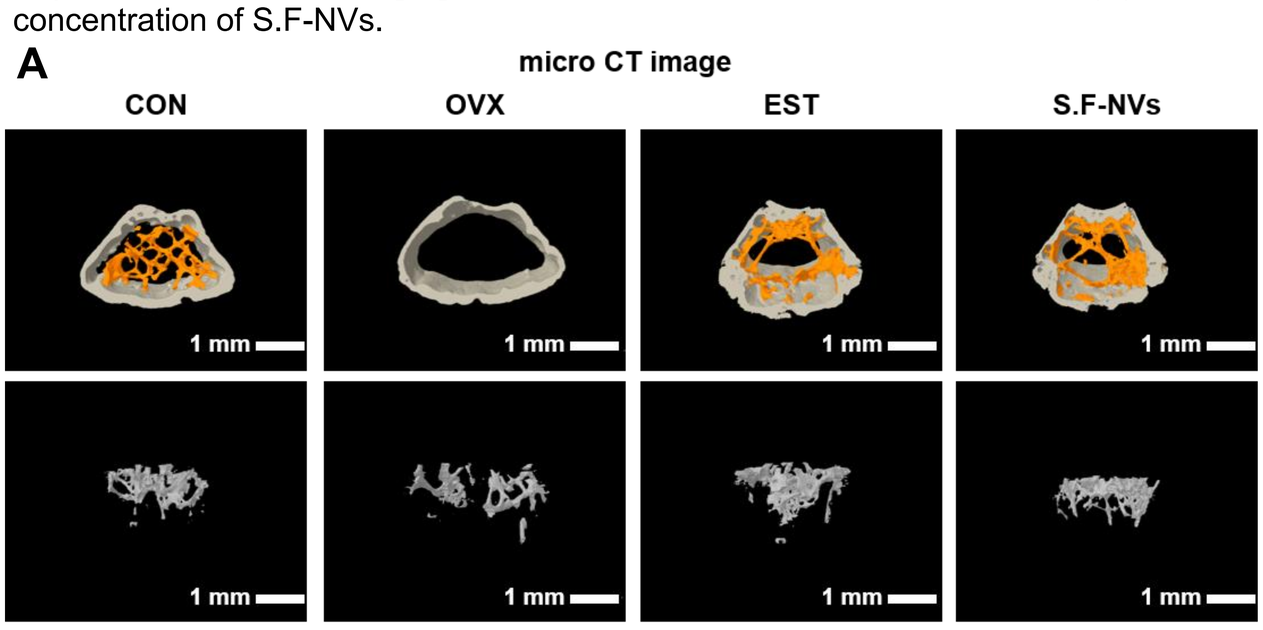


Fig 2. S.F-NVs attenuated OVX-induced bone loss in mice. Representative micro-CT images showing trabecular bone loss in OVX mice and its recovery after EST or S.F-NV treatment.

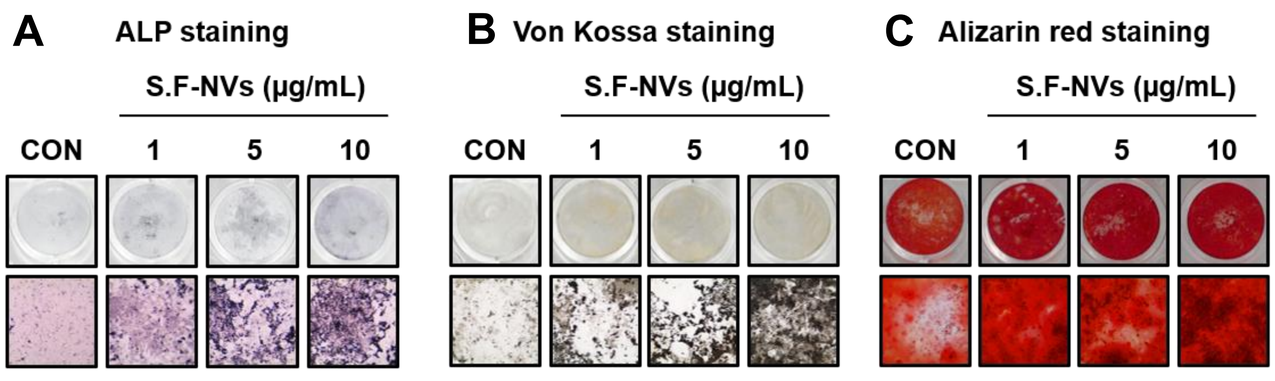


Fig 3. S.F-NVs enhanced osteogenic differentiation and mineralization in mouse primary osteoblasts. (A) ALP staining, (B) von Kossa staining, and (C) Alizarin red staining.

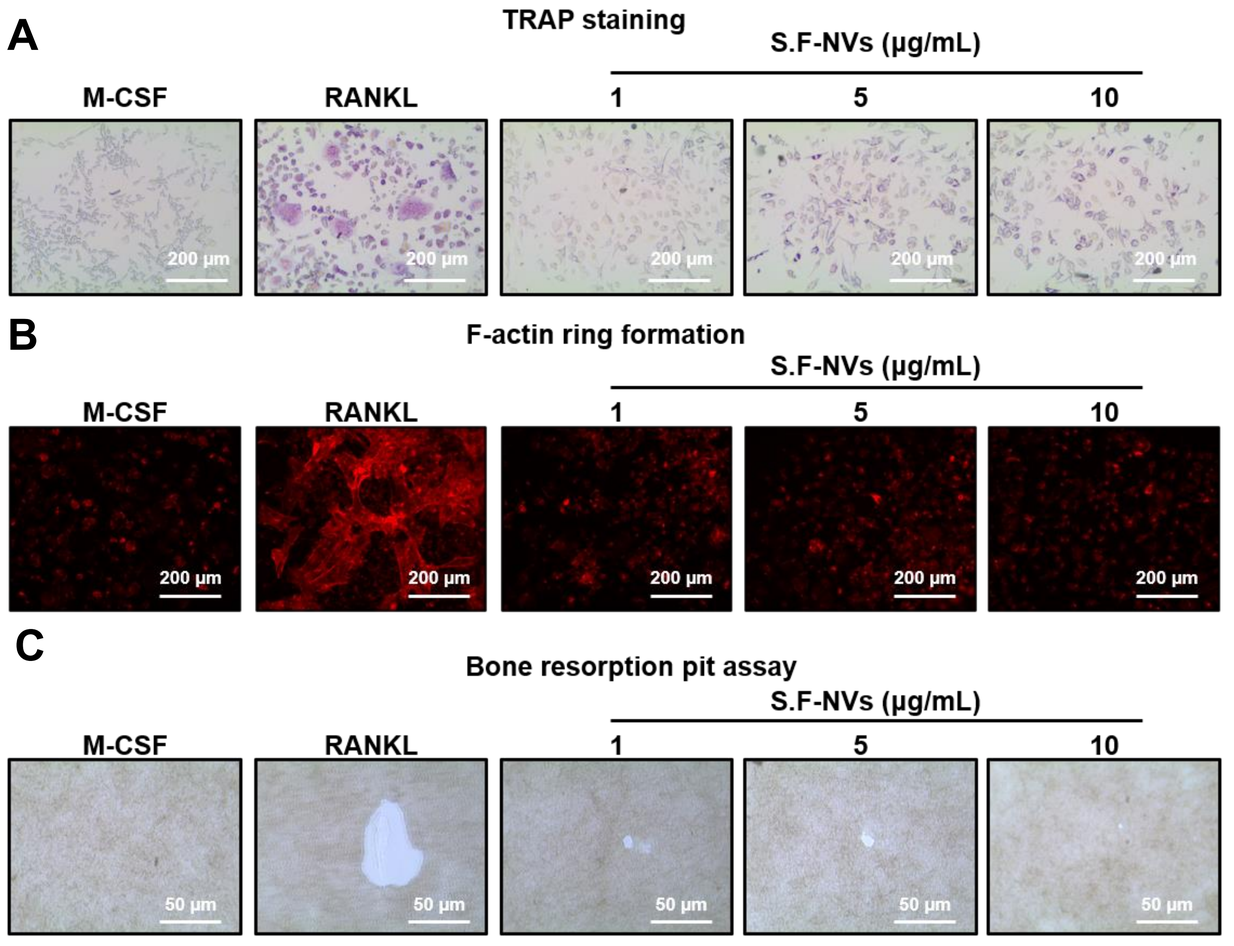


Fig 4. S.F-NVs suppressed RANKL-induced osteoclast formation and resorptive activity. (A) TRAP staining, (B) F-actin ring formation, and (C) bone resorption pit assay.

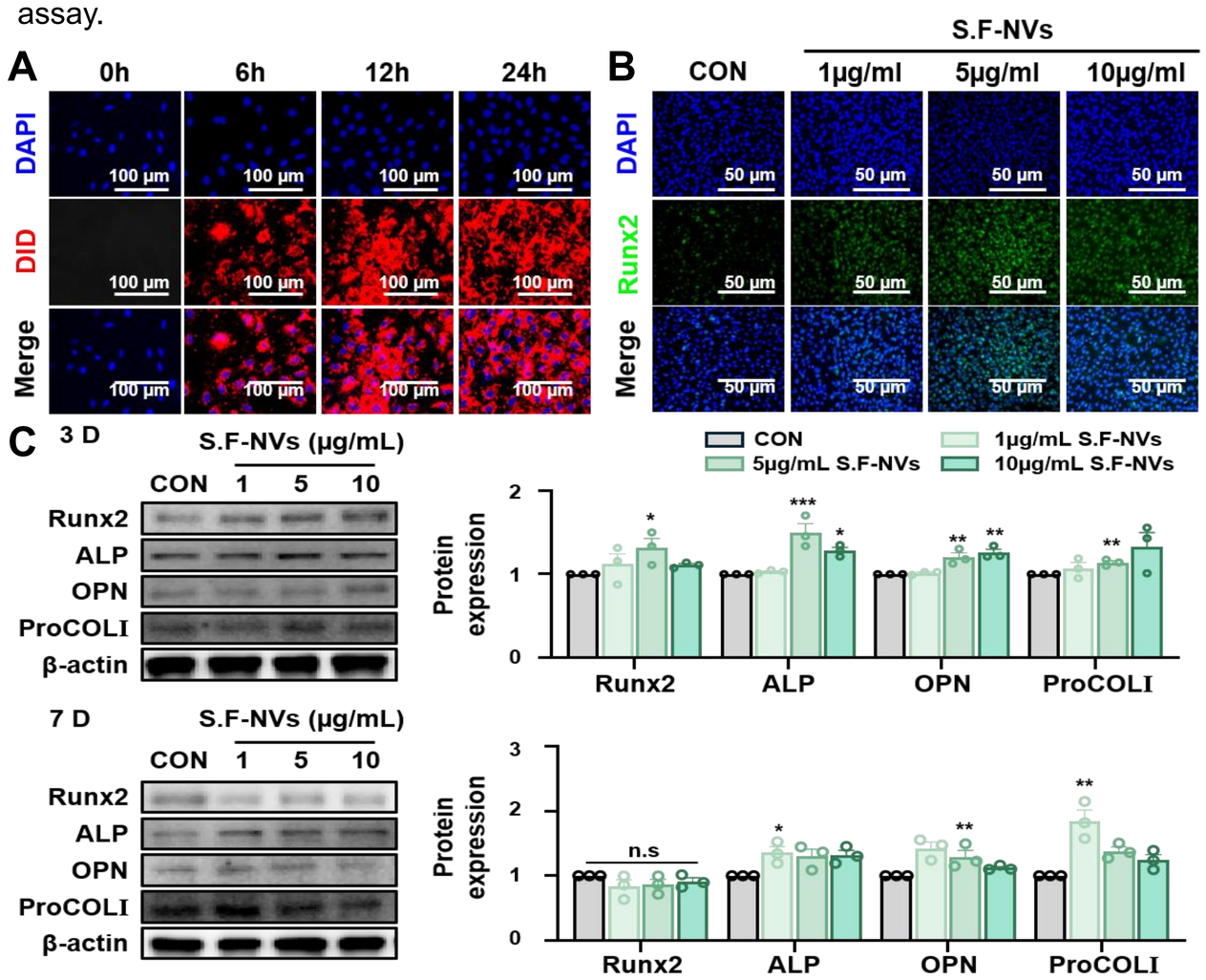


Fig. 5. S.F-NVs enhance osteogenic differentiation in MC3T3-E1 cells. (A) Time-dependent uptake of DiD-labeled S.F-NVs by MC3T3-E1 cells. (B) Runx2 immunofluorescence staining. (C) Western blot analysis and densitometric quantification of osteogenic markers.

Fig 6. S.F-NVs activated BMP2/4 signaling during osteoblast differentiation. (A) 3-day and 7-day western blot analysis of BMP2/4 and p-Smad1/Smad1.

Conclusion

S.F-NVs enhanced bone-forming activity and inhibited osteoclast formation, restoring the balance of bone remodeling in vitro and in ovariectomized mice. These results support S.F-NVs as a promising marine-derived nanovesicle candidate for osteoporosis management.

References

Chen X, Wang Z, Duan N, Zhu G, Schwarz EM, Xie C. Osteoblast-osteoclast interactions. Connect Tissue Res. 2018. 59:99–107.

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