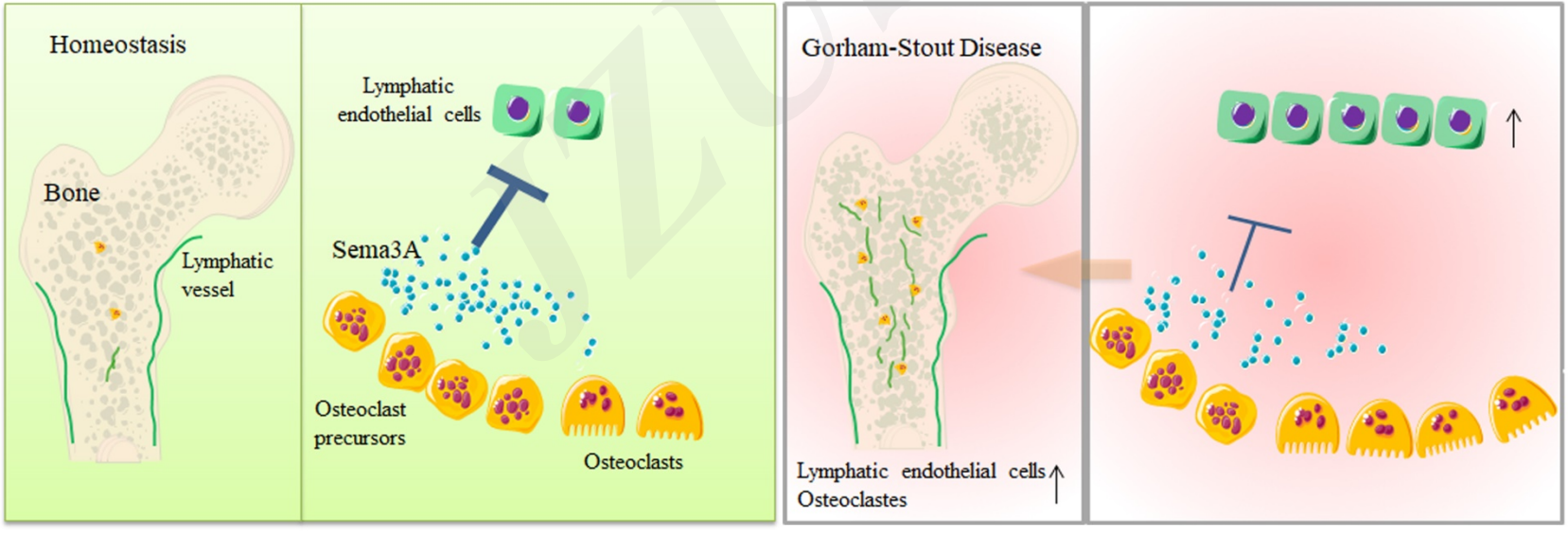
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Reduced expression of semaphorin 3A in osteoclasts causes lymphatic expansion in a Gorham-Stout disease (GSD) mouse model

Key words: Semaphorin3A (Sema3A); Gorham-Stout Disease (GSD); Osteoclasts (OCs); Osteolysis; Lymphatic endothelial cell (LEC)

Research Summary

Sema3A, an axon guidance factor, plays an crucial role on osteoprotection. In this study, we investigated the effect of OCs on LECs and found that expression of Seme3A was decreased in OCs, which enhanced the growth, migration, and tube formation of LECs in vitro. Overexpressing Sema3A in bone marrow alleviated osteolysis induced by LECs and inhibited the growth of LECs. Our results indicate that Sema3A is a potential target for GSD treatment.



Innovation points

- **The reduction of Sema3A expression in OCs enhances LEC growth, migration, and tube formation.**

- **Overexpression of Sema3A effectively alleviates osteolysis induced by LECs and inhibits LECs' expansion *in vivo*, which provide a new therapeutic target for the treatment of GSD.**

- **Knockdown of Sema3A in bone marrow is a new approach for establishing a GSD mouse model.**

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Innovation points

Fig. 1 | OC but not OC precursors conditioned media promoted LEC growth, migration, and lymphatic vessel formation in vitro.

Fig. 2 | RNA sequencing revealed that expression of Sema3A in OCs was decreased compared with that in OC precursors .

Fig. 3 | Seme3A suppresses the growth, migration and tube formation of LECs.

Fig. 4 | Sema3A expression is decreased in GSD mice, and Sema3A administration reduces GSD bone lesions and LECs.

Fig. 5 | Sema3A shRNA enhances GSD bone lesions and LEC expansion.

Fig. 6 | Overexpression of Sema3A in LECs reduces the GSD bone phenotypes.