KDDF
Korea Drug Development Fund

Asset #2
Weill Cornell Medicine

Targeting the SLIT3 Pathway to Promote Bone Formation

Therapeutic Area	Bone Disease, Endocrinology	**Indications**	Osteoporosis
Modality	Protein	**Development Stage**	Hit to Lead/Lead Optimization

Overview

Background

- One in two women and one in four men experience a fracture due to osteoporosis in their lifetime. However, the application of currently available therapeutic methods is limited by either the side effects or by the maximum therapy duration
- Biophosphonates are the most widely prescribed but are associated with nausea, abdominal pain and heartburn-like symptoms
- Denosumab produces similar or better bone density results but is associated with rare but serious side effects
- Bone-building medications such as teriparatide and romosozumab may be used in patients who fail or are intolerant to other therapies
- Unmet Need: Methods to prevent and reverse osteoporosis that act through novel mechanisms

Technology Advantages

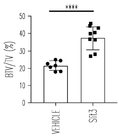
- Novel methods that involves targeted administration of osteoanabolic agents to promote bone formation, boost bone strength, and enhance bone healing
- Slit guidance ligand 3 (SLIT3) is a potent proangiogenic factor that enhances bone fracture healing and counteracts bone loss
- SLIT3 provides a complementary pathway to PTH-based agents, suggesting they may be used sequentially or in combination to enhance efficacy
- Distinct mechanism of action from approved therapies
- May be used sequentially or in combination with PTH-based anabolic agents
- Local drug delivery minimized extra-skeletal toxicities
- Can be delivered in combination with a carrier or medical device

Key Data

Administration of recombinant SLIT3 has therapeutic effects on bone fracture healing in mice.

A

B

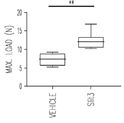


E

(A) Representative μCT images of mouse femurs 21 days post-fracture with IV injection of SLIT3 or PBS (Scale bar = 1 mm for μCT). (B) μCT measurement of BV/TV in callus area of femurs after IV injection of SLIT3 or PBS 21 days after fracture (n≥4, per group).

(E) Representative μCT linages of the trabecular bone in the distal femur of mice after sham-operation (Sham), or in ovariectomized (OVX) mice, where the OVX mice were treated with vehicle, SLIT3, or parathyroid hormone (PTH) injection. Scale bars, 1mm.

C



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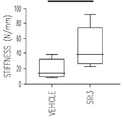

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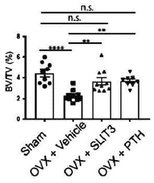

(C) Results of bio-mechanical test of maximum compressive load of femurs after IV injection of SLIT3 or PBS 21 days after fracture (n≥4, per group). (D) Results of bio-mechanical test of stiffness of femurs after IV injection of SLIT3 or PBS 21 days after fracture (n≥4, per group).

(F) relative quantitative analysis of bone volume/total volume in trabecular bone in the distal femur of mice after sham-operation (Sham), or in ovariectomized (OVX) mice, where the OVX mice were treated with vehicle, SLIT3, or parathyroid hormone (PTH) injection. Values represent mean ± s.e.m; *P < 0.05, **P < 0.01, ***P < 0.001 and **** P < 0.0001 by a Fisher's exact test unpaired two-tailed Student's t-test or by one-way ANOVA followed by a Tukey's posttest in all other panels.

IP Status & Publication(s)

Intellectual Property

Patent Number
PCT-US2019-018115 (2019.02.14)

Patent Family
PCT, US

Publication(s)

- Xu, R. et al. (2018). Targeting skeletal endothelium to ameliorate bone loss. Nature Medicine, 24(6):823-833.