



Weill Cornell Medicine

Targeting the SLIT3 Pathway to Promote Bone Formation

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Background & Unmet Need

- 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 Overview

- **The Technology:** Novel methods that involves targeted administration of osteoanabolic agents to promote bone formation, boost bone strength, and enhance bone healing
- **Discovery:** Slit guidance ligand 3 (SLIT3) is a potent proangiogenic factor that enhances bone fracture healing and counteracts bone loss
- **PoC Data:** In a mouse model of osteoporosis, SLIT3 had comparable efficacy to PTH-based anabolic agents
- Local therapeutic delivery was achieved using a SLIT3-loaded collagen sponge, which limits potential for extra-skeletal toxicities
- SLIT3 provides a complementary pathway to PTH-based agents, suggesting they may be used sequentially or in combination to enhance efficacy

Inventors:

Matthew Greenblatt
Laurie Glimcher
Ren Xu

Patents:

[US Application Filed](#)

Publications:

[Xu et al. Nat Med. 2018.](#)

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Cornell Reference:

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Technology Applications

- Treatment and prevention of bone loss (osteoporosis)
- Promotion of bone healing and strength
- Use with a range of orthopedic procedures to enhance healing or osteointegration
- Inhibition of SLIT3 may prevent unwanted bone formation

Technology Advantages

- 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

Supporting Data / Figures

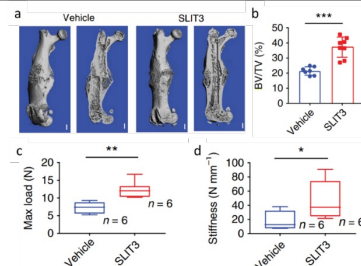


Figure 1: Administration of recombinant SLIT3 has therapeutic effects on bone fracture healing in mice.

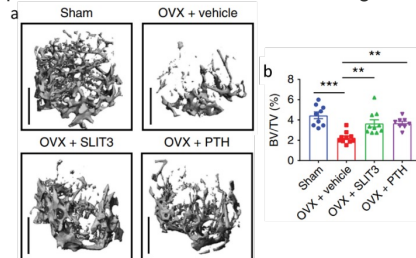


Figure 2: Administration of recombinant SLIT3 has therapeutic effects comparable to parathyroid hormone (PTH) on ovariectomy (OVX)-induced bone loss in mice.

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