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ENGINEERED RANK PROTEIN FOR TREATMENT OF OSTEOPOROSIS

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Value Proposition: *Single chain RANK ligand that can selectively inhibit pathological bone loss.*

Technology Description

Researchers at Washington University in St. Louis have developed a genetically engineered mutant RANKL protein that prevents bone loss by selectively inhibiting RANK activation. Antibody treatments for osteoporosis prevent bone loss and osteoclast formation by binding the RANK ligand (RANKL) and thereby inhibiting RANKL/RANK interactions. However, this completely removes RANKL which leads to increased infection and off-target effects.

This engineered protein inhibits osteoclast formation in vitro and bone resorption in vivo and could potentially be generalized to create additional therapies directed toward other TNF superfamily receptors, such as TNFR1 for rheumatoid arthritis and psoriasis or DR5 for acute myeloid leukemia and breast cancer.

Stage of Research

Proof of concept in vitro and in vivo

Publications

Warren JT, Nelson CA, Decker CE, Zou W, Fremont DH, Teitelbaum SL. Manipulation of receptor oligomerization as a strategy to inhibit signaling by TNF superfamily members. Sci Signal. 2014 Aug 19;7(339):ra80. doi: 10.1126/scisignal.2004948. PMID: 25140055; PMCID: PMC4206197.

Applications

Antibody treatment for osteoporosis

Key Advantages

- Mutant RANKL does not interact with osteoprotegerin, leading to less off-target effects and potentially less risk for infection.
- Genetic engineering method could be generalized to generate therapeutics that selectively inhibit other pathological TNF superfamily pathways.

Patents

- Patented: Oligomers for TNF superfamily inhibition (US Patent No. 9,914,761)

Related Web Links – Steven Teitelbaum Profile; Teitelbaum Lab