EFFECTS OF A MUTATED SCLEROSTIN PEPTIDE ON BONE AND LEAN MASS IN MICE

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INTRODUCTION

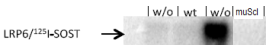
1) **Sclerostin, a product of osteocytes, is known to inhibit Wnt signaling by binding the LRP5/6 receptor** (ten Djike et al. 2008).
2) **Its production is reduced by mechanical stimulation** (Robbing et al. 2008).
3) **Paradoxically, serum sclerostin levels correlated positively with BMD** (Mödder et al 2011; Garnero P et al. 2012; Asaru A et al. 2012).
4) **Associations between fracture risk and serum sclerostin levels are discordant** (Arasu, Joe et al. 2012; Szulc et al. 2013).
5) **Hence, the biological significance of circulating sclerostin remains unknown.**

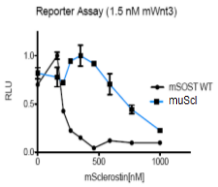
AIM

TO INVESTIGATE THE EFFECTS OF CIRCULATING SCLEROSTIN AGONIST (Scl) AND ANTAGONIST (muScl) PEPTIDES ADMINISTRATION

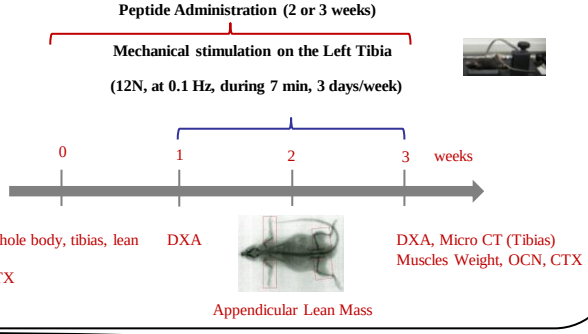
MATERIALS AND METHODS

- **In vitro**, muScl fully competed with radioactive 125 I-SOST for binding to LRP6 and showed shows an impaired activity to inhibit Wnt signaling



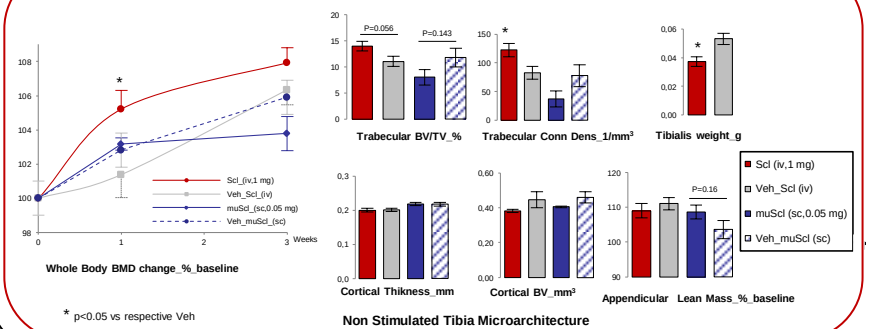


- **Experiment 1:** 2 month-old mice received Scl peptide (iv, 1mg/kg/d) or muScl (s.c 0.05 mg/kg/d) or veh for 3 weeks.
- **Experiment 2:** 3 month-old mice received muScl by minipumps (0.01 mg/kg/d and 0.05 mg/kg/d) or veh for 2 weeks.



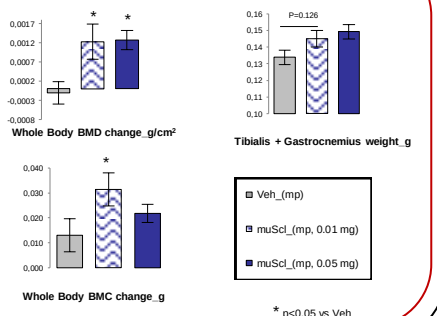
EFFECTS OF SCLEROSTIN PEPTIDES ON BONE, MUSCLE AND LEAN MASS

EXPERIMENT 1



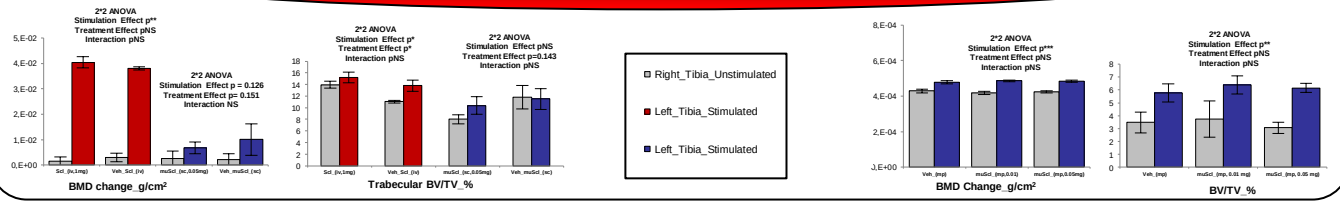
* p<0.05 vs respective Veh

EXPERIMENT 2



* p<0.05 vs Veh

EFFECTS OF MECHANICAL STIMULATION COMBINED WITH SCLEROSTIN PEPTIDES ON BONE



SUMMARY AND CONCLUSIONS

1) **Sclerostin agonist (Scl) was associated with a modest increase of whole body BMD and trabecular BV/TV whereas it decreased muscle mass.**
2) **Sclerostin antagonist (muScl) had inconsistent effects on bone depending on way and dose administration but increased muscle mass.**
3) **These preliminary observations suggest a new role of circulating sclerostin in the regulation of muscle mass.**