INTRODUCTION

1) Sclerostin, a product of osteocytes, is known to inhibit Wnt signaling by binding the LRPs6 receptor (ten Dijke et al. 2008).
2) Its production is reduced by mechanical stimulation (Robbing et al. 2008).
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 125I-SOST for binding to LRPS6 and showed 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.

**Peptide Administration (2 or 3 weeks)**

Mechanical stimulation on the Left Tibia
(12N, at 0.1 Hz, during 7 min, 3 days/week)

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<th>Time (weeks)</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
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</thead>
<tbody>
<tr>
<td>DXA (Whole body, tibias, lean mass)</td>
<td>Veh_Scl</td>
<td>muScl</td>
<td>Veh_Scl</td>
<td>muScl</td>
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<tr>
<td>OCN, CTX</td>
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<tr>
<td>Appendicular Lean Mass</td>
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**EFFECTS OF SCLEROSTIN PEPTIDES ON BONE, MUSCLE AND LEAN MASS**

**EXPERIMENT 1**

- Whole Body BMD change % baseline
- Trabecular BV/TV %
- Trabecular Conn.Dens_1/mm²
- Tibial weight g
- Cortical Thickness_mm
- Cortical BV/mm²
- Appendix Lean Mass % baseline

**EXPERIMENT 2**

- Whole Body BMD change_g/cm²
- Trabecular BV/TV %
- Tibialis + Gastrocnemius weight_g

**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.