associated with the risk of falls but higher GDF-15 was associated with poorer balance and slower gait speed (P<0.001).

Conclusions: Increased GDF-15 was associated with an increased risk of hip fractures, suggesting that greater cell senescence increases hip fracture risk. This may not be attributable to lower BMD, but perhaps to poor balance while walking slowly causing falls that are more likely impact the hip.

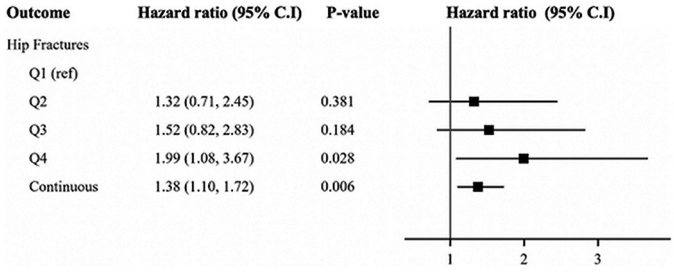

Figure 1. Hip fracture risk by quartile of GDF-15 and continuous level of GDF-15.

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Concurrent Oral Poster Presentations 1: Basic / Translational

P033

Depletion of TRAP/Acp5 abolishes the bone forming effects of mechanical loading in male mice

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Tartrate resistant acid phosphatase (TRAP/Acp5) is a known biomarker of osteoclastic bone resorption activity. In addition to osteoclasts, TRAP is also expressed in osteoblasts and osteocytes, but the specific function of TRAP in bone formation is poorly understood. In this study, we aimed to investigate the role of TRAP in bone formation induced by external mechanical loading. Three-months-old male TRAP KO and WT mice were subjected to axial mechanical loading on their right tibiae, three times per week for two weeks (40 cycles, peak strain 1100strains). Internal controls of non-loaded left limbs were utilized to determine the independent effects of loading on bone formation. Micro computed tomography (CT) was used to examine the architecture of the bones. The variation in cortical bone microstructure over the length of the tibiae was mapped using site-specificity analysis (SSA) (1). TRAPKO mice had 12% shorter tibia than WT mice ($p<0.001$), and osteopetrosis as shown by higher BV/TV, Tb.Th, Tb.N and Tb.BMD (+66%, $p<0.001$; +30%, $p<0.001$; +27%, $p<0.01$; and +51%, $p<0.001$ respectively) and a reduced Tb.Sp (-21%, $p<0.001$). Loading increased trabecular BV/TV, Tb.Th, Tb.N and Tb.BMD, and reduced Tb.Sp in WT mice (+33%; $p<0.001$, +21%; $p<0.001$, +10%; $p<0.01$, +25%; $p<0.001$ and -6%; $p<0.05$ respectively). In contrast, loading failed to increase BV/TV, Tb.N, Tb.Sp or Tb.BMD in TRAPKO mice, and their increase in Tb.Th was significantly smaller than in WT mice (+11%; $p<0.05$). SSA showed that loading increased cortical area proximally in WT mice ($p<0.01$). This response was abrogated in TRAPKO mice. In conclusion, we report that the loading-associated increase in trabecular and cortical bone seen in WT mice is diminished or abrogated in TRAPKO mice. These results suggest an important role of TRAP in loading-induced bone formation.

Reference

1. Windahl et al, 2021. Methods in Molecular Biology, 2221:275-289.

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P015

Tissue engineered mimetic periosteum for efficient delivery of rhBMP-2

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Background: Despite its unique regenerative capacity, bone healing can be compromised, leading to delayed fracture regeneration and consequently nonunion. Due to the scarcity of autografts and the problems associated with a supraphysiological use of rhBMP-2, novel tissue engineering strategies arise as a promising solution to overcome nonunions and related bone pathologies.

Purpose: To clinically deal with fracture nonunion, we designed engineered mimetic autografts consisting of a personalized polycaprolactone (PCL) scaffold surrounded by a porous PCL membrane mimicking the periosteum synthesized by melt electrowriting (MEW) (Figure 1).

Methods: MEW membrane was functionalized with poly ethyl acrylate (PEA) and Fibronectin for efficient rhBMP-2 binding and delivery. The regenerative capacity and therapeutic potential of these scaffolds were tested *in vitro* for osteoblast differentiation and *vivo* in a critical size femur defect in Sprague Dawley rats (n=6-7 animals/group) (ethical approval 073-20). Regenerative effects were assessed by qPCR, q-mCT and histological analysis. Non-parametric Kruskal Wallis test was used for statistical analysis.

Results: We selected the two lowest dose implants (10 mg/ml, 51.94±8.84 ng and 25 mg/ml, 186.8±17.33) to assess release profile over time and for *in vivo* therapeutic effect. In vitro, single loading of 186 ng of rhBMP-2 allows similar differentiation potential that standard osteogenic differentiation medium where fresh rhBMP-2 was added twice weekly (Figure 2). *In vivo*, regarding bone regeneration, quantitative μCT analysis shows great bone healing of defects treated with rhBMP-2 at concentrations of 25 μg/ml (186 ng) and 10 μg/ml (52 ng). **Control group**, 6.80±2.47 mm^3; **10 μg/ml BMP-2 group** 19.53±4.266 mm^3, *p=0.0324; **25 μg/ml BMP-2 group** 24.48±11.30 mm^3, **p=0.0087. In addition, histological analysis was carried out to determine the osteoconductive potential of our PCL core (Figure 3).

Conclusion: In conclusion, PEA functionalized mimetic periosteum show an unpreceded increase in bone healing, greatly enhancing rhBMP-2 effects.

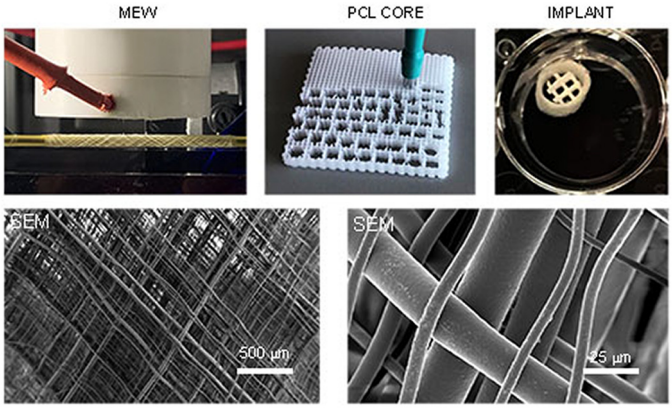

Figure 1

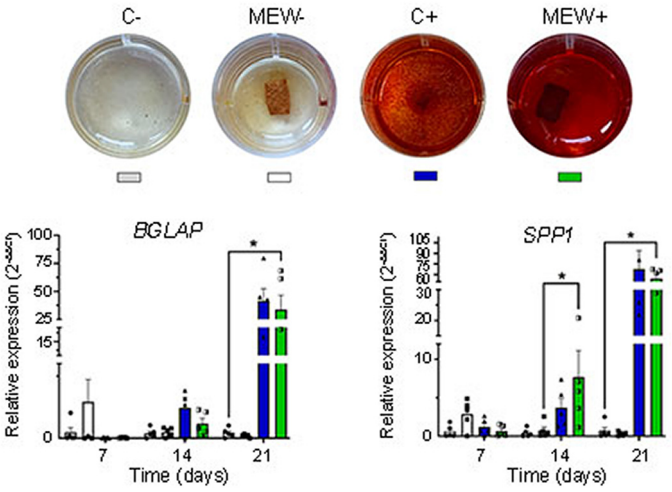

Figure 2

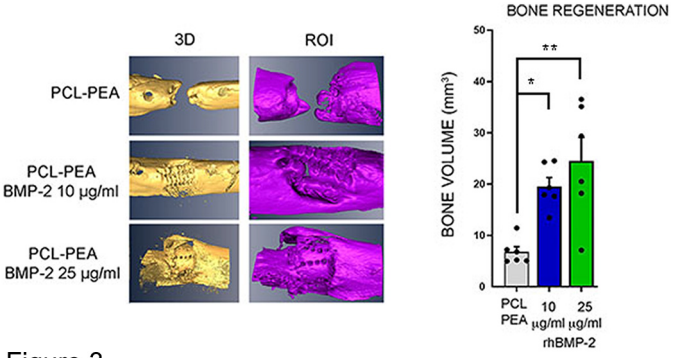

Figure 3

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P046

Local microdamage accumulation and impaired osteocyte viability in human cortical bone is linked to type 1 diabetes mellitus

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Introduction: Type 1 diabetes mellitus (T1DM) is a chronic metabolic disease of insulin deficiency, with a 7-fold increased risk of hip fractures. Osteocytes are the primary bone cells connected through lacuno-canalicular network orchestrating bone remodeling. Their proper function is pivotal for maintaining bone homeostasis. Micropetrosis is defined as osteocyte lacunar mineralisation, which implies preceding osteocyte apoptosis. Our earlier work indicated that T1DM has a local effect on osteocyte viability, resulting in increased micropetrotic lacunae at the periosteal region of femoral bone. We hypothesised that the osteocyte network on diabetic bone would be functionally impaired towards imbalanced bone turnover.

Purpose: We investigated the effect of T1DM on osteocyte viability and its consequences for microdamage detection in human femoral cortical bone.

Methods: Femoral cortices of the mid-diaphysis from 22 individuals from both sexes (T1DM n=8, 55.0±10.6 years; control n=14, 53.1±9.5 years) were collected during autopsy with IRB approval. Microdamage accumulation in the anterior quadrant on rhodamine-infiltrated samples was evaluated using confocal microscopy. Caspase-3 immunohistochemistry and TUNEL were applied to quantify osteocyte apoptosis.

Results: Microcrack numbers in the endocortical region were similar (p=0.365), yet the periosteal region in T1DM showed significantly higher number of microcracks per bone area (p=0.048).TUNEL indicated a marginally higher percentage of osteocyte apoptosis in the periosteal region in T1DM (p=0.180). Caspase data revealed significantly higher occurrence of apoptotic osteocytes per bone area in both endocortical (p=0.035) and periosteal (p=0.013) regions.

Conclusion: This study demonstrated a significantly higher number of microcracks in the periosteal region of femoral cortical bone in T1DM. Furthermore, elevated osteocyte apoptosis was noted in periosteal and endocortical regions in T1DM. We present that T1-diabetic bone exhibits an impaired osteocyte network and a local microdamage accumulation. Such impaired bone quality might further lower bone turnover, contributing to decreased bone mechanical competence and potentially an elevated fracture risk with T1DM bone disease.

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P052

Complement receptor C5aR1 on osteoblasts regulates osteoclastogenesis during ovariectomy-induced bone loss in mice

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The proinflammatory anaphylatoxin C5a is generated by activation of the complement system. There is evidence that the C5a/C5aR1 axis is involved in physiological bone turnover and inflammatory bone disorders. Mice with a global deletion of C5aR1