in this coupling, and several factors have been proposed in the literature. However, most of these factors were only studied *in vitro* or in murine models.

Purpose: To investigate spatial expression of proposed coupling factors and their receptors within human bone remodeling events.

Methods: Highly sensitive RNA in situ hybridization combined with TRAcP immunostaining on sections from 9 adolescent controls (patients undergoing corrective surgery for Coxa Valga) with Masson Trichrome staining of adjacent sections to enable identification of cortical remodeling events.

Results: In cortical pores with active bone remodeling, *LIF*-receptor (*LIFR*) expression was high in osteoprogenitors in the lumen and on eroded surfaces (osteoblastic reversal cells). In contrast, expression of *LIFR* was lower in bone lining cells of quiescent pores and bone-forming osteoblasts of formative pores. *LIFR* was not expressed by osteoclasts, which instead had a high *LIF* expression. Likewise, expression of the putative coupling factor *SEMA4D* was restricted to osteoclasts, while its receptor *PLXNB1* was expressed in neighbouring reversal cells and in bone-forming osteoblasts. However, *PLXNB1* was not expressed in osteoprogenitors in lumen of resorptive pores. Similarly, *PDGFB* was expressed by osteoclasts, while receptors *PDGFRA* and *PDGFRB* were expressed by reversal cells and in bone-forming osteoblasts. Like *LIFR*, *PDGFRB* was expressed by osteoprogenitors in the lumen of resorptive pores, whereas *PDGFRA* was less abundant within these osteoprogenitors.

Conclusions: This study demonstrates that proposed osteoclastic coupling factors LIF, PDGFB and SEMA4D are expressed by bone-resorbing osteoclasts in human intracortical remodeling events. Moreover, their receptors are expressed by nearby osteoblastic reversal cells. This supports that these coupling factors may be important in osteoclast-osteoblast coupling *in vivo* in humans.

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P126

Inositol Phosphatase SHIP1 – a Regulator of Osteoclast Lineage Cell Development and Activity

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Introduction: Src-homology (SH) 2 domain-containing inositol-5-phosphatase 1 (SHIP1) is a negative regulator of the PI3K/Akt pathway that is expressed in hematopoietic cells. Osteoclast (OC) development depends on two essential pathways activated by receptor activator of NF-κB ligand (RANKL) and colony-stimulating factor-1 (CSF-1). Both pathways involve PI3K in their signalling and may therefore be regulated by SHIP1. SHIP1-deficient mice (*($SHIP^{styx/styx}$)* are characterized by low bone density that has been suggested to be caused by an increased number of hyperactive OC.

Purpose: This study aimed to investigate cellular mechanisms leading to low bone mass in SHIP1-deficient mice.

Methods: MicroCT analysis of vertebrae and femora was performed to evaluate bone structure *in vivo*. To study OC development *in vitro*, progenitor cells (OPC) from SHIP1-deficient $SHIP^{styx/styx}$ and control mice were cultured with RANKL and CSF-1. Osteoclastogenesis was assessed using an XTT cell viability assay and by determining TRAP activity. Furthermore, the capacity of OC to dissolve amorphous calcium phosphate (CaP) was determined.

Results: *In vivo*, BV/TV of vertebrae and femora of $SHIP^{styx/styx}$ mice was decreased compared to *wt* animals (40% and 35%, respectively, $p<0.01$). Trabecular number in vertebrae from $SHIP^{styx/styx}$ mice was increased by 26%, while thickness was decreased by 30% ($p<0.01$). In femora from $SHIP^{styx/styx}$, trabecular thickness was reduced by 25% ($p<0.05$), whereas trabecular number remained unchanged. *In vitro*, $SHIP^{styx/styx}$ OPC showed a 1.5-fold increased proliferation compared to controls ($p<0.001$), yet the number of OPC-derived OC was reduced by 40%. The capacity of $SHIP^{styx/styx}$ OC to dissolve CaP was decreased by 60% compared to controls ($p<0.001$).

Conclusions: Our data indicates a central role for SHIP1 in OC development and activity *in vitro*. The low bone mass phenotype in $SHIP^{styx/styx}$ mice, however, may be caused by reduced bone formation or by the wasting disease and systemic inflammatory condition characteristic of SHIP1-deficient mice.

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P127

Increased bone resorption in mice bearing WHIM Syndrome mutations does not rely on increased intrinsic OCL differentiation capacity

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WHIM Syndrome (WS) is a rare immunodeficiency caused by gain-of-CXCR4-function mutations affecting homologous desensitization of the receptor altering the lymphoid differentiation and blood leukocyte numbers. Taking advantage of a mouse model