into osteoclasts, that displayed a more motile phenotype and enhanced bone resorption activity (Resorbed Area/cell μm^2, HD: 886.7±61.2, GSD: 4100.0±938.8. p=0.01). Gene expression analysis of GSD osteoclasts revealed 106 modulated transcripts, 40 and 66 under- and over- expressed, respectively. These transcripts are involved in Beta-arrestin, PI3 Kinase and EGF receptor pathways. Moreover, large microRNA array of GSD osteoclasts revealed the upregulation of 3 miRNA involved in Metallopeptidase and PI3K activity. MSC from a patient did not show defect of osteogenic differentiation, whereas GSD-osteoblasts had impaired activity as shown by reduced mineralization and by altered pathways of bone morphogenesis and ossification modulation identified by transcriptomic analysis. GSD-osteoblasts had also an increased osteoclastogenic potential. miRNA analysis of GSD osteoblasts revealed a modulation of 12 miRNA involved in PDGFB signalling and NF-kB activity pathway.

Our results highlighted the molecular alterations in GSD patients and pave the way for the identification of molecular pathways that could be the target for new therapeutic approaches for GSD.

doi:10.1016/j.bonr.2020.100655

COP30

LIGHT as regulator of bone homeostasis during osteolytic bone metastasis formation in non-small cell lung cancer patients

Giacomina Brunetti[a], Dimas C. Belisario[b], Giuseppina Storlino[c], Graziana Colaianni[a], Lucio Buffoni[d], Giuseppe Ingravallo[c], Carl F. Ware[e], Silvia Colucci[a], Riccardo Ferracini[f], Maria Grano[c], Ilaria Roato[b]

[a]*Department of Basic and Medical Sciences, Neurosciences and Sense Organs, University of Bari, Bari, Italy*

[b]*Center for Experimental Research and Medical Studies (CeRMS), A.O.U. Città della Salute e della Scienza di Torino, Torino, Italy*

[c]*Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy*

[d]*Department of Oncological Sciences, University of Torino, Torino, Italy*

[e]*Infectious and Inflammatory Disease Center, Sanford Burnham Prebys Medical Discovery Institute, La Jolla, United States*

[f]*Department of Surgical Sciences (DISC), IRCCS, A.O.U. San Martino, Genoa, Italy*

Tumor necrosis factor superfamily member 14 (*TNFSF14*), LIGHT is one of the cytokines produced by tumor and immune cells, which promotes homeostasis of lymphoid organs, liver and bone. Non-small cell lung cancer (NSCLC) commonly metastasizes bone, altering bone homeostasis and causing osteolysis. Here we investigated the role of LIGHT in NSCLC-induced osteolytic bone disease.

The LIGHT expression in monocytes was higher in patients with metastatic bone lesions than in non-bone metastatic ones (66.5 ± 24.5 vs 43.3 ± 25.2 mean ± SD, $p = 0.001$), in healthy donors (66.5 ± 24.5 vs 8.5 ± 4.6 $p = 0.0002$), and in non-bone metastatic patients than in healthy donors (43.3 ± 25.2 vs 8.5 ± 4.6, $p = 0.0001$). Serum LIGHT levels were also significantly higher in bone metastatic patients than in non-bone metastatic ones (186.8 ± 191.2 pg/ml vs 115.8 ± 73 pg/ml, $p = 0.04$) and in healthy donors (186.8 ± 191.2 pg/ml vs 85.7 ± 38.4 pg/ml, $p = 0.04$).

A neutralizing mAb anti-LIGHT added to osteoclast (OC) cultures of both bone and non-bone metastases inhibited osteoclastogenesis, but the decrease was statistically significant only for bone metastatic patients (272 ± 98 vs 132 ± 74, $p = 0.01$). To investigate the role of LIGHT in NSCLC- induced bone lesion *in vivo*, we performed an intratibial injection of a mouse lung cancer cell line LLC-1, in wild-type (WT) and LIGHT KO mice. The WT-injected mice displayed a significant reduction of about 20% for BV/TV, Tb.N, Tb.Th, and Tb.Sp compared to the WT-vehicle mice (p< 0.01). These parameters did not show significant variation for KO-injected mice vs vehicle or for WT-injected mice vs KO-injected mice. These data indicate LIGHT as a regulator of bone homeostasis during NSCLC metastatic invasion, thus it may be a novel therapeutic target in osteolytic bone metastases.

doi:10.1016/j.bonr.2020.100656

Concurrent Oral Poster Presentations 1: Basic/ Translational

P001

Transcriptome analysis reveals potential biomarkers of *CLCN7*-dependent Autosomal Dominant Osteopetrosis Type 2 (ADO2)

Iona Norwood, Denis Szondi, Nadia Rucci, Anna Teti, Antonio Maurizi

DISCAB, University of L'Aquila, L'Aquila, Italy

ADO2 is a rare genetic disease characterized by dense yet fragile bones. To date, the radiological approach remains the gold standard for ADO2 diagnosis. However, recent observations unveiled that ADO2 is a systemic disease affecting various organs beyond bone, including lung, kidney, muscle and brain. Monitoring disease status and progression would greatly benefit from specific biomarkers shared by the affected organs. In this work, data derived from RNA deep sequencing (RNA-dSeq) of bone, lung, kidney, muscle, brain and osteoclasts isolated from wildtype and *Clcn7*^{G213R} ADO2 mice was subjected to Gene Ontology analyses, which identified shared modulated biological processes, molecular functions and cellular components, with Response to stimulus (p=4.26E-19), Cell communication (p=7.41E-17) and Extracellular space (p=3.34E-41) overrepresented in all ADO2 organs tested and in osteoclasts, and RNA processing (p=1.14E-06), Nucleic acid binding (p=3.70E-05) and Microtubule cytoskeleton (p=7.11E-04) underrepresented. KEGG pathway analysis also revealed the presence of common pathways altered in ADO2 organs and in osteoclasts, including Cytokine-cytokine receptor interaction (p=6.72E-06), Hematopoietic cell lineage (p=3.04E-05), JAK-STAT signaling pathway (p= 0.004), Chemokine signaling pathway (p=0.04), Protein processing in endoplasmic reticulum (p=0.006) and Ubiquitin mediated proteolysis (p=0.01). A deep analysis of the altered pathways allowed us to extrapolate a list of genes modulated in all ADO2 organs, including *Epor*, *Ccl8* and *Cd38* (p< 0.05), encoding the erythropoietin receptor, the monocyte chemoattractant protein 2 and the cyclic ADP ribose hydrolase, respectively. These genes were modulated also in circulating ADO2 monocytes (p< 0.05), thus representing potential candidate biomarkers of the disease. Given that monocytes give rise to osteoclasts and macrophages and that these two cell types are involved in ADO2 pathogenesis in bone and in visceral organs, respectively, we conclude that these transcriptional biomarkers could represent useful and inexpensive tools for ADO2 diagnosis and monitoring of disease status.

doi:10.1016/j.bonr.2020.100657

P004

Extracellular vesicles are new bone turnover diagnostic tools to discriminate osteoporosis induced by estrogen deprivation or by unloading

Alfredo Cappariello[a,b], Argia Ucci[b], Maurizio Muraca[c], Anna Teti[b], Nadia Rucci[b]

[a]*Children Hospital Bambino Gesù, Rome, Italy*

[b]*Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy*