POS0346
IDENTIFICATION OF NEW MUTATIONS IN THE SQSTM1 GENE IN PATIENTS WITH PAGET’S DISEASE OF BONE. GENOTYPE-PHENOTYPE CORRELATION
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Background: The Paget’s disease of bone (PDB) is characterized by a chronic and focal disorder of bone remodeling. PDB is currently considered a complex and multifactorial disease, as a result of a synergistic association of genetic variants with environmental risk factors. The genetic component of PDB is relevant to identify biomarkers associated with osteoporosis and fragility fracture versus without osteoporosis.

Methods: We analysed clinical data and bone marrow samples collected at diagnosis in SM patients from our Reference Centre for Maccerosis (CEREMAST) and fulfilling the SM WHO criteria. All patients signed an informed consent. Twelve SM patients with OP and fragility fracture (OP group) were age- and gender-matched with 12 SM patients without OP or fragility fracture (non-OP group).

Results: Both OP and non-OP groups included 8 women and 4 men, with similar average age (OP 56.1 +/- SD 8.7 vs non-OP 57.1 +/- 9.3). The 12 patients from the OP group had at least 1 vertebral fracture (VF) with an average number of VF of 4.9 +/- 2.6. Lumbar and hip bone mineral density was significantly lower in the OP group. The transcriptomic analysis revealed a specific profile associated with osteoporotic vertebral fractures in SM, with 26 differentially expressed genes (see Figure 1). The analysis highlighted an involvement of NECTIN2 and of IL6/STAT3. Pathway analysis suggested a role for genes involved in cell cycle regulation, T cell activation, protein kinase activity and differentiation and activation of monocyctic cells.

Conclusion: Our results highlight that a transcriptomic analysis of bone marrow is relevant to identify biomarkers associated with OP in SM. In addition to the pathogenic role of clonal mast cells and of monocytic lineage, this condition may involve non-clonal immune cells such as T cells.

Disclosure of Interests: Yannick Degboe Grant/research support from: Novartis grant, Arnaud Constantin: None

Acknowledgements: This work has been supported by the GRIOR (Groupe Français de Recherche et d’Information sur les Ostéoporoses)

Figure 1. Heatmap of the differentially expressed genes in bone marrow from SM patients with osteoporosis and fragility fracture versus without osteoporosis.

POS0347
CHARACTERIZATION OF THE TRANSCRIPTOMIC SIGNATURE OF BONE MARROW CELLS IN OSTEOPOROSIS ASSOCIATED WITH SYSTEMIC MASTOCYTOSIS
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Background: Systemic mastocytosis (SM) is a rare monoclonal mast cell disease, associated with vertebral osteoporosis (OP) in ~30% of the patients. This OP frequently leads to multiple vertebral fractures, in particular in young or premenopausal patients. Soluble mediators secreted by the pathogenic mast cells and subsequent activation of osteoclasts are thought to explain the development of such OP. However, data about the nature and the regulation of the pro-osteoporotic factors is limited. We hypothesized that a transcriptomic approach, assessing bone marrow cells involved in this pathological condition, can identify the specific determinants of fragility fractures in SM.

Methods: We analysed clinical data and bone marrow samples collected at diagnosis in SM patients from our Reference Centre for Maccerosis (CEREMAST) and fulfilling the SM WHO criteria. All patients signed an informed consent. Twelve SM patients with OP and fragility fracture (OP group) were age- and gender-matched with 12 SM patients without OP or fragility fracture (non-OP group).

Results: Both OP and non-OP groups included 8 women and 4 men, with similar average age (OP 56.1 +/- SD 8.7 vs non-OP 57.1 +/- 9.3). The 12 patients from the OP group had at least 1 vertebral fracture (VF) with an average number of VF of 4.9 +/- 2.6. Lumbar and hip bone mineral density was significantly lower in the OP group. The transcriptomic analysis revealed a specific profile associated with osteoporotic vertebral fractures in SM, with 26 differentially expressed genes (see Figure 1). The analysis highlighted an involvement of NECTIN2 and of IL6/STAT3. Pathway analysis suggested a role for genes involved in cell cycle regulation, T cell activation, protein kinase activity and differentiation and activation of monocyctic cells.

Conclusion: Our results highlight that a transcriptomic analysis of bone marrow is relevant to identify biomarkers associated with OP in SM. In addition to the pathogenic role of clonal mast cells and of monocytic lineage, this condition may involve non-clonal immune cells such as T cells.

Disclosure of Interests: Yannick Degboe Grant/research support from: Novartis grant, Arnaud Constantin: None declared, Adeline Ruys sen-Witrand: None declared, Carle Paul: None declared, Patrice Dubreuil: None declared, Cristina Bulai Livide anu: None declared

Acknowledgements: This work has been supported by a Novartis grant, Arnaud Constantin: None declared, Adeline Ruys sen-Witrand: None declared, Carle Paul: None declared, Patrice Dubreuil: None declared, Cristina Bulai Livide anu: None declared