Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Osteology and Biomechanics, Hamburg, Germany
[e]*University Medical Center Hamburg-Eppendorf UKE, Department of Trauma and Orthopedic Surgery, Hamburg, Germany*

Background: Bone marrow (BM) is a common homing organ for disseminated tumor cells (DTCs, the seed of metastases) derived from various types of malignant epithelial tumors, including breast cancer. Previously, we have shown that the presence of single DTCs in the BM is an independent predictor of metastatic relapse in breast cancer and that retinoic acid–induced 2 (RAI2) is a marker for early tumor cell dissemination to the BM. RAI2 was shown to not only being significantly associated with DTCs status but also poor prognosis, especially in hormone receptor positive tumors. The primary goal of this project is to better understand the precise role of RAI2 for the development of bone metastasis in breast cancer.

Methods: Xenograft models were established by injecting intracardial and orthotopically (mammary fat pad) RAI2 KO (CRISPR/Cas9 mediated RAI2 depletion) and parental KPL1 and MCF7 cells in immune deficient SCID/J mice. To investigate *in vitro* effect of RAI2 depletion in breast cancer cells on the BM cells, we performed osteoclast (OC) differentiation assays either using conditioned media (CM) or extracellular vesicles (EVs) from parental and RAI2 KO (MCF7 and KPL1) cells. Secreted proteins were analysed with Olink technology and NGS was performed on the miRNAS content of the EVs from the different cell line models.

Results: Increased tumour dissemination (numbers of CTCs and DTCs) was observed when RAI2 KO cells were injected versus the parental cell line. Besides, both CM and EVs from RAI2 KO cells significantly increase OC differentiation. Two secreted proteins and five miRNA candidates were identified to be involved in the crosstalk between tumour and bone cells.

Conclusions: RAI2 is a new metastasis suppressor gene inhibiting the dissemination of cancer cells in the BM through a crosstalk with OC.

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P086

Psychosocial impact of COVID-19 pandemic on cancer patients with bone metastases (PsyCO-B): a multicentre prospective observational study

Stella D'Oronzo[a], Francesco Salonne[a], Natasha Scardino[a], Stefania Stucci[b], Giulia Paparella[c], Paolo Taurisano[c], Chiara Abbatantuono[c], Maria Fara De Caro[c], Camillo Porta[a]

[a]*University of Bari Aldo Moro, Department of Biomedical Sciences and Human Oncology, Bari, Italy*
[b]*University Hospital Policlinico, Medical Oncology Unit, Bari, Italy*
[c]*University of Bari Aldo Moro, Department of Basic Medical Science-Neuroscience and Sense Organs, Bari, Italy*

Background: COVID-19 pandemic has affected our daily habits and quality of life (QoL). Cancer patients with bone metastases (BM) are among the most concerned individuals, due not only to their clinical condition as a primary cause of morbidity, but also to social distancing which compromises their psychological and relational well-being.

Purpose: To determine the psychosocial impact of COVID-19 pandemic on patients with BM.

Methods-Cancer patients with radiological and/or histological diagnosis of BM were enrolled following written informed consent. Six questionnaires were administered: Hospital Anxiety-Depression Scale; WHO QoL-BREF; Attitude Toward Seeking Professional Psychological Help; Brief Illness Perception Questionnaire; Brief COPE; Impact Event Scale-Revised. Clinical, pathological and socio-demographics were collected and analyzed by descriptive statistics. After selection of the co-variates by univariate analysis, regression models were developed for multivariate analysis. Statistical analyses were performed using SPSS software, and p-values≤0.05 were considered significant.

Results: The study was approved by Local Ethics Committee. Between October and December 2021, 23 patients were enrolled, whose median age was 62 (range: 34-83). Among primary tumors, the most common were breast (38%), renal (28%) and lung cancer (9%). In most cases (66.6%) BM had been diagnosed after the pandemic outbreak. A statistically significant association emerged between younger age and depression onset ($p<0.05$). Females had to cope with more "intrusive thoughts", and used religious coping strategies more frequently than males ($p<0.05$ in both instances). A significant correlation emerged between the burden of skeletal disease and QoL impairment ($p<0.05$). Finally, patients diagnosed with BM after the pandemic outbreak expressed a stronger need for psychological help ($p=0.01$).

Conclusion: These preliminary results show that receiving a diagnosis of BM during the pandemic negatively affected patients' QoL and increased their need for psychological support. Patient enrollment is still ongoing and will provide more accurate data to define an "identikit" of patient at high-risk of psychosocial distress.

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P087

Pre-osteoblasts and endothelial progenitors differently affect homing of breast cancer cells to the bone marrow

Franziska Wirth[a], Alexander Lubosch[a], Caren Zöller[a], Inaam Nakchbandi[a]

[a]*University Hospital Heidelberg, Institute for Immunology, Heidelberg, Germany*

Breast cancer cells home to the bone marrow, where they presumably hijack the hematopoietic stem cell niche. This niche consists of poorly defined stromal subpopulations. Our group found that a decrease in a stromal cell subpopulation increases cancer cell homing and metastatic lesions. We aimed to further characterize the components of the premetastatic niche and evaluate how they affect hematopoiesis.

Transgenic mouse models were used that express the osterix promoter attached to cre-recombinase (defining pre-osteoblasts and found in hematopoietic cells) or vav-cre (endothelial and hematopoietic cells). Mating these with mice carrying floxed genes allows deletion of fibronectin or b1-integrin in the population that expresses cre.

Using dtomato-reporter mice confirmed expression of osterix in 1% of bone marrow stromal cells. Deletion of fibronectin using osterix-cre diminished various stromal cell subpopulations ($p<0.001$, $N=55/40$), while the number of cancer cells that homed to bone marrow increased ($p<0.05$, $N=55/40$). Hematopoiesis was not affected. In contrast, deletion of b1-integrin, the main fibronectin receptor, did not affect stromal cells, cancer cell homing, or hematopoiesis. These data suggest that fibronectin originating from pre-osteoblasts supports other stromal cells and inhibits cancer cell homing.

Reporter mice showed that vav was expressed in 80% of stromal cells and all hematopoietic-stem-and-progenitor cells (HSPCs). Deletion of fibronectin using vav-cre neither affected cancer cell homing nor hematopoiesis. In contrast, loss of b1-integrin diminished stromal cells ($p<0.01$, $N=26/11$) and increased cancer cell homing ($p<0.05$, $N=28/11$), despite the rise in hematopoietic-stem-and-progenitor cell (HSPCs) numbers ($p<0.001$, $N=13/16$). Thus, in this case, cancer cell homing was enhanced even though hematopoietic stem cell niches were presumably occupied.

In summary, fibronectin from preosteoblastic cells acts on other stromal cells that presumably express vav and prevents cancer cell homing. Furthermore, cancer cells do not always hijack empty hematopoietic stem cell niches in the bone marrow.