

fibronectin motif) surfaces. However, only those exposing the IGDQ sequence induced significant migration of MDA-MB-231 cells. The observed migratory behaviour suggests the presence of cell subpopulations associated with a 'stationary' or a 'migratory' phenotype, the latter determining a considerable cell migration at the sub-cm length scale.

Material and methods We created gold-titanium (Au-Ti) surface and we coated them with a gradient of IGDQ-peptide and PSH (tetraethylenglycol) as a filler (PACMAN). The role of a5b1 and avb3 was studied using knockdown of b3 integrin using siRNA, shRNA and CRISPR/Cas9 strategies in MDA-MB-231 cells.

Results and discussions According to literature and to our previous results published in, Marega *et al*, *Small* (2016) we focus on the integrins a5b1 and avb3, already known to be implicated in cell migration, angiogenesis and resistance to cell death. They can be activated indirectly by EGFR pathway or directly by IGD type I fibronectin motif. Our preliminary results evidenced the implication of avb3 in distal migration and a potential compensatory system through a5b1 in shb3 cell line. Cells migrated following the motogenic peptide gradient. The fibronectin type I is implied in cell migration through the formation of focal adhesion with an activation of avb3 integrin.

Conclusion The influence of both integrin invalidation (alone or together) will be studied on cell migration in usual culture plates and on IGDQ-exposing surfaces. The subpopulations of native MADA-MB-231 cells with a 'stationary', 'intermediary' and a 'migratory' phenotype, obtained on PACMAN surfaces, are characterised using a single-cell RNA-sequencing in order to identify new pathways regulating the metastasis process (on going).

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LONG NON CODING RNA H19 (LNCH19) IS REQUIRED FOR THE HYPOXIA MEDIATED MULTIPLE MYELOMA PROGRESSION

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Introduction Multiple myeloma (MM) is a malignant disorder of post-germinal centre B cells, characterised by the clonal proliferation of malignant plasma cells within the bone marrow (BM). The hypoxic condition that develops in the BM niche during progression of MM, has been shown to play a major role in i) the dissemination of MM, ii) the proliferation of MM cells and iii) the induction of drug resistance finally determining a poor prognosis for MM patients. The molecular mechanisms driving hypoxic responses is the activation and nuclear translocation of the Hypoxia-inducible factor 1-alpha, (HIF1 α) that, in turns, induce the expression of genes controlling angiogenesis, hypermetabolism, stemnes maintenance, resistance to chemotherapy, and tumour metastasis. The lncRNA H19, an imprinted non-coding RNA which expression was found up-regulated in many tumours including MM, is among the targets of HIF1 α .

We previously attributed to the lncH19 a role into control of hypoxic response; in particular we demonstrated, in both glioblastoma and colon cancer, that the lncH19, is necessary and required to sustain HIF1 α activity. Here we propose to

investigate the role of lncH19 in hypoxia mediated MM progression.

Material and methods Transcriptional analysis (RT-PCR) of MM cell lines (RPMI and MM1S) exposed to normoxia or hypoxia (1% O₂) was done in order to evaluate lncH19 levels under hypoxic stimulation. To investigate the role of lncH19 in hypoxia mediated MM progression, transcriptional, protein and functional assays have been performed on MM cell lines, silenced or not for lncH19, under normoxia or 24 hour hypoxic stimulation in low oxygen chamber

Results and discussions Our data indicate that MM cell lines respond to hypoxic stimulation by HIF1 α nuclear translocation and activation of hypoxic responsive genes including the lncH19. Our data revealed that lncH19 silencing inhibits HIF1 α nuclear translocation with a subsequent reduction in the expression of hypoxia induced genes, associated to MM progression, such as snail and VEGF. Moreover, adhesion assay of MM cells on Mesenchymal Stromal Cells revealed that lncH19 silencing abrogates the increased adhesion induced by hypoxic condition.

Conclusion lncH19 is required for the induction of hypoxic responses in MM cells thus representing a new therapeutic target for MM. Further studies are required to better define the molecular mechanism through which H19 may control HIF1 α activity.

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IDENTIFICATION OF CANDIDATE GENES UNDERLYING SOFT TISSUE SARCOMA PROGRESSION USING A PROGRESSION SERIES OF MURINE FIBROSARCOMA CELL LINES

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Introduction Soft tissue sarcomas are known for their great variability in clinical behaviour, ranging from almost indolent lesions to rapidly metastasing tumours. Genes responsible for sarcoma progression have been poorly characterised by now. Towards this end, we established a unique single-background progression series of murine sarcoma cell lines, consisting of the slowly proliferating nonmotile and noninvasive cell line JUN-2, rapidly proliferating, motile and invasive cell line JUN-3, and the cell line JUN-2fos-3 that exhibits a unique transformation pattern, with little deregulation of cell growth and proliferation, but pronounced motility and invasiveness.

Material and methods This unique distribution of transformation related-traits made us possible to identify two separate groups of genes tentatively involved in sarcoma progression in a single transcriptomic analysis – on the one hand, proliferation-related genes could be identified by their differential expression in JUN-3 compared to both JUN-2 and JUN-2fos3, and, on the other hand, motility and invasiveness-related genes could be identified by their common expression pattern in JUN-2fos3 and JUN-3 cells compared to JUN-2. The high-throughput gene expression analysis has been performed using the GeneChip Mouse Genome 430 2.0 Array (ThermoFisher Scientific).

Results and discussions In total, we identified 277 upregulated and 212 downregulated unique transcripts in JUN-2 and JUN-2fos3 compared to the JUN3 cells (adjustP <10⁻⁴).