of the isolated exosomes, as well as to analyze their effect in functional assays.

0766 - EVIDENCES POINTING THAT BONE MARROW ORIGINATING TUMOR CELLS WITH LUNG COLONIZING ABILITY, RATHER THAN TUMOR CELLS REMAINING WITHIN THE BONE MARROW, ARE RELATED TO A MESENCHYMAL STEM CELL PHENOTYPE

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Abstract/Resumen: A critical challenge in the clinical management of osteosarcoma (OS) is the appearance of lung metastasis. This bone marrow – associated tumor represents the most frequent bone tumor in pediatric and young adult populations. In this context, 20% of OS patients are diagnosed with metastatic OS, but a high percentage of the remaining cases diagnosed without metastasis could already present micrometastasis undetectable through conventional methods. Our previous results indicated that a differential gene expression distinguished OS cells with higher ability to home into the lungs. Interestingly, molecular differences were subtle at the level of cellular content but more prominent at the level of the secretory compartment. These molecular features were reproduced by a functional behavior relevant to a colonizing ability to the lungs. In order to gain insight into spatial arrangements of OS cells that diverged in their lung colonizing ability, that may contribute to understand advantages to home into the lungs and could relate to metastatic mechanisms, we approached 3D OS cultures. We observed that OS cells that remain at the primary tumor site had lesser ability to establish 3D growth, while cells leaving the tumor and colonizing the lungs established 3D growth successfully; this last feature was shared by mesenchymal stem cells (MSC). This would point that cell-cell contact is a prominent feature in lung colonizing cells. Since our previous results demonstrated that the secretome of divergent OS cells is the compartment that mostly distinguished the ability to home into the lungs, we analyzed GOs in the secretory fraction in divergent OS cells and bone marrow MSC. MSC share the original niche where the bone tumor arises, and related to possible closeness between MSC and OS cells, we demonstrated that the cells that leave the primary tumor rather than the cells remaining at the primary niche of residence for OS, share similarity with MSC. This points at the necessity to target stem-like tumor cells that leave the tumor and colonize secondary sites. Conventional therapies to treat OS, which are directed to the primary tumor OS site, may be unsuccessful considering those stem-cell like OS populations residing in the primary site.

0770 - PARACRINE EFFECT MEDIATED BY EXTRACELLULAR VESICLES DERIVED FROM IGF-I OVEREXPRESSING HUMAN UMBILICAL CORD PERIVASCULAR CELLS IN A MURINE MODEL OF EXPERIMENTAL LIVER FIBROSIS

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Abstract/Resumen: Cirrhosis is the result of chronic liver damage/regeneration cycles and fibrosis accumulation. Human umbilical cord perivascular cells (HUCPVC) are mesenchymal stromal cells that could allow tissue regeneration by secretion of soluble factors and extracellular vesicles (EV). We previously demonstrated that HUCPVC engineered to produce insulin growth factor like-I (IGF-I-HUCPVC) ameliorate liver fibrosis in mice. Our aim is to evaluate the role of EVs in the therapeutic effect of IGF-I-HUCPVC in liver fibrosis. Conditioned media (CM) or EV depleted CM (DCM) were collected from HUCPVC infected with adenovirus codifying with IGF-I or green fluorescence protein (GFP). EVs were isolated from CM by differential centrifugation and characterized by electron microscopy, dynamic light scattering and flow cytometry to test shape, size and EV markers expression respectively. IGF-I levels were assayed in EV after lysis and/or dialysis by ELISA. Fibrosis was induced in BALB/c mice by administration of thioacetamide for 8 weeks (600 mg/kg/week). On week 6, IGF-I-HUCPVC and GFP-HUCPVC derived EV, CM or DCM were intravenously administrated (3 doses, 15 µg/dose/mice, every 5 days) and at week 8 liver samples were collected. Hepatic Stellate Cells (CFSC-G2 cell line) and hepatic macrophages (Mø) were incubated in vitro with EV, CM or DCM, and gene expression evaluated by qPCR. CFSC-G2 incubation with CM or EV derived from IGF-I-HUCPV downregulates the expression of COL1A2 and a-SMA in comparison with DCM-IGF-I-HUCPVC ($p<0.001$). Then, we found that lysis of dialyzed EV-IGF-I-HUCPVC results in an increase of IGF-I levels ($p<0.001$). In vivo, CM and EV derived from IGF-I-HUCPVC reduced collagen deposit while EV-depleted CM does not ($p<0.001$). In vitro, iNOS, IL-6 and TNF-a; are downregulated in Mø after treatment with EV-IGF-I-HUCPVC compared to controls ($p<0.001$). Our results showed that EV mediate the therapeutic effect of IGF-I-HUCPVC and ameliorates liver fibrosis.

0785 - TBX20 OVEREXPRESSION INDUCES CELL PROLIFERATION AND ANGIOGENESIS IN VITRO

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Abstract/Resumen: In the last years, several therapies aimed at myocardial regeneration have been investigated to treat acute myocardial infarction (AMI). To reach this aim, the main approaches are to induce neovascularization (angiogenesis) and myocardial self-regeneration (myocardiogenesis). It has been shown that the overexpression of TBX20 transcription factor in transgenic mice induces cardioprotective effects, suggesting that the overexpression of TBX20 could be a therapeutic alternative for cardiac regeneration. Our objective was evaluated the effect of the overexpression of TBX20 over cell proliferation and angiogenic induction in vitro. Baculoviral vectors overexpressing human TBX20 (BvTBX20) and control vectors (BVNull) were generated. Then, H9c2 cells were transduced with these vectors using a MOI of 300. At 2- and 5-days post-transduction cell proliferation was evaluated by MTS assay and cell count. Supernatants from transduced cells were used to perform a tubulogenic assay in HMEC cells. Cell proliferation rate was highest at 5 days post-transduction in the BvTBX20 group vs BvNull assessed by MTS assay (BvTBX20: 107 ± 1; vs. Bvnull: 100±1 % cell proliferation, $p<0.01$, t- test), and cell count (BvTBX20: 136,500 ± 15,256 cells; vs. Bvnull: 92,166 ± 11,250 cells, $p<0.05$, t-test). At 2 days post-transduction no significant differences were found. In the tubulogenic assay a higher amount of rings was found in the BvTBX20 group vs BvNull at 2 (4.34 ± 0.40 vs. 1.43 ± 1.28) and 5 days (7.35 ± 2.40 vs. 2.77 ± 1.04, $p<0.05$, t- test). Conclusion: The overexpression of TBX20 transcription factor increases cell proliferation in rat myoblast cell line H9c2 and promotes angiogenesis in vitro. These results suggest that TBX20 overexpression could be a therapeutic alternative for tissue regeneration.