0795 - STEM - ASSOCIATED FEATURES IN TUMOR CELLS ABLE TO COLONIZE SECONDARY TUMORAL SITES

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Abstract/Resumen: Osteosarcoma (OS), the most frequent bone tumor in pediatrics, presents critical clinical challenges in lung metastasis and chemoresistance emergence. Understanding OS switch into a metastatic phenotype and the interaction OS-stromal cells relevant in the new niche, would help in developing better diagnostic and therapeutic tools. In order to distinguish aspects that would allow OS cells to leave the bone niche and survive in a new tissue environment, we evaluated behavioral features acquired by OS cells with ability to establish secondary tumor growth in the lungs, approaching the degree of differentiation, doxorubicin (doxo) exclusion and distribution properties and molecular signatures. Our results indicate that lung-colonizing OS cells diminished its osteoblastic potential while modified the intracellular localization of chemodrugs. In this way, doxo switched from a nuclear to a cytoplasmatic distribution in cells with lung colonizing ability (0.884 ± 0.015 SAOS2; 0.546 ± 0.131 LM7). These features coincided with a higher level of expression of stem-related genes and lower expression of differentiation-associated markers even at basal conditions in the metastatic cells. On the other hand, the higher osteogenic activity of OS cells with non-colonizing features was even reflected as a paracrine osteo-inductive effect. In addition, OS cells with high and low lung-colonizing capacities have opposite impact in mesenchymal stem cells (MSCs). Further, OS cells colonized-mouse lungs had a greater chemoattractive induction on MSCs. A major acquisition in tumor cells with metastatic features is a switch into a stem-like state that could favor their survival in the pulmonary niche, opening new possibilities for specific chemotherapeutic schemes. We provide new insights on OS cells differing in lung homing ability, with particular emphasis on multidrug resistance and interaction with MSC, which would impact in early diagnosis and therapeutic management.

0841 - BACULOVIRAL VECTOR ENCODING MUTANT HIF-1ALPHA AS A POSSIBLE TREATMENT FOR PERIPHERAL ARTERIAL DISEASE

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Abstract/Resumen: Peripheral artery disease (PAD) is an ailment characterized by decreased arterial blood flow to the lower limbs. Given the lack of effective treatments, angio-arteriogenesis has been proposed. We hypothesized that the administration of a baculovirus encoding mutant HIF-1ALPHA (Bv.mHIF-1A) would induce collateral vessels neoformation in the ischemic limb. Methods: A. In vitro studies: 1) Transgene expression: Skeletal myoblast (SkM) isolated from rabbit adductor muscle were transduced with Bv.mHIF-1A at MOI= 100, and HIF-1A expression was evaluated by RT-qPCR and Western blot. 2) Angiogenic potential of transduced cells: the tubulogenic assay was performed with supernatants of SkM and SkM-mHIF-1A cultures. B. In vivo studies: 12 rabbits underwent sterile excision of the femoral artery of the left posterior limb. Seven days later, rabbits were randomized to receive in the ischemic muscle 10 injections containing 1E9 copies of the Bv.mHIF-1A vector (treated group, n= 6) or 1E9 copies of Bv.null (control group, n= 6). Two weeks post-treatment digital angiography was performed in both posterior limbs. HIF-1A mRNA levels in SkM-mHIF-1A cells was 1,000-fold higher than in non-transduced cells ($p<0.05$, t-test). HIF-1A protein levels were also overexpressed. Supernatants derived from SkM-mHIF-1A formed more tubular networks than those from non-transduced SkM cells (7.38 ± 0.69 vs. 4.99 ± 1.01 rings/mm², $p<0.01$; t-test). Finally, at 14 days post-treatment the density angiographyically visible collaterals was higher in Bv-mHIF-1A -traeated rabbits (8.12 ± 0.42 colaterales/cm²) than in those treated with Bv-null (6.13 ± 1.15 colaterales/cm²; $p<0.05$, t-test). Conclusion: The Bv.mHIF-1A induced angiogenesis in vitro and collateral vessels neoformation in the ischemic muscle of rabbits at 14 days after treatment. Further safety and efficacy studies at longer follow up periods are needed to estimate the potential usefulness of this approach in the clinical setting.

0845 - 3-D PRINTING OF OF BIODEGRADABLE SCAFFOLDS TO RESTORE SCAR TISSUE: PLA PROOF OF CONCEPT.

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Abstract/Resumen: Regenerative medicine (RM) has become relevant particularly because more than 150 million people worldwide have functional problems in tissues or organs. One of the strategies to restore function is the application of biomaterials with pre-administered cells. Materials to be used constitute one of the fundamental points in this process, since they positively or negatively influence the survival of the cells. One of the best known biomaterials is polylactic acid (PLA), a polyester that in the body degrades into lactic acid, which is easily removed. 3D printing is being applied in RM to address the need for tissues and organs suitable for transplantation, and implies additional complexities, not only because of the possibility of combining materials and cells, but also because of the possibility of incorporating growth and/or differentiation factors. We approached the feasibility of printing biologically plausible tissue structures for organ replacement using 3D printers and PLA as biomaterial. To this end we printed tubes as scaffolds that would substitute scar tissue. By Fusion 360 we designed tubes of 14.0 mm long (tolerance of ± 0.1 mm) and 5.4 mm in diameter (tolerance of ± 0.05 mm) of 1.72 mm thick PLA, that were sterilized by UV light. The printing was done on a modified Makerparts2 printer with a 0.2 mm diameter spout. Size, macrostructure and porosity would suit recellularization. We are currently approaching the use of fibroblasts to adhere to the scaffold to help in the regeneration process of the target tissue and provide anchoring for epithelial cells. Cells from excess, discarded tissue samples (surgeries at the Dermatology department, HIBA) will be used to anchor on the generated structures. The choice of resorbable materials that shape suitable artificial prosthesis (scaffold) is essential, allowing the biological system to function as a bioreactor using the scaffold as the structure from which the new organ will be reorganized.

0848 - HLA TYPING AS A QUALITY CONTROL FOR PURITY IN CELLULAR THERAPY PRODUCTS.