Characterization of calvarial stem cells toward the optimization of cranioplastic strategies

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OBJECTIVE:Background and aims. Mesenchymal stromal cells (MSC) are well-known bone progenitors within the bone marrow niche. This has been widely characterized in long bones developing through endochondral ossification, while fewer data are available on the biology of the skull bone osteogenic niche.
Craniofacial sutures provide a unique niche for MSCs for craniofacial bone homeostasis and repair.
Since surgical cranial remodelling is often associated with morbidities of variable degrees, the aim of this study was to characterize the calvarial MSC niche in human bone specimens, in order to identify suitable tool to implement and ameliorate the cranial reconstruction strategies.
MATERIAL-METHODS:Methods. Calvarial tissues were collected from surgical waste of patients undergoing cranial remodelling and served for MSC isolation. MSC isolated from bone marrow served as controls. MSC's immunophenotype was confirmed by flow cytometry. The following lineage-specific markers were analysed in MSC, under growth and osteoinductive conditions, by immunofluorescence and qPCR: THY1 (skeletal stemness-marker), GLI1 (putative calvarial stemness-marker), AXIN2 (mesenchymal cell fate determinant), TEK and ENPEP (bone marrow stem cells differentiation markers). MSC were also grown on a novel 3D-printed PMMA based support in order to study cellular viability and cytotoxicity (by MTT test).
RESULTS:Results. All calvarial MSC homogeneously expressed the THY1+/GLI1+/AXIN2+/ITGAV+/TIE2-/ENPEP- phenotype, indicating that explant cultures allow selecting comparable cell populations, regardless of the patient phenotype. Upon in vitro osteogenic induction, the expression of THY1 and GLI1 decreased, whereas AXIN2 levels increased, in calvarial-derived cells. MTT test highlighted a higher level of biocompatibility of the 3D-printed biomaterial. Indeed, the mortality of MSC cultured on the biomaterial was about 9% after 72 hours.
CONCLUSION:Conclusion. MSCs isolated from calvarial sutures expressed a specific marker profile. In particular, THY1+/GLI1+ representing the stem cells within the human calvarial niche. MSC could implement the efficacy of osteo-biomaterial for innovative therapeutic strategies exploitable for craniofacial bone remodeling.

Keywords: mesenchymal stromal cells, suture niche, craniofacial bone reconstruction, craniofacial surgery, bone regeneration

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