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Differential SOD2 and GSTZ1 profiles contribute to contrasting dental pulp stem cell susceptibilities to oxidative damage and premature senescence

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Abstract

Background: Dental pulp stem cells (DPSCs) are increasingly being advocated as viable cell sources for regenerative medicine-based therapies. However, significant heterogeneity in DPSC expansion and multi-potency capabilities are well-established, attributed to contrasting telomere profiles and susceptibilities to replicative senescence. As DPSCs possess negligible human telomerase (hTERT) expression, we examined whether intrinsic differences in the susceptibilities of DPSC sub-populations to oxidative stress-induced biomolecular damage and premature senescence further contributed to this heterogeneity, via differential enzymic antioxidant capabilities between DPSCs.

Methods: DPSCs were isolated from human third molars by differential fibronectin adhesion, and positive mesenchymal (CD73/CD90/CD105) and negative hematopoietic (CD45) stem cell marker expression confirmed. Isolated sub-populations were expanded in H₂O₂ (0-200 μM) and established as high or low proliferative DPSCs, based on population

doublings (PDs) and senescence (telomere lengths, SA- β -galactosidase, p53/p16^{INK4a}/p21^{waf1}/hTERT) marker detection. The impact of DPSC expansion on mesenchymal, embryonic, and neural crest marker expression was assessed, as were the susceptibilities of high and low proliferative DPSCs to oxidative DNA and protein damage by immunocytochemistry. Expression profiles for superoxide dismutases (SODs), catalase, and glutathione-related antioxidants were further compared between DPSC sub-populations by qRT-PCR, Western blotting and activity assays.

Results: High proliferative DPSCs underwent > 80PDs in culture and resisted H₂O₂-induced senescence (50-76PDs). In contrast, low proliferative sub-populations exhibited accelerated senescence (4-32PDs), even in untreated controls (11-34PDs). While telomere lengths were largely unaffected, certain stem cell marker expression declined with H₂O₂ treatment and expansion. Elevated senescence susceptibilities in low proliferative DPSC (2-10PDs) were accompanied by increased oxidative damage, absent in high proliferative DPSCs until 45-60PDs. Increased SOD2/glutathione S-transferase ζ 1 (GSTZ1) expression and SOD activities were identified in high proliferative DPSCs (10-25PDs), which declined during expansion. Low proliferative DPSCs (2-10PDs) exhibited inferior SOD, catalase and glutathione-related antioxidant expression/activities.

Conclusions: Significant variations exist in the susceptibilities of DPSC sub-populations to oxidative damage and premature senescence, contributed to by differential SOD2 and GSTZ1 profiles which maintain senescence-resistance/stemness properties in high proliferative DPSCs. Identification of superior antioxidant properties in high proliferative DPSCs enhances our understanding of DPSC biology and senescence, which may be exploited for selective sub-population screening/isolation from dental pulp tissues for regenerative medicine-based applications.

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Assessing the effect of human mesenchymal stem cell-derived conditioned media on human cancer cell lines: A systematic review

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Abstract

Background: Mesenchymal stem cells (MSCs) exhibit differential effect (augmentation or inhibition) on cancer cells depending on the tissue of origin. Given the increasing demand to use MSCs in regenerative medicine, it is vital to ensure that the MSCs being employed are not pro-carcinogenic.

Objective: To assess the effect of human MSC derived conditioned media (CM) on human cancer cell lines.

Materials and methods: PubMed, SCOPUS, and Web of Science were searched using the keyword combination 'human mesenchymal stem cell and conditioned media and human cancer cell line and in-vitro'.

Results: MSC-CM pro-carcinogenic molecules were IL-6, IL-8, FGF10, VEGF, PDGF, TGF- β 1, IGF-1, GRO- α , OSP, MMPs, TNF α , IL-4, IL-10, IL-13, IL-17, IL-1 β , G-CSF, MCP-1, MIP-1 α , MIP-1 β , RANTES, MIG, IP-10, HGF α , ETX, DKK1; anti-carcinogenic molecules were IFN- β , OST, LIGHT, FRTK3, INF- γ , IP-10, LAP, IL-1RA, IL-2, IL-5, IL-7, IL-12, IL-15, IFN- α , IFN- γ . Effector pathways were STAT 1, JAK2/STAT3, Ras-Raf-MEK-ERK, Wnt/ β -catenin, NF- κ B, ERK1/2, PI3K/ Akt/mTOR, MAPK/ERK. BMSC, ADMSC, UCMSC, WJMSC, DPMSMC, AMSC, and UTCMSMC had a differential effect on carcinogenesis. GMSMC, LMSMC, FDMSC were anti-carcinogenic. OMSMC was pro-carcinogenic.

Conclusion: Use of MSC-CM with a pro-carcinogenic effect must be restricted in cancer patients irrespective of the nature of the application.