FEATURES

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Tissue Engineered Early Tooth Development

Li Xiao and Takeki Tsutsui

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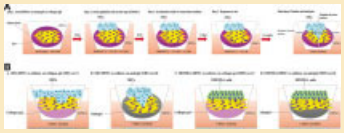

Epithelium invagination is the key feature of early tooth development. Although using oral epithelial stem cells and mesenchymal stem cells from a mouse embryo can rebuild a bioengineered tooth, information is not yet available concerning the use of human adult epithelial and mesenchymal cells to represent early tooth development. In the work by Xiao and Tsutsui, in this issue, the authors built a three dimensional model to represent an epithelium invagination-like structure using human normal oral epithelial cells (OECs) and dental pulp stem cells (DPSCs). When OECs and DPSCs were co-cultivated on matrigel for about 4 weeks, typical invagination of epithelial cells and condensation of the underlying mesenchymal cells were observed. Epithelial invagination related molecules, CD44 and E-cadherin, and mesenchymal condensation involved molecules, N-cadherin and Msx1 expressed at a high level in the tissue model, suggesting the epithelial invagination is functional. The authors' findings also point out that to reconstruct the epithelium invagination, special scaffolding (such as matrigel) and epithelial cell type are important (e.g. immortalized human oral epithelial cells NDUSD-1, which did not express p75, Shh and Wnt10b, could not form epithelium invagination under the same conditions).

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hWJSCs Do Not Transform to Tumor-Associated Fibroblasts

Arjunan Subramanian, Gan Shu-Uin, Ngo Kae-Siang, Kalamegam Gauthaman, Arijit Biswas, Mahesh Choolani, Ariff Bongso, and Fong Chui-Yee

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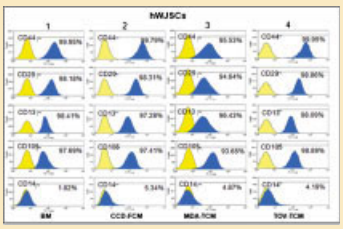

Human bone marrow mesenchymal stem cells (hBMMSCs) were shown to transform into tumor-associated fibroblasts (TAFs) when in the vicinity of breast cancer tumors and play an important role in tumor enhancement and metastasis. Do MSCs from Wharton's jelly of the umbilical cord (hWJSCs) behave the same? In comparative studies, Subramanian et al. showed that hWJSCs do not transform into TAFs when exposed for 30 days to breast (MDA) and ovarian (TOV) cancer cell conditioned media (CM) but hBMMSCs transformed from short to thin long fibroblasts, proliferation rates increased, CD marker expression decreased and they showed positive staining for the tumor-associated markers FSP, VEGF, EGF and Tn-C. Real-time PCR and multiplex luminex bead analysis of the hBMMSCs showed upregulation of TAF-related genes (FSP, FAP, Tn-C, Tsp-1, EGF, bFGF, IL-6, a-SMA, VEGF and TGF-ß). Subramanian et al. further confirmed from the luciferase assay that hWJSCs previously exposed to MDA-CM and TOV-CM for 30 days had no stimulatory growth effect on luciferase-tagged MDA or TOV cells unlike hBMMSCs. The results concluded that hWJSCs do not transform to the TAF phenotype and may not be associated with enhanced growth of solid tumors making them a potentially safe choice of MSCs for cell based therapies.

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Sex and Age are Important Influences in Stem Cells

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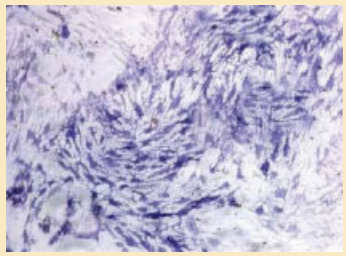
Scientists have found that cell sex is a variable that considerably influences the regeneration abilities of muscle-derived stem cells (MDSCs). This evokes some fundamental and interesting problems of whether cell sex influences a stem cell's other biological characteristics and whether there are any other variables which may also influence a stem cell's biological characteristics. Wang *et al.* comprehensively compare the biological characteristics of human adipose tissue-derived stem cells (H-ADSCs) in two variables: cell sex and cell age. Their results show that the sex of H-ADSCs influences their proliferation, differentiation, paracrine and anti-apoptosis abilities, and the age of the H-ADSCs' host may influence the cells' differentiation and anti-apoptosis abilities. Wang *et al.* provide novel insight into stem cells' self characteristics which may help to explain the broad heterogeneity that has been reported in other stem cell populations. Further study is needed to determine if similar results will occur in vivo.



Wharton's Jelly Stem Cell Inhibition in Multiple Cancer Cell Types

Kalamegam Gauthaman, Fong Chui Yee, Suganya Cheyyatraivendran, Arijit Biswas, Mahesh Choolani, and Ariff Bongso

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Wharton's jelly stem cells (WJSCs) were shown to abolish breast cancer cells (MDA-MB-231) in vitro and in animal models. Is this tumour inhibitory activity specific to breast cancers alone and can it be mediated via non-cellular contact using WJSC extracts? Gauthaman et al. show that human Wharton's jelly stem cell conditioned medium (hWJSC-CM, 50%) and lysate (hWJSC-CL, 15µg/ml) inhibit breast adenocarcinoma (MDA-MB-231), ovarian adenocarcinoma (TOV-112D) and osteosarcoma (MG-63) cells in vitro. Cell shrinkage, blebbing and vacuolations were observed in the cancer cells and MTT, BrdU and Transwell migration assays showed inhibition of cell growth by hWJSC-CM and hWJSC-CL. Cell cycle assay showed increases in sub-G1 and G2/M phases suggestive of apoptosis and metaphase arrest. AnnexinV-FITC and TUNEL positive cells seen in TOV-112D and MDA-MB-231 suggested that inhibition was via apoptosis while anti-BECLIN1 and anti-LC3B antibodies seen with MG-63 indicated autophagy. Up-regulation of pro-apoptotic BAX and down-regulation of anti-apoptotic BCL2 and SURVIVIN genes were observed in all three cancer cell types and the autophagy genes (ATG5, ATG7, BECLIN1) were up-regulated in MG-63 cells. Gauthaman et al. concluded that hWJSCs possess tumour inhibitory properties not exclusive to breast cancer cells alone and these effects could be mediated via hWJSC extracts.