Wharton's Jelly-derived Mesenchymal Stem Cell - Conditioned media induces apoptosis of pancreatic cancer

Neha Chopra
Sir Ganga Ram Hospital, India

Pancreatic cancer has an extremely poor prognosis, due to not only being a highly complex and aggressive malignancy but also due to its chemo-resistance. Stem cell-based treatments are being increasingly explored especially for those cancers that cannot be treated with targeted therapy. In the last decade, Mesenchymal Stem Cells (MSCs) have attracted significant attention as a result of their accessibility, tumor-oriented homing capacity and the transplantation feasibility. Till date, MSC-based therapy for pancreatic cancer has not been demonstrated.

To study the interaction between human Wharton's jelly-derived mesenchymal stem cells (hWJMSCs) and pancreatic cancer cells, co-culture assays were performed (ratio of 1:1; 48 hrs). An inverse proportionate expression of Bax and Ki67 was observed when MiaPaCa-2/PanC-1 was treated with hWJMSCs (32.5% and 13% respectively). To verify these results, PKH-26 -labeled hWJMSCs were overlaid on pancreatic tumor cells (1D). It was observed microscopically that PKH-26 -labeled hWJMSCs proliferated two-fold in comparison to tumor cells. The effect of MSCs directly affecting the pancreatic tumor cell was reconfirmed with a proliferative marker Ki67. Functional properties EpCAM/CXCR4 (metastatic markers), Vimentin & E-cadherin (EMT markers) were evaluated using Flow cytometry and qPCR. EpCAM was significantly ($p=0.0002$) decreased when treated with hWJMSCs in comparison to untreated tumor cells (MiaPaCa-2- 23% vs 37%; PanC1- 20% vs 50%). However, no significant change in CXCR4 expression was observed.

To understand the cellular cross-talk between hWJMSCs and pancreatic tumor cells, the conditioned media derived from hWJMSC (CM) was studied. Expression of Bax was significantly further increased (58%) when treated with CM in comparison to hWJMSCs alone (32.5%). However, inhibition of EpCAM expression did not differ from hWJMSCs alone treatment. Migration and invasion potential of tumor cells were inhibited when treated with CM (MiapaCa-2- 2.2 vs 9 cells/field; PanC-1- 5 Vs 10.5 cells/field), compared to untreated tumor cells. On frequency distribution histograms (flow cytometry) apoptotic events were characterized by a distinctive "sub-G1" peak that represents oligonucleosomal DNA fragments. MiaPaCa-2 and PanC1 cells treated with CM showed significant ($p<0.005$) reduced number of cells entering G1 phase of the cell cycle ie., at G0M phase. This result was also evident as per DNA-fragmentation assay.

Thus, our results suggest that Wharton's jelly derived mesenchymal stem cells secretome can modulate the proliferation and migratory (oncogenic) capabilities of pancreatic tumor cells. In other words, paracrine factors released by hWJMSC might be act as a cytotoxic biological agent.

Biography

Neha Chopra is pursuing her PhD from Jamia Hamdard in association with Sir Gangaram hospital, New Delhi. She was a university topper in post graduate program and presently a DST-INSPIRE fellow. Her work from post graduate thesis is under publication in an international journal. She has presented her PhD research work at national and international conferences (AACR). She has co-authored a book chapter and currently in process of submitting 2 original research papers.

neha.bioresearch@gmail.com