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Development of mesenchymal stem cell (MSC) therapies for cancer with 3-D culture systems

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Mesenchymal stem cells (MSCs) have many potential applications in cancer therapy. In particular, there is interest in exploiting the notable tumor-tropic properties of MSCs to deliver anti-cancer factors directly into tumors. Previously we reported that when MSCs are prepared as spheroids in 3-D hanging drop cultures, expression of tumor-suppressive factors (TRAIL, IL-24, CD82) was augmented and MSC size was effectively reduced resulting in improved vascular mobility and tumor-homing potential of the cells. Therefore, here we tested the effects of MSCs in spheroids on growth and phenotype of various cancer cells.

Within hanging drop co-cultures of MSCs and breast cancer cells (BCCs), the MSCs rapidly surrounded the BCCs and promoted formation of cancer spheroids then disappeared 24-48 hours later. Further experiments revealed that BCCs internalized and degraded MSCs in spheroids, a process resembling cell cannibalism/entosis. The resulting BCCs showed markedly delayed tumorigenicity after injection into mice and displayed features of cellular dormancy. Moreover, sphere-derived MSCs (SDMs) delivered intravenously effectively reduced growth of breast cancer metastasis in lungs of mice. Importantly high cell viability, small cell size, and elevated expression of tumor-suppressive factors were not diminished with cryopreservation of SDMs suggesting that cell banks can be prepared for 'off-the-shelf' patient therapies. The results here provide new insight into the interactions between MSCs and cancer cells and indicate that MSCs prepared as spheroids have enhanced tumor-suppressive properties. Collectively, 3-D cultures of MSCs and cancer cells are useful to model the tumor niche in further research and to effectively precondition MSCs for cancer therapies.

Biography

Thomas Bartosh completed his PhD degree in Cell Biology and Genetics from The University of North Texas HSC. He joined the Institute for Regenerative Medicine (IRM) at Texas A&M University in 2008 to develop therapies with mesenchymal stem cells (MSCs). Currently, he an Assistant Professor of Internal Medicine and Director of flow cytometry and microscopy at the IRM. He studies the advantages of using three-dimensional (3-D) culture methods to activate MSCs and exploit their inherent therapeutic potential. This approach was pioneered by Dr. Bartosh at the IRM and has been highlighted in numerous publications.

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