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Extracellular mechanical forces ruling the stem-ness of human adult mesenchymal stem cells

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Stem cells are at the center of expectations for regenerative medicine. We may be able to develop new and more potent regenerative therapeutics strategies if we can decipher the extracellular-intracellular mechanisms responsible for developmental patterning in the embryo and adult. Mechanical forces can switch cell fate between growth, differentiation and death. It has been shown that most mechanical signaling pathways are induced and mediated by integrin receptors and integrin linked kinases. Regenerative capacity of a tissue relays on quiescent stem cells resident within the tissue. Different approaches have been introduced to utilize this capacity from different tissues. Adipose derived stem cells are a heterogeneous population of cells with multi-potent regenerative capacity. In this study we demonstrated how different methods of separation of cells from lipoaspirate can greatly affect their regenerative capacity.

Methods: Enzymatic separation was performed on lipoaspirate using four different enzymes from three different companies. For mechanical separation we used an ultrasonic instrument manufactured by Sonics. We compared cell number per gram of lipoaspirate, apoptosis, colony forming unit capacity, cell surface marker expression, integrin expression and senescence index between groups and within groups. We analyzed data using ANOVA-PAST statistical program. Data presented are mean+/- SE (N=16 and n=3).

Results: 1- Enzymatic separation performed by Collagenase I manufactured by BioSpecifics yields statistically significant fewer cell number per gram of fat tissue $p<0.05$, but no statistically significant differences in CFU-f numbers. 2- Enzymatically and mechanically separated cells expressed very low levels of hematopoietic markers and high levels of mesenchymal stem cell markers. 3- Enzymatically separated cells expressed B1-Integrin and CD54 >60% and >30% respectively. 4- Mean of C12FDG fluorescent, a senescence marker, was 32+/- 6.7 in cells separated enzymatically, compared to the positive control 2456+/- 122. 5- In mechanical separation smaller tips, higher amplitudes and longer impulses induce cell death. 5- Mechanical separation yields statistically significant less cell number per gram of fat tissue compared to enzymatic separations ($p<0.005$), cells are not plastic adherent, do not form CFU-f and lose expression of B1-integrin and CD54 irreversibly.

Conclusion: The field is still young and it seems likely that cellular therapies using autologous stem cells will be effective for certain conditions. Utilization of the regenerative capacity of adult stem cells requires diligent confirmation of all processes if the ultimate goal is to preserve their full regenerative capacity for therapeutic strategies

Biography

After completion of her PhD in 2003, Maryam Niapour succeeded to a fellowship in Acute Myeloid Leukemia Research at University of Toronto in 2005. She is currently scientific director of a state-of-art clinical research faculty in Toronto, leading two clinical trials projects. Her research interests are focused towards the development, assessment and validation of therapeutic strategies for regenerative medicine including cellular therapies with adult mesenchymal stem cells. Since2007, she has published nine peer reviewed scientific papers and has presented in numerous national and international seminars

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