THE EFFECTS OF HYPOXIA- INDUCIBLE FACTOR-1 α (HIF-1α) ON THE PROLIFERATION AND MIGRATION OF HUMAN ADIPOSE DERIVED MESENCHYMAL STROMAL CELLS IN VITRO

Amirah Mahfuzah Zulkifli[1], Nam Hui Yin[1], Tunku Kamarul Zaman Tunku Zainol Abidin[1]

[1]Universiti Malaya

Introduction: Mesenchymal stromal cells (MSCs) are a promising source for therapy. However, long-term in vitro culture and expansion may result in reducing MSCs-efficacy. MSCs resided in a stem-cell niche microenvironment, characterized by the presence of low oxygen concentration via the activation of hypoxia-inducible factor 1 alpha (HIF-1α). HIF-1α stabilization is known to improve cell functions including cell adhesion, migration, and proliferation. Yet, the role of HIF-1α in adipose-derived MSCs (ADMSCs) activity is not fully elucidated. In the present study, we examined the effects of cobalt chloride (CoCl2), a hypoxia mimetic mediator, on the migration and proliferation of ADMSCs in vitro.

Methodology: MSCs from fat pads were isolated and expanded until passage-2. The cells were characterized using their surface markers and differentiation potential. Different CoCl2 concentration (0-400μM) was added to the culture for 24, 48, and 72 hours. At different time points, cell morphology was analyzed, and cell proliferation was assessed using alamarBlue® assay. Cell migration was examined using the wounding assay.

Results: The ADMSCs used in this study fulfilled the minimal criteria of MSC based on 1) their plastic adherence, 2) exhibit expression of CD90 and CD105 while lacking expression of CD34 and CD45, 3) able to undergo tri-lineage differentiation, namely adipogenic, osteogenic and chondrogenic. Our results show that cell proliferation of ADMSCs was enhanced when 100μM was applied, most notably after 24 hours. There is no difference in cell morphology between the groups, but the cells appear to have detached at higher concentrations of CoCl2. The cells also migrated faster under CoCl2 treatment.

Conclusion: This study suggests that HIF-1α, induced by CoCl2 treatment, can influence the behavior of ADMSCs and promote superior cell proliferation at specific levels. These findings may provide evidence supporting the use of in vitro hypoxic environments mimicked by CoCl2 in improving tissue engineering applications.