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Study of miRNA-146a as a down regulator of CXCR4 expression in acute myeloid leukemia

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CXCR4/CXCL12 interaction plays an important role in both homing and retention of hematopoietic stem cells in the bone marrow. Leukemic cells express high levels of CXCR4, which supports their growth and survival in the bone marrow. Antagonism of CXCR4 mobilizes stem cells into the bloodstream e.g., by AMD3100. MiRNA-146a is one of the miRNAs most down-modulated in AML blasts. A highly significant inverse correlation between miR-146a expression and CXCR4 membrane protein level was found. Thus, up-regulation of MiRNA-146 may lead to down-regulation of the CXCR4 protein levels. 36 de novo AML cases were subjected to immunophenotypic characterization of surface and cytoplasmic expression of CXCR4 of isolated leukemic cells. 24-hour stimulation with Vitamin D3 and AMD3100 was done followed by re-estimation of surface and cytoplasmic expression of CXCR4. Cells were cultured in special in vitro cell migration assay wells to detect effects of drugs on migration. The miRNA146a gene expression by real time PCR quantitation in leukemic cells before and after stimulation with vitamin D3 and AMD3100 was performed. AMD3100 increased miR146a expression which in turn down modulated CXCR4 expression. Vitamin D3 also increased miRNA expression but less significantly. There was no statistically significant difference between effects of AMD3100 and Vitamin D3 on CXCR4 expression and cell migration. This suggests that Vitamin D3 may be considered as an alternative to AMD3100. Further research will indicate if Vitamin D3 can be used as an adjuvant therapy to increase mobilization of leukemic stem cells from the bone marrow and improve response to chemotherapy.

Biography

Nouran Nabil Momen has completed her Master's degree in Clinical and Chemical Pathology from Kasr Al Ainy School of Medicine, Cairo University and has recently completed her Doctorate degree (MD) in Clinical and Chemical Pathology from Kasr Al Ainy School of Medicine, Cairo University, Egypt.

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