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STROMA-LEUKEMIA INTERACTION STUDIES

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The bone marrow niche is comprised of endothelial cells, osteoblasts, osteoclasts, perivascular cells and MSCs. The population comprising of all these cells play an important role in growth and maintenance of hematopoietic stem cells (HSCs). The various signaling molecules secreted by MSCs including cytokines, chemokines help in control and development of hematopoietic stem cells. Various life threatening cancers such as leukemia and multiple myeloma are characterized by the aberrant production, differentiation and inability of HSCs to undergo apoptosis (1). The communication between HSCs and MSCs is responsible for survival of leukemic cells after chemotherapy and further altering their phenotype. The properties of MSCs also gets altered by the cross communication between HSCs and MSCs. A number of medications have been developed based on the interacting molecules involved in MSCs-HSCs interactions which have been used for the treatment of variety of hematological disorders including leukemia(2). To study the interactions between MSCs and HSCs, two cell lines, HL60 and THP1, were used to investigate the influence of cell-cell contact between leukemic cell lines and MSCs. HL60 is a cell line from a human Caucasian promyelocytic leukemia patient with a bad prognosis. THP1, a cell line for acute monocytic leukemia, is in the intermediate to poor prognosis group of AML. The differentiation of MSCs were examined after 7 days of co-culture with a leukemic cell line, and it was found to be controlled by the immediate microenvironment provided by the leukemic cell lines leading to decrease in differentiation potential (3). In addition to that the expression of MSC characterization markers CD73, CD90, CD105 as well as adhesion markers such as integrins CD44, CD49D, CD49E involved in migration, attachment to extracellular matrix and other important cellular functions were also studied. The adhesion of MSCs was found to be increased after interaction with leukemic cells. Similarly, cell-cell mediated signaling between MSCs and leukemic cells was involved in changing the expression integrins as CD49D, CD49E. Direct cell-cell contact signaling between MSCs and cell lines also influenced the drug sensitivity of the leukemic cell lines. From the experiments conducted it was concluded that the microenvironment provided during the coculture of leukemic cells and MSCs regulates the phenotypic and other properties of the leukemic cell and vice versa.

References

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