Differentially Expressed Genes and their Functional Relationships in a Blast-Mesenchymal Cell Co-Culture Model.

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The reciprocal interactions between tumor cells and their microenvironment have been shown to modulate tumor growth, survival and metastasis. In Acute Lymphoblastic Leukemia the bone marrow stroma plays essential roles for tumor maintenance, as illustrated by the fact that the leukemic blasts die faster without its support *in vitro* and that it is the primary site where residual leukemic cells survive during cancer treatment. This study aims to identify the survival signals received by leukemic blasts from stromal cells, in order to find pathways that could be important as targets for cancer therapy. To achieve this objective we performed global gene expression analysis of leukemic blasts co-cultured with mesenchymal cells and of blasts alone. The microarray data were analyzed using RMA algorithm and the differentially expressed gene list was subsequently submitted to gene ontology analysis, followed by a pathway analysis. This strategy led to the identification in leukemic blasts of genes belonging to key cellular processes which are related to cell motility and migration, proliferation, tissue remodeling and epithelial to mesenchymal transition. The mesenchymal cells did not show significant changes in the gene expression profile. The results indicate that the contact between leukemic blasts and mesenchymal cells induces alterations in the expression profile of the blasts that promote survival, and additionally, that the survival signals are not mediated by soluble factors delivered by the mesenchymal cells. Key genes identified with altered expression in the blasts were selected and their differential expression will be confirmed by qRT-PCR.

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