

ORAL PRESENTATION

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Differentially expressed genes responsible for insensitivity of CD34+ cells to kinase inhibitors in patients with chronic myeloid leukemia

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Background

Chronic Myeloid Leukemia (CML) is a clonal myeloproliferative disorder characterized by formation of *BCR-ABL* fusion that encodes the p210 oncoprotein, which has a tyrosine kinase activity that confers an adaptive advantage to leukemic cells. Imatinib mesylate (IM) acts specifically on p210. Imatinib is able to reduce the differentiated cells (CD66b+) efficiently, but it has not the same effect on the stem cells (CD34+), which can be kept alive during treatment. Our aim was to identify expressed genes in CD34+ and CD66b+ cells as candidates for kinase inhibitors transport.

Materials and methods

CD34+ and CD66b+ cells were isolated from bone marrow (BM) and peripheral blood (PB) of five patients with CML, in optimal response, and 1 control. The samples were sequenced on SOLiDTM platform for whole transcriptome analysis. We analyzed the Gene Ontology annotation, and the software Cufflinks were used to identify the differential expression of genes in patients (BM x PB) and controls (BM x PB).

Results

In pooled patient samples, we identified the expression of *SLC22A1* influx gene in both, BM and PB samples, without any significant change ($p \leq 0,05$), and expression of *SLCO1A2* influx gene only in PB sample. Thus its presence could not be identified in any of the control samples. The overexpression of ABC efflux gene family (*ABCB1*; *ABCG2*; *ABCC1*), were found only in BM cells of patients.

The presence of other two genes responsible for the drug efflux was also found exclusively in BM pool sample of patients, *SLC47A1* and *SLC47A2*.

Conclusions

Over-representation of drug influx and absence of drug efflux channels in mature cells, and the reverse in stem cells of patients with CML may explain the insensitivity of CD34+ cells to IM treatment and consequent failure to eliminate minimal residual disease.

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