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Expression of angiotensin-converting enzymes (ACE, CD143) and shaperons (BiPs, calnexin, calreticulin) by leukemic dendritic cells (LDCs) in acute myeloid leukemia (AML) patients

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Abstract

Background: DCs play a key role in the immune response. LDCs and DCs are characterized by high levels of co-stimulatory molecules. The difference between LDCs and DCs is a high expression of surface ACEs on DCs.

Aim: To confirm the block of ACE transport to surface LDCs, controlled by shaperons, we quantified the intracellular and surface ACE, BiP, and mRNA expression levels of ACE and BiP, calnexin, calreticulin in DC and LDC were measured.

Methods: Blood samples were collected from 12 AML patients and 10 donors. Mononuclear cells were differentiated into DCs by culturing with 180 n?g/ml calcium ionophore for 4 days at 37°C and 33°C (activated shaperons). Stained surfaces, intracellular ACEs (2 mAbs-clones 1D8, 9B9) and BiPs (mAb KDEL) were analyzed by flow cytometry. MRNA expression levels of ACEs, BiPs, calreticulin, and calnexin were evaluated with RT PCR.

Results: The surface ACEs on LDCs at 37°C was 3±2% (mAb9B9), 2% (mAb1D8), and BiPs 6%, at 33°C 45±10%, 57±8%, and 63±7%, respectively; on DCs at 37°C it was 46±9%,5±2%, and BiPs 36±4%, at 33°C 34±3%, 6±2%, 21±4%, respectively.

The intracellular ACEs in LDCs at 37°C was 71±9%, 52±8%, and BiPs 92±7%, at 33°C 6±2%, 5±2%, 52±6%, respectively; in DCs at 37°C was 50±10%, 27±7%, BiPs 69±7%, at 33°C 40±10%, 33±7%, 88%, respectively. Gene expression was measured by RT PCR using the TaqMan procedure and calculated in relative units using GAPDH expression for normalization. The expression of ACEs increased in 4 out of 7cases in DCs at 33°C compared to DCs at 37°C, and in 8/9 cases of LDCs at 33°C compared to LDCs at 37°C. The expression of BiPs increased in 6/8 cases in DCs, and in 3/6 cases of LDCs. For calnexin, appropriate measures showed 6/8 for DCs, 3/6 for LDCs; for calreticulin 2/8 for DCs, and 3/6 for LDCs, respectively.

Conclusion: The data demonstrates the block of ACE transport to the surface of LDCs at 37°C and the different reactions of LDCs and DCs in stress conditions (33°C increased surface ACEs, BiPs, and ACE gene expression by LDCs).

Keywords: Acute myeloblastic leukemia, AML, dendritic cells