Upregulation of CD200 is associated with Foxp3\(^+\) regulatory T cell expansion and disease progression in acute myeloid leukemia

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Received: 19 September 2012 / Accepted: 30 October 2012 © International Society of Oncology and BioMarkers (ISOBM) 2012

Abstract Immunosuppression in acute myeloid leukemia (AML) is an important mechanism of tumor escape. CD200, as an immunosuppressive molecule, is overexpressed in some hematological malignancies and it has also been shown to be an independent prognostic factor in AML. In the current study, simultaneous CD200 expression and Foxp3\(^+\) regulatory T cell levels were investigated in Iranian patients with AML by flow cytometry. We also assessed the effect of CD200–CD200R blockade on Th1 and T-reg cytokine production and T cell proliferation in autologous AML- and monocyte-DC mixed lymphocyte reactions (MLRs). ELISA assay was performed to detect IL-2, IL-12, IFN-\(\gamma\), IL-10, and TGF-\(\beta\) production in MLR supernatants. Expression of Foxp3, IL-10, and TGF-\(\beta\) mRNAs in MLRs were detected by real-time PCR. Our results demonstrated significant overexpression of CD200 \((P=0.001)\) in association with higher frequencies of Foxp3\(^+\) T cells in AML patients \((r=0.8, P<0.001)\). Blocking of CD200–CD200R interaction demonstrated a significant decrease in TGF-\(\beta\) and IL-10 expression in AML-DC MLRs and a significant increase in IL-12 and IFN-\(\gamma\) expression in monocyte-DC MLRs. Elevated T cell levels with lower Foxp3 intensity was also shown in CD200–CD200R-blocked MLRs. Expression of IL-10 mRNA declined significantly only in AML-DC MLRs where CD200–CD200R interaction was blocked and the same result was observed for TGF-\(\beta\) and Foxp3 mRNA in both AML- and monocyte-DC MLRs. These data present a significant role for CD200 in suppressing anti-tumor immune response through stimulation of regulatory mechanisms in AML patients and suggest that CD200 may have a prognostic value in this malignancy and its blockade may be used as a target for AML immunotherapy.

Keywords CD200 · Acute myeloid leukemia · T-reg · Immunosuppression · Disease progression

Introduction

Acute myeloid leukemia (AML) is a hematopoietic malignancy of the myeloid lineage, characterized by increase of precursor cells in the bone marrow (BM) and peripheral blood (PB) [1]. Although chemotherapy is administered, more than 50% of AML cases go into relapse [2–4].