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LETTER TO THE EDITOR

mPGES-1 in leukemic cells of AML patients

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We read with a great interest the article by Li et al. [1] demonstrating the mechanism leading to MK886-induced apoptosis in HL-60 cells [a human acute myelogenous leukemia (AML) cell line] by downregulation of microsomal prostaglandin E synthase-1 (mPGES-1) and, thus, reduced prostaglandin E_2 (PGE_2) synthesis. Authors indicate that their study reveals, for the first time, that mPGES-1 is overexpressed in HL-60 cells as compared with control blood mononuclear cells and that mPGES-1 inhibitors should be considered as promising candidate for leukemia treatment. We think that the results obtained with leukemic cell lines may be different from those obtained from freshly isolated leukemic cells. Phospholipase A_2 (PLA_2), cyclooxygenases (COX-1 and COX-2) and mPGES-1 are the key enzymes that control PGE_2 synthesis [2, 3]. We have previously reported PLA_2 enzymatic activities [4, 5], COX-1 [6], COX-2 [7] and PGE_2 synthesis [8] in freshly isolated leukemic cells from AML patients. PGE_2 acts through EP_2 receptors [9] and stimulates AML cell growth [6]. We have investigated mPGES-1 transcripts in leukemic cells from AML patients to confirm whether mPGES-1 is expressed more highly than in control blood mononuclear cells. Real time PCR analysis reveals that mPGES-1 mRNAs are detected in 100% (24/24) of leukemic cells from AML patients and 100% (7/7) of control blood mononuclear cells (Fig. 1). However, no significant differences ($P = 0.5$, Mann–Whitney U test) were found between mPGES-1 transcript levels in AML patients (relative expression of 36.7 ± 7.9; mean ± SEM in 24 patients) and control blood mononuclear cells (relative expression 37.4 ± 10.5; mean ± SEM in seven donors). In conclusion, data obtained using HL-60 cells are different from those obtained using freshly isolated blood mononuclear cells. The current results do not support the hypothesis that mPGES-1 inhibitor should be considered as a promising candidate for leukemia treatment.

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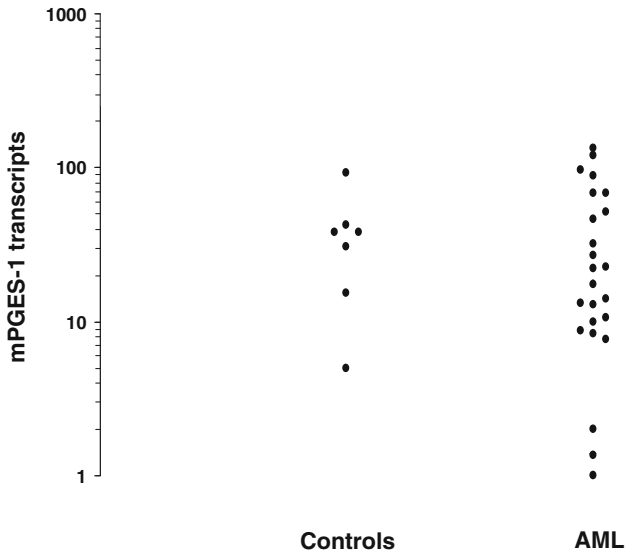

Fig. 1 mPGES-1 transcripts in leukemic cells of AML patients. The World Health Organization (WHO) has proposed a classification system divides AML into several broad groups: AML with genetic abnormalities, AML with multilineage dysplasia, AML related to previous chemotherapy or radiation and AML not otherwise specified. The latter group contains a subgroup, AML without maturation, which consisted of the weaker immature group (referenced in the past nomenclature as AML M_0, M_1 and M_2). AML blasts without maturation were investigated. Leukemic cells from 24 AML patients and blood mononuclear cells from 7 healthy volunteers were recovered as previously reported [4, 5]. Real time PCR was performed in duplicate using TaqMan assay reagents according to the manufacturer's recommendations (Applied Biosystems, Foster City, CA) (mPGES-1 product reference: Hs01115610-m1). Gene expression levels were normalized to GAPDH RNA (product reference Hs99999905-s1). Amounts of transcripts were compared to sample with the lowest level of transcripts (an AML sample which was arbitrary quoted 1)

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