

TREM-1 expression in leukemia and a functional link between leukemia and TREM-1 in stem/progenitor cells and microvesicles

Wenyang Li, Xiaoling Yi, Wei Liu, Li Jiang, Cu Lu, Shiang Huang and Huiyu Li
Huazhong University of Science and Technology, China

Objectives: Triggering receptor expressed on myeloid cells (TREM)-1 was initially recognized as a transmembrane glycoprotein expressed in neutrophils and monocytes/macrophages. TREM-1 shed from the membrane of activated phagocytes without the transmembrane and intracellular domains can be found as soluble TREM (sTREM)-1 in body fluids and is thought to negatively regulate TREM receptor signaling. TREM-1 can trigger and amplify the inflammatory response. The role of TREM-1 in leukemia is unknown. The aims of this study was to investigate the TREM-1 expression in leukemia and a functional link between leukemia and TREM-1 in stem/progenitor cells and microvesicles (MVs) in their microenvironments.

Methods: 60 specimens were collected from patients with AML or CML from 2012 to 2013. The expression of TREM-1 on cells and MVs were detected by flow cytometry. Enzyme-linked immunosorbent assay was used to measure the expression levels of soluble TREM-1 (sTREM-1). For the assessment of the modulatory effects of leukemic cell on TREM-1 expression, we use cell culture.

Results: In this study, our results provide the first evidence that TREM-1 was expressed in leukemic cells. The expressions of TREM-1 were 13.745 ± 1.918 and 17.586 ± 4.77 in CML and AML cells, respectively. The expression of TREM-1 in CML was weaker than that in AML. The expression of TREM-1 in leukemia cells was lower compared with the normal control. There was statistically significant differences between leukemic cells and normal cells ($P=0.001$ for CML, $P=0.004$ for AML).

In addition, the elevated circulating sTREM-1 level was observed in patients with leukemia. sTREM-1 levels in AML group was 56.80 ± 33.16 pg/mL and 43.72 ± 23.93 pg/mL in CML group. sTREM-1 levels were elevated in AML and in CML and were significantly different compared with normal control ($P < 0.01$).

In order to assess a functional link between leukemia and TREM-1 expression in stem/progenitor cells, we cultured CD34+/CD38-, CD34+/CD38+ cells with supernatant from cultural K562 cells. As a result, the expression of TREM-1 went from 759.65 ± 23.45 to 319.87 in CD34+/CD38- cells and expression of TREM-1 went from 880.2 ± 23.45 to 394.9 ± 19.35 in CD34+/CD38+ cells in a period from zero to 24 hours; same results were obtained from cultured stem/progenitor cells with supernatant from cultural THP-1 cells. These suggested that the leukemia could induce the decreased expression of TREM-1 in stem/progenitor cells in time-dependent manner. TREM-1 expression peaked at 24 hours in stem/progenitor cells.

MVs are small vesicles that are shed from almost all cell types including leukemic cells into their surroundings. In our study, the expression of TREM-1 on MVs isolated from umbilical cord blood went from 89.2 ± 21.2 to 3.97 ± 2.54 after cultured with supernatant from cultural K562 cells in a period from zero to 24 hours. The expression levels were dramatically decreased, indicating that leukemia could inhibit the expression of TREM-1 on MVs from umbilical cord blood cells. The same results were obtained from MVs derived from umbilical cord blood cultured with the THP-1 conditional medium. Furthermore, our results showed that sTREM-1 levels was increased in supernatants of umbilical cord blood cultured with supernatant from cultural K562 cells (6.04 ± 3.92 pg/mL for zero hour; 17.51 ± 3.8 pg/mL for 48 hours $P < 0.05$). Compared with quiescent cord blood cells, leukemia induced blood cells secreting high levels of sTREM-1 in vitro.

Conclusion: In this study, our results provide the first evidence that TREM-1 was decreased expressed in leukemic cells and leukemic cells secreted high level of sTREM-1. Soluble TREM-1 was negatively correlated with expression of TREM in leukemia. The leukemia could induce the decreased expression of TREM-1 in normal stem/progenitor cells and MVs and facilitates the generation of sTREM-1.

huiyuli26@aliyun.com