

Opposite effects of VWF during megakaryocytic vs erythroid differentiation

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Hemopoiesis is formed by stem cells (SC), progenitor cells and short-lived precursors, that continuously interact with the extracellular matrix and the cells in the bone marrow microenvironment. The complexity of hematopoiesis consists in the requirement of a highly regulated progression through different steps of proliferation and maturation, that span from the self-renewal of SC, their commitment, the arrest of proliferation and terminal differentiation of mature, functional elements with a defined lifespan. The downstream progeny of Human SC (HSC) have been characterized, and lineage restricted oligopotent progenitor cells for lymphoid (common lymphoid progenitor, CLP) and myeloid (common myeloid progenitor, CMP), granulocyte-monocyte progenitor (GMP) and megakaryocyte-erythrocyte progenitor (MEP) lineages have been identified. In normal hematopoiesis, cytokine and growth factors (i.e. erythropoietin – EPO – and thrombopoietin – TPO –) are essential for these various functions, and act by binding to their cell-surface receptors and triggering complex cascades of intracellular signaling. We recently found that VWF is able to increase platelet production during TPO-induced MK differentiation, acting as a cytokine. It was also able to restore normal platelet production in TPO-treated CD34 cells obtained from VWD2B patients.

Here, we tested the role of VWF both in MK and erythroid differentiation.

VWF boosted the TPO-induced differentiation of human CD34-derived MK, as expected. On the contrary, EPO-induced erythroid differentiation of CD34 cells was inhibited by addition of VWF to the culture medium.

Our data demonstrate that VWF plays different roles during both erythropoiesis and megakaryocytopoiesis, making it attractive to speculate that VWF could be involved in the control of the MEP commitment. Further experiments are needed to elucidate the effects of VWF on the common precursor.

Key words

Stem cells, VWF, TPO, EPO, erythropoiesis, megakaryocytopoiesis