Vasoactive intestinal polypeptide suppresses proliferation of human cord blood-derived hematopoietic progenitor cells by increasing TNF-α and TGF-β production in the liver

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ABSTRACT. The physiology of hepatic hematopoiesis is largely unknown, although studies have indicated that vasoactive intestinal polypeptide (VIP) is involved in this disease. To validate this hypothesis, we assessed the effects of VIP on human cord blood CD34⁺ cells. We also measured VIP levels and the capacity of vasoactive intestinal polypeptide receptor (VIPR) to bind to VIP in the rat liver during different developmental phases. VIP inhibited the proliferation of cord blood-derived CD34⁺ cells from concentrations of 10⁻⁷-10⁻¹² M. The highest suppression was achieved with 10⁻⁸ M VIP at day 10.
Intracellular levels of tumor necrosis factor (TNF)-α and transforming growth factor (TGF)-β in CD34+ cells treated with VIP were increased by 50.70 and 43.46%, respectively. Variations in VIP levels in the rat fetal liver generally increased rapidly with the stage of fetal development. In addition, the affinity of VIPR for VIP increased from relatively low levels in the rat fetal liver and peaked at birth, after which it gradually decreased. VIP had a suppressive effect on the proliferation of human cord blood-derived CD34+ cells, partially by increasing the production of TNF-α and TGF-β. Low VIP levels in the fetal liver and gradually increasing levels after birth may in part be responsible for suppressing hematopoietic stem cell and progenitor proliferation in the liver.

**Key words:** Cord blood cells; Fetal development; Hepatic hematopoiesis; Vasoactive intestinal polypeptide