The emerging role of immunomodulatory agents in fetal hemoglobin induction

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Letter to Editor

Beta-thalassemia is considered as genetic disorder characterized by insufficiency or absence of β-globin gene expression with accumulation of α-globin chains in erythroid precursor cells resulting in ineffective erythropoiesis (1, 2). Recently, attempt for augmentation of fetal hemoglobin (HbF) production has been established as a novel therapeutic strategy in blood transfusion independent beta-thalassemia. Several studies have been demonstrated the effective role of immunomodulatory agents including rapamycin, resveratrol, thalidomide and pomalidomide in HbF over-expression (3-6). Our recent data clearly indicated the effectiveness of thalidomide in γ-globin gene expression in the erythroid progenitor cells (7).

Although immunomodulatory agents have not cytotoxicity effects on erythroid precursors, rapamycin and resveratrol suppressed the with cell proliferation, while using thalidomide and pomalidomide stimulates cell growth (6).

These findings may suggest that immunomodulatory agents have different molecular mechanisms in HbF induction. Further researches based on molecular and epigenetic mechanisms of actions in HbF induction and could able to reveal the interfered mechanisms of γ-globin gene up-regulation.

In this regard it has been shown that the effects of Pomalodomide as an immunomodulatory agents is associated with histone H3 acetylation of γ-globin promoter, while thalidomide is activating P38 MAPK signaling as well as increasing histone H4 acetylation (4,5).

Besides, we have demonstrated that thalidomide decreased of histone H3K27 methylation in erythroid progenitor cells (8).

Also, as combination of an immunomodulatory agent and other HbF inducer compounds, higher levels of HbF could be expected moreover, it has been postulated that by using combination of both agents with different mechanisms of γ-globin gene induction could provide higher levels of HbF (9).

In conclusion, using combination of such immunomodulatory drugs and agents with histone acetylation potency may provide more effective compound in HbF induction.

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