

Indoleamine 2,3 Dioxygenase and Regulatory T Cells in Acute Myeloid Leukemia

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Abstract : Background and Objectives: The microenvironment of acute myeloid leukemia (AML) is suppressive for immune cells. Regulatory T cells (Tregs) have been recognized to play a role in helping leukemic cells to evade immunosurveillance. The mesenchymal stem cells (MSCs) are essential contributors in immunomodulation of the microenvironment as they can promote differentiation of Tregs via the indoleamine 2,3-dioxygenase (IDO) pathway. The aim of the present work was to evaluate the expression of IDO in bone marrow derived MSCs and to study its correlation to percentage of Tregs. Methods: 37 adult bone marrow samples were cultured in appropriate culture medium to isolate MSCs. Successful harvest of MSCs was determined by plastic adherence, morphology and positive expression of CD271 and CD105; negative expression of CD34 and CD45 using flowcytometry. MSCs were examined for IDO expression by immunocytochemistry using anti-IDO monoclonal antibody. CD4+ CD25+ cells (Tregs) were measured in bone marrow samples by flowcytometry. Results: MSCs were successfully isolated from 20 of the 37 bone marrow samples cultured. MSCs showed higher expression of IDO and Tregs percentage was higher in AML patients compared to control subjects ($p=0.002$ and $p<0.001$ respectively). A positive correlation was found between IDO expression and Tregs percentage (p value= 0.012 , $r=0.5$). Conclusion: In this study, we revealed an association between high IDO expression in MSCs and elevated levels of Tregs which has an important role in the pathogenesis of AML, providing immunosuppressive microenvironment.

Keywords : acute myeloid leukemia, indoleamine 2,3-dioxygenase, mesenchymal stem cells, T regulatory cells

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