

Transcriptional interplay during myelopoiesis

Myelopoiesis is the maturation of hematopoietic stem cells (HSCs) into mature myeloid cells like neutrophils, eosinophils and macrophages. During myelopoiesis progenitors such as common myeloid progenitors (CMPs), granulocyte-macrophage progenitors (GMPs) and megakaryocyte-erythroid progenitors (MEPs) differentiate into committed mature cells of the respective lineages. During development progenitors lose in a hierarchic manner their multi-lineage potential. In order to become fully mature cells, promyelocytes are dependent on certain cytokines like colony stimulating factors, binding to their corresponding receptors to induce cell growth and differentiation. The granulocyte colony stimulation factor (G-CSF) as well as the granulocyte-macrophage- colony stimulation factor (GM-CSF) have been implicated in neutrophil generation. Macrophage colony-stimulating-factor (M-CSF) induces myelopoiesis by directly activating progenitors through induction of PU.1.

The process of myelopoiesis is strictly controlled to scope arising challenges during systemic infections and prevent blood disorders and diseases like acute myeloid leukemias. Understanding myeloid differentiation and defects during myelopoiesis is critical for explaining aberrant changes in immune cell distributions.

Previous studies have described the transcription factor Myc interacting zinc finger protein 1 (Miz-1) to not only be involved in early lymphocyte development, but also in lymphomagenesis through interaction with c-Myc. Our findings highlight the transcriptional activity of Miz-1 during myelopoiesis in mice.

Performing colony forming unit assays indicated a decrease in macrophage progenitor formation. In addition, flow cytometry analysis revealed altered distributions of mature macrophages in Miz-1 deficient mice. Furthermore, these mice showed an impaired expression of CD115 on the cell surface of monocytes and macrophages. The CD115 receptor plays a major role in M-CSF signaling and is essential for maturation of myeloid precursors to proceed. This developmental blockage of myelopoiesis was accompanied by decreased expression of the master regulator PU.1 in both monocytes and macrophages as revealed by quantitative real-time PCR and western blot. Further investigation of these findings will provide a deeper understanding of fundamental events during myelopoiesis.

Keywords : myelopoiesis, macrophage

Authors :

References : , , ,

Authors

Nina Henning 1, Christian Kosan 1,

1. Institute of Biochemistry and Biophysics, Friedrich-Schiller University, Jena, GERMANY