

Proceedings of German Society for Stem Cell Research (PGSSCR)

Nucleolin activates expression of CD34 and Bcl-2 in CD34-positive hematopoietic cells

Grinstein E, Santourlidis S, Fischer J, Uhrberg M, Wernet P.

Institute of Transplantation Diagnostics and Cellular Therapeutics, Heinrich Heine University Medical Center, 40225 Duesseldorf, Germany, Correspondence E.mail: edgar.grinstein@web.de

Published on 16 May 2007

Introduction:

CD34 glycoprotein in human hematopoiesis is expressed on a subset of progenitor cells capable of self-renewal, multilineage differentiation and reconstitution. Nucleolin is an abundant factor of growing and cancerous cells, involved in regulation of gene transcription and RNA metabolism, whose transcripts are enriched in murine hematopoietic stem cells, as opposed to differentiated tissue. Here we investigated the involvement of nucleolin in gene regulation in human CD34-positive hematopoietic cells.

Materials and Methods:

Interactions of nucleolin with CD34 promoter region were detected by EMSA and chromatin immunoprecipitation, and activation of the CD34 promoter region - by co-transfections of a nucleolin cDNA expression vector together with CD34 promoter reporter constructs. Levels of gene expression were monitored by immunoblotting, real-time RT-PCR and FACS.

Human bone marrow-derived CD34-positive cells KG1, stably transfected with a nucleolin cDNA expression vector, were employed. CD34-positive cells from apheresis collections were enriched using CD34 MicroBeads.

Results:

It is shown that, in human CD34-positive hematopoietic cells, nucleolin increases the abundance of the CD34 and Bcl-2 transcripts and proteins, and cell surface CD34 protein expression is enhanced by nucleolin. Nucleolin-mediated activation of the CD34 gene transcription results from sequence-specific interactions with the CD34 promoter region. *Nucleolin* expression prevails in CD34-positive cells mobilized into peripheral blood (PB), as opposed to CD34-negative PB mononuclear cells. Therefore, in intact CD34-positive mobilized PB cells, a recruitment of nucleolin to the CD34 promoter region is detected.

Discussion and Conclusions:

Our study reveals a novel role of nucleolin for gene regulation in CD34-positive hematopoietic cells and likely for the maintenance of these cells. We report that nucleolin is a crucial activator of the CD34 gene transcription. We suggest that nucleolin may be involved in controlling basic functions of CD34-positive hematopoietic cells, and its deregulation may contribute to the development of acute myelogenous leukemias.

JSRM
www.pubstemcell.com