Gene expression differences in cytokines/chemokines, G-protein signaling molecules, and multiple extracellular matrix proteins add to the known protein and functional characterization of the lines, leading to new insight into the differences in their support function for hematopoietic progenitors.

Lynn Graf, Mineo Iwata, and Beverly Torok-Storb

Correspondence: Lynn Graf, Fred Hutchinson Cancer Research Center, 1100 Fairview Ave N, D1-100, PO Box 19024, Seattle, WA 98109; e-mail: lgraf@fhcrc.org

Supported in part by grants HL62923, CA15704, and DK56465 from the National Institutes of Health, Bethesda, MD.

References

1. Roecklein BA, Torok-Storb B. Functionally distinct human marrow stromal cell lines immortalized by transduction with the human papilloma virus E6/E7 genes. Blood. 1995;85:997-1005.
2. Torok-Storb B, Iwata M, Graf L, Gianotti J, Horton H, Byrne MC. Dissecting the marrow microenvironment. Ann N Y Acad Sci. 1999;872:164-170.
3. Marton MJ, Derisi JL, Bennett HA, et al. Drug target validation and identification of secondary drug target effects using DNA microarrays. Nat Med. 1998;4: 1293-1301.
4. Iwata M, Graf L, Awaya N, Torok-Storb B. Functional interleukin-7 receptors (IL-7Rs) are expressed by marrow stromal cells: binding of IL-7 increases levels of IL-6 mRNA and secreted protein. Blood. 2002;100:1318-1325.

To the editor:

Acidic and neutral sialidase in the erythrocytes of patients with Type 2 diabetes: influence on erythrocyte lifespan

Venerando et al reported an increased quantity of sialic acid at the surface of erythrocytes in diabetic patients and associated the increase with decreased activity of neutral sialidase, an enzyme for which they had previously demonstrated a role in physiologic desialylation of red cells.[1] In their discussion they hypothesized that this excess in sialic acid was responsible for a shorter life span of erythrocytes in diabetes mellitus.

This second assertion is in contradiction with what is commonly known about phagocytosis of senescent red cells. Indeed, several lines of evidence support the contrary hypothesis. The mechanism proposed for this selective recognition and uptake of desialylated red cells is that the macrophage recognizes the adjacent galactose group, which is unmasked by desialylation of glycophorin glycans. Several studies support this hypothesis.

First, in vivo studies showed that neuraminidase-treated erythrocytes are sequestrated more quickly by resident macrophages of the spleen, liver, and bone marrow.[2,3,4] Their life span is also decreased.[2]

Second, centrifugation and lectin recognition studies have showed that older erythrocytes carry less sialic acid residue than younger ones. Moreover, these erythrocytes can be resialylated in vitro, suggesting that the rest of the sialic acid–binding group remains intact. Older red cells can be more resialylated than younger ones.[2]

Third, a receptor for galactose residue has been identified at the surface of peritoneal macrophages that are capable of performing erythrophagocytosis in vitro.[2,3,5]

Fourth, in vitro studies showed that older erythrocytes are preferentially by murine peritoneal macrophages, a reaction that can be inhibited by lactose, which is used as a competitive inhibitor of galactose recognition.[2]

To our knowledge no recent data have invalidated this theory.

Thibault Richard, Karim Zouaoui Boudjeltia, Michaël Piagnerelli, and Michel Vanhaeverbeek

Correspondence: Thibault Richard, ISPPC André Vésale, Laboratory of experimental medicine, 706, route de Gozée 6110, Montigny Le Tilleul, Belgium; e-mail: tqr@swing.be.

References

1. Venerando B, Fiorilli A, Tettamanti G. Presence in human erythrocyte membranes of a novel form of sialidase acting optimally at neutral pH. Blood. 1997; 90:2047-2056.
2. Bratosin D, Masurier D, Mazurier J, et al. Cellular and molecular mechanisms of senescent erythrocyte phagocytosis by macrophage: a review. Biochimie. 1998;80:173-195.
3. Deiss A. Destruction of erythrocytes. In: Richard Lee G, Foerster J, Lukens J, et al, eds. Wintrobe's Clinical Hematology. Baltimore, MD: Williams & Wilkins; 1999:267-299.
4. Simchon S, Jan KM, Chien S. Studies on sequestration of neuraminidase-teated red blood cells. Am J Physiol. 1988;254:H1167-H1171.
5. Traving C, Schauer R. Structure, function and metabolism of sialiv acids. Cell Mol Life Sci. 1998;54:1330-1349.

To the editor:

Expression of Ikaros isoforms in patients with acute myeloid leukemia

Recently, Yagi et al[1] reported on expression of Ikaros isoforms in patients with childhood acute myeloid leukemia (AML). Ikaros expression was assessed by nested polymerase chain reaction (PCR) and immunoblotting. The authors found that Ikaros isoform 6 (Ik-6) was detected in 7 of 10 cases of M4 and M5, but in none of the remaining FAB (French-American-British) subtypes. They conclude that the pathogenesis of myelomonocytic/monocytic AML may involve aberrant regulation of apoptosis by Bcl-XL up-regulation due to unscheduled expression of Ik-6.

Over the past several years, there has been a controversy regarding the expression of Ikaros isoforms in human leukemia. Sun et al reported that leukemic cells from infants with B-cell acute lymphoblastic leukemia (ALL) expressed dominant-negative Ikaros isoforms Ik-4, Ik-7, Ik-8, and their deletion mutants.[2] They also reported similar observations with childhood T-cell ALL[3] and childhood ALL[4] using reverse transcriptase (RT) PCR and immunoblotting. Contrary to their reports, we demonstrated overexpression of dominant-negative Ikaros isoform Ik-6 in patients with blast