Technology Offer

LEF-1, a Central Target in Neutrophil Granulopoiesis with Involvement in Leukemia and Neutropenia

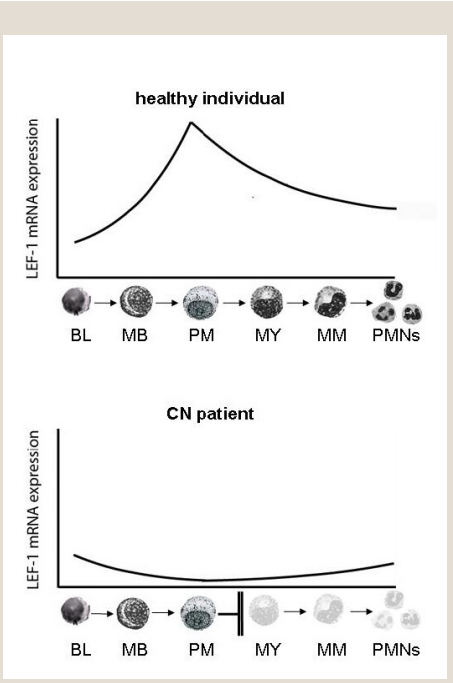
Reference Number: TO 15-00013

ascenion

A Company of the Life-Science Foundation for the Promotion of Science and Research

Challenge

Severe congenital neutropenia (CN) is a disorder of myelopoiesis resulting in recurrent life-threatening infections due to a lack of peripheral blood neutrophils. CN is also considered a pre-leukemic syndrome, because more than 20% of patients with CN progress to acute myelogenous leukaemia (AML). AML is characterized by uncontrolled proliferation of myeloid progenitors arrested in their maturation process. Several recent studies propose a common regulatory pathway for proper proliferation and differentiation of myeloid progenitors.



LEF-1 mRNA level in granulopiesis

Technology

LEF-1 has been found to be a decisive transcription factor in granulopoiesis controlling proliferation, lineage commitment and granulocytic differentiation via regulation of its target genes.

Commercial Opportunity

In-licensing or collaboration to identify therapeutic compounds that can alter LEF-1 activity.

Developmental Status

In vitro modulation of LEF-1 level in several cell-culture applications have verified a central role for LEF-1 in granulopoiesis:

- Reconstitution of LEF-1 expression in CN patient cells abolishes the differentiation block of hematopoietic progenitors, and leads to differentiation into mature granulocytes.
- Repression of endogenous LEF-1 by specific shRNA inhibits proliferation and induces apoptosis of progenitors from healthy individuals and myeloid cell-lines.

Patent Situation

EP and US patent applications have been filed based on WO2008/034637A1.

Further Reading

Skokowa and Welte (2007). LEF-1 is a decisive transcription factor in neutrophil granulopoiesis. Ann N Y Acad Sci. Mar 14; Epub ahead of print

Sokowa et al. (2006). LEF-1 is crucial for neutrophil granulocytopoiesis and its expression is severely reduced in congenital neutropenia. Nat Med. Oct;12(10):1191-7

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