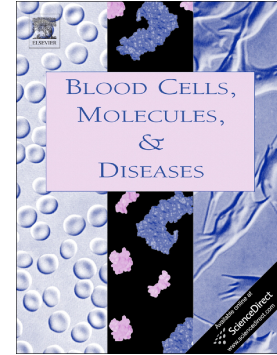


Accepted Manuscript

Mutation in an exonic splicing enhancer site causing chronic granulomatous disease

Martin de Boer, Karin van Leeuwen, Judy Geissler, Bernd H. Belohradsky, Taco W. Kuijpers, Dirk Roos



PII: S1079-9796(17)30266-8

DOI: doi: [10.1016/j.bcmed.2017.08.012](https://doi.org/10.1016/j.bcmed.2017.08.012)

Reference: YBCMD 2219

To appear in: *Blood Cells, Molecules and Diseases*

Received date: 23 June 2017

Revised date: 17 August 2017

Accepted date: 18 August 2017

Please cite this article as: Martin de Boer, Karin van Leeuwen, Judy Geissler, Bernd H. Belohradsky, Taco W. Kuijpers, Dirk Roos, Mutation in an exonic splicing enhancer site causing chronic granulomatous disease, *Blood Cells, Molecules and Diseases* (2017), doi: [10.1016/j.bcmed.2017.08.012](https://doi.org/10.1016/j.bcmed.2017.08.012)

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Mutation in an exonic splicing enhancer site causing Chronic Granulomatous Disease

Martin de Boer¹, Karin van Leeuwen¹, Judy Geissler¹, Bernd H. Belohradsky², Taco W. Kuijpers^{1,3}, Dirk Roos¹

¹ Sanquin Research, and Landsteiner Laboratory, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands. ² Dr. von Haunersches Kinderspital, Ludwig-Maximilians-University, Munich, Germany. ³ Emma Children's Hospital, Department of Pediatric Hematology, Immunology and Infectious Diseases, Academic Medical Center, Amsterdam, The Netherlands.

Corresponding author: Dr. Dirk Roos, Sanquin Research, Plesmanlaan 125, 1066 CX Amsterdam, The Netherlands. d.roos@sanquin.nl

Abstract

In a male patient suffering from X-linked chronic granulomatous disease (CGD) we found a c.389G>T mutation in exon 5 of the *CYBB* gene. We have analyzed why 95% of the transcripts of this gene lacked exon 5, leading to a frameshift and premature termination codon. The mutation was located in a region comprising three putative exonic splicing enhancer binding sites, for SRSF1, SRFS2 and SRFS6, according to the ESEfinder Tool (<http://rulai.cshl.edu/cgi-bin/tools/ESE3/ese finder.cgi>). With the Analyser Splice Tool we calculated the probability of skipping of exon 5 in *CYBB* mRNA, and by means of Sroogle the number of putative binding motifs for splicing enhancer and splicing silencer proteins (<http://astlab.tau.ac.il/index.php>). These analyses clarify why this exon was skipped in the majority of the mRNA. The normally spliced transcript contains an amino acid change p.Arg130Leu. This poorly expressed transcript gives rise to a protein with low expression but presumably normal activity, leading to a respiratory burst activity in the patient's neutrophils of about 15% of normal.

Download English Version:

<https://daneshyari.com/en/article/5591410>

Download Persian Version:

<https://daneshyari.com/article/5591410>

[Daneshyari.com](https://daneshyari.com)