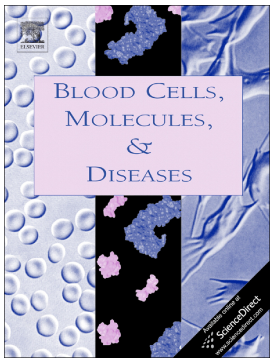

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Mutation in an exonic splicing enhancer site causing Chronic Granulomatous Disease

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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/esefinder.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.