Screening for c-mpl mutations in patients with congenital amegakaryocytic thrombocytopenia identifies a polymorphism [letter]


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Screening for \(c\text{-mpl}\) mutations in patients with congenital amegakaryocytic thrombocytopenia identifies a polymorphism

Congenital amegakaryocytic thrombocytopenia (CAMT) is an uncommon disorder, characterized by an isolated thrombocytopenia and the almost complete absence of megakaryocytes in the bone marrow. Several studies have indicated that the origin of CAMT is an intrinsic stem cell defect.\(^1\)\(^3\) Recently, we and others have demonstrated the presence of mutations in the thrombopoietin-receptor gene, \(c\text{-mpl}\), as a possible cause of CAMT.\(^4\)\(^-\)\(^7\) Although some mutations directly predict loss of Mpl function, it has not been established that others, notably those that lead to an amino acid substitution, also directly predict this loss.

To exclude that the mutations we found in our patients represent non-disease-related polymorphisms, we screened 50 healthy donors (100 alleles) for the presence of the different mutations by either sequence analysis or allele-specific restriction analysis.\(^4\)

In conclusion, mutations that predict amino-acid substitutions found by genetic screening of patients with CAMT can be due to polymorphisms of the \(c\text{-mpl}\) gene. The relation of such mutations to disease should be proven by functional studies with the mutated protein.

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