*Xmn*I polymorphism frequency in heterozygote beta thalassemia subjects and its relation to Fetal hemoglobin levels

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Thalassemias are common monogenic disorders caused by partial or complete reduction synthesis of one or more globin chains.[1] The normal concentrations of fetal hemoglobin (Hb F) in adults without Hb alterations range from 0% to 1%.[2] It is known that stimulation of Hb F production is beneficial to homozygous beta-thalassemia individuals[3] and that the *Xmn*I polymorphism may be related to increases.[4] The objectives of this study were to evaluate the frequency of the *Xmn*I polymorphism in heterozygous beta-thalassemia subjects and in individuals without Hb alterations, to estimate the polymorphism frequency related with beta thalassemia mutations and to correlate the presence of the *Xmn*I polymorphism with Hb F levels. A total of 325 peripheral blood samples from control (n=169) and beta thalassemia trait individuals (n=156) were submitted to classical tests for hemoglobinopathies.[5] The presence or absence of the *Xmn*I polymorphism was analyzed in both groups by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).[6] Statistical analysis employed the Statistica 7.0 computer program (Statsoft Inc.) with significance being set for a p-value < 0.05.

The *Xmn*I polymorphism was observed in 36.5% of heterozygous beta-thalassemia patients and in 41.4% of control subjects. There was no statistically significant difference between the two groups (p-value = 0.32). There were significantly higher concentrations of Hb F (p-value = 0.01) in individuals with the polymorphism compared to those without (Table 1).

The CD39 was found in 60.25% of cases, corroborating other published results that this is the most common mutation in Southeastern and Southern Brazil.[7] Additionally, the IVS-I-110 (25.64%) and IVS-I-6 (5.12%) were found as were other unidentified mutations (8.9%). There was no statistical difference between the presence of the *Xmn*I polymorphism and beta thalassemia mutations (p = 0.99).

In conclusion, the *Xmn*I polymorphism influences Hb F concentrations in patients with the beta-thalassemia trait. The presence of the polymorphic site showed no difference between heterozygous beta-thalassemia carriers and control subjects. The average levels of Hb F in individuals with heterozygous beta-thalassemia and with the *Xmn*I polymorphism were higher than normal, showing the influence of this site on the gene expression of γ-globin.

Table 1 - Fetal hemoglobin concentrations in patients with heterozygous beta-thalassemia

	*Xmn*I Polymorphism		
	+/+ (n=2)	+/- (n=55)	-/- (n=99)
Fetal hemoglobin concentration %	3.75 ± 2.61	2.58 ± 2.59*	1.55 ± 1.98*

Data presented as means ± standard deviation
* Statistically significant difference between heterozygous and wild type homozygous individuals (Mann-Whitney test, p-value = 0.011)

Conflict-of-interest disclosure:
The authors declare no competing financial interest

Submitted: 10/21/2011
Accepted: 11/22/2011

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DOI: 10.5581/1516-8484.20110128

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