QUANTIFICATION OF *IN-VIVO* EXPRESSION OF THE β–IVS-I-NT#6 THALASSAEMIA MUTATION .

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A recently described β chain variant, Hb Valletta (or $\alpha_2\beta_2$87PRO; Felice et al, BLOOD, 74, 7, suppl. 1, 141a, 1989) has been observed among 1.8% of the Maltese population among whom β+ & βo thal occur with a combined heterozygous incidence of 2.4 %. This provides an opportunity to quantify objectively, through the proportion of Hb A or of β(A) chains in double heterozygotes, the degree of functional deficit due to the β+ thal mutations which prevail in this area.

In this communication we describe the ocurrence of the β–IVS-I#6 mutation in two heterozygotes. One had Hb F Malta I (or $\alpha_2\gamma_2$117ARG) at birth, and on re-evaluation at 18 months of age was found to have Hb Valletta in association with β+ thal. The other was an eight year old boy with Hb S in association with β+ thal and who was being seen in our clinic. Hb identification and quantification was by isoelectric focussing and anion exchange or reverse phase HPLC. The β-IVS-I #6 mutation was identified by dot blotting of DNA, amplified by PCR, and hybridisation with allele specific oligonucleotides. The proportion of β(A) chains in the Hb Valletta β+ thal (β-IVS-I#6) condition was 29% of total β globin (γ = 29.3% and (G)γ = 0.71) while the proportion of Hb A in the Hb S β+ Thal (β-IVS-I# 6) condition was comparable at 25% [= βA / (βA + βS)]. These data show objectively that the β-IVS-I#6 mutation suppresses β chain production only to about 40% of normal, and as documented by clinical observation in homozygous patients it is a relatively mild defect. Quantification of other mutations present in the Maltese population is being pursued.

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