GENETIC STUDIES IN

SANFILIPPO SYNDROME, TYPE B

By

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ABSTRACT

The deficient activity of the enzyme N-acetyl-α-glucosaminidase (NAG) causes the genetic disease Sanfilippo syndrome, type B (SFB). SFB is inherited in an autosomal recessive manner and belongs to the group of lysosomal storage diseases known as the Mucopolysaccharidoses.

Six SFB families, comprising over 200 individuals, were sampled for blood, urine, whole and parotid saliva. A serum assay (von Figura et al., 1973) was used to measure NAG activity in 12 SFB obligate heterozygotes and 363 Caucasian controls. Minimal overlap between these two distributions was found, with the obligate heterozygote mean only 31% of the control mean. One obligate heterozygote presented as an apparent new mutation for SFB.

One control and her mother were demonstrated to be SFB carriers, providing an estimate for SFB carrier frequency of 1/363. Linkage analysis did not reveal a positive linkage of NAG with 26 marker loci but did exclude seven loci at 10 cM or less.

Heritability analysis was computed with 30 half-sib twin families, using the half-sib twin model and parent-offspring regression. The results suggest that a substantial heritability for NAG activity may exist in the Caucasian population.

The investigation of 126 Black controls found that the mean NAG activity and variance of the Black controls is significantly ($p<0.001$) greater than that of the Caucasian controls. Significant differences ($p<0.001$) in heat inactivation between individuals at the opposite ends of the distribution for NAG activity and the successful fit of the expected distribution of two alleles with the observed data suggests that the variance seen in the Black population is due to the presence of two or more polymorphic alleles at the NAG locus.

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