Chromosomes 14 and 21 as possible candidates for mapping the gene for Sanfilippo disease type IIIC

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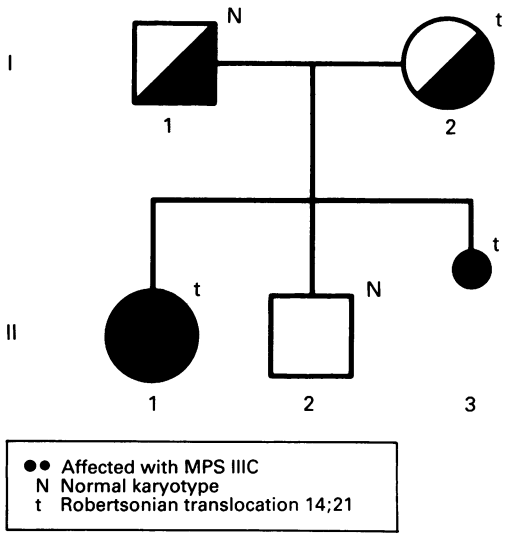
An 8 year old girl, a single child of unrelated parents, was found to be affected with type C Sanfilippo disease. The diagnosis of MPS III in this girl was based on a characteristic clinical picture, including urinary excretion of heparan sulphate and chondroitin sulphate as shown by electrophoresis. Investigation of the enzymes involved in the various types of Sanfilippo disease showed a deficiency of acetyl CoA-glucosamine acetyl transferase (table), which indicated MPS type IIIC.

The mother was offered prenatal diagnosis in two subsequent pregnancies at the ages of 35 and 39 (figure). In the pregnancy which resulted in II·2 normal results of biochemical (table) and cytogenetic analyses (46,XY) were obtained; the child is now 6 years of age and healthy. In the next pregnancy (II·3) a greatly increased amount of heparan sulphate was found in the amniotic fluid by 2D electrophoresis, as has previously been shown for MPS types IIIA and B.[2] Based on this result the pregnancy was terminated and MPS IIIC was confirmed by the finding of N-acetyltransferase deficiency in fibroblasts cultivated from the fetal skin (table). Chromosome analysis in this fetus (II·3) showed a balanced Robertsonian translocation, involving chromosomes 14 and 21. Thereafter, we found the same translocation in the affected girl, II·1, and in her mother, I·2.

The presence of a 14;21 translocation in the two affected sibs and a normal karyotype in the unaffected one may be only coincidental. However, it is also possible that the mutation responsible for MPS IIIC is the result of rearrangement in the pericentric region of one of the two chromosomes involved. Thus, one of the two mutated loci necessary for an autosomal recessive disease to be expressed would be transmitted with the translocation from the mother and only the father would be a carrier of the 'regular' mutation.



Pedigree of the family. Prenatal tests, biochemical and cytogenetic, were performed in II·2 and II·3. In case II·3 there was a selective termination of pregnancy.

The gene for MPS IIIC has not yet been mapped, and we suggest that chromosomes 14 and 21, particularly their pericentric regions, should be taken into account as possible candidates for mapping the gene.

Fibroblastic cell lines are available from the Department of Genetics, Warsaw (Reg no 58/P/90) and the Department of Clinical Genetics, Rotterdam (Reg no 83 RD 210).

1 Hopwood JJ, Elliot H. The diagnosis of the Sanfilippo C syndrome, using monosaccharide and oligosaccharide substrates to assay acetyl-CoA: 2 amino-2-deoxy-α-glucoside N-acetyltransferase activity. *Clin Chim Acta* 1981;11:67–75.

2 Kleijer WJ, Huijmans JGM, Blom W, *et al.* Prenatal diagnosis of Sanfilippo disease type B. *Hum Genet* 1984; 66:287–8.

Acetyl CoA-glucosamine acetyltransferase activity in the 8 year old girl affected with MPS IIIC and in two subsequent pregnancies of her mother at the ages of 35 and 30.

	Cell type	Activity (nmol/h/mg protein)*	
		Case	Controls
Index case II·1	Skin fibroblasts	0·3	1·3–6·0 (n = 18)†
			1·0–1·4 (n = 4)‡
Prenatal test II·2	Amniocytes	1·3	1·1–4·4 (n = 9)
Prenatal test II·3	Not available§	—	
Fetus II·3	Skin fibroblasts‖	0·5	1·3–6·0 (n = 18)

* Enzyme assay as described.[1] † Normal controls. ‡ Obligate heterozygotes. § An affected fetus was indicated by an abnormal electrophoresis pattern of glycosaminoglycans in amniotic fluid. ‖ Cultivated after termination of pregnancy II·3.

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