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Cystic fibrosis: analysis of linkage of the disease locus to red cell and plasma protein markers

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Cystic fibrosis (CF) is the most common autosomal recessive disorder in Caucasian children; it affects approximately 1 out of 2000 live-births in North America (reviewed in Talamo et al, 1983). The patients suffer from chronic pulmonary disease and pancreatic enzyme insufficiency. They also have a highly elevated level of sweat electrolytes which, although of little clinical consequence itself, is the most reliable diagnostic feature of the disease. All these symptoms are consistent with CF being an exocrine disorder. However, despite extensive research efforts, the basic biochemical defect in CF remains unknown.

Genetic heterogeneity has been considered as a possible explanation for the high frequency of the disease. However, all available data are only consistent with the assumption that CF is due to mutation(s) at a single locus (Andersen and Hodges, 1946; Steinberg et al, 1956; Danks et al, 1984; Romeo et al, 1985). It should be possible, therefore, to discover a genetic marker closely linked to the disease locus by genetic linkage studies. Previous investigators have provided evidence against close linkage of CF with the genetic determinants for the ABO, Rh, K, Fy, Jk, Le, P and MNS blood groups, and HLA (Steinberg et al, 1956; Steinberg and Morton, 1956; Goodchild et al, 1976). A recent report has suggested a possible linkage between *F13B* and CF (Eiberg et al, 1985) but the lod score is far from conclusive.

We have examined 11 red cell and plasma protein markers, namely ACP1, AHSG, AK1, C3, GC, IGHG, GPT, PGM1, PI, PLG, and TF, using blood samples from 26 Canadian CF families each with at least two affected children. Probability of linkage between CF and these markers was analysed using either the LIPED (Ott, 1973) or the Mark III program (Côtèq, 1975). As shown in table I, none of these markers are closely linked to CF. However this information may be of interest to other investigators.

Table I. Linkage data for 11 chromosome marker loci and CF

Marker loci (chromosomal location)	Lod (z) scores at various recombination fractions (θ)				
	0.05	0.10	0.20	0.30	0.40
ACP1 (2p23 or p25)	−3.382	−1.866	−0.658	−0.207	−0.040
AHSG (3q)	−3.103	−0.986	0.209	0.271	0.095
AK1 (9q34)	−4.334	−2.689	−1.180	−0.463	−0.109
C3 (19pter-q13.2)	−4.074	−2.115	−0.616	−0.130	−0.010
GC (4q11-q13)	−4.150	−2.513	−1.066	−0.407	−0.095
IGHC (14q32.3)	−2.848	−0.728	0.490	0.499	0.186
GPT (8q13 or 16pter-p11)	−2.033	−0.966	0.124	0.089	0.053
PGM1 (1p22.1)	−5.248	−2.563	−0.574	−0.013	0.038
PI (14q24-q32)	−4.903	−2.366	−0.563	−0.062	0.015
PLG (4)	−6.373	−3.613	−1.373	−0.477	−0.103
TF (3q21-q25)	−7.949	−4.575	−1.770	−0.619	−0.134

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