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European Working Group
on Cystic Fibrosis Genetics

No Evidence for Segregation Distortion of Cystic Fibrosis Alleles among Sibs of Cystic Fibrosis Patients

In 1988, an excess of male carriers of cystic fibrosis (CF) mutations among sibs of CF patients was reported by Kitzis et al. [1]. In particular, a significant deviation from a 1:1 sex ratio was observed among heterozygous carriers in favor of males, and among homozygous normals in favor of females. When the study reported by Kitzis et al. [1] was carried out, before the identification of the CFTR gene, carriers were detected by means of RFLPs tightly linked to the CF locus. Following the identification of the CFTR gene, direct carrier detection has become possible in those CF families where mutations are identified, thus avoiding possible errors deriving from misdiagnosis and/or recombination with the linked markers. We decided, therefore, to further investigate the question of a possible sex ratio distortion among carrier sibs of CF patients taking advantage of the large amount of data already available. Only families which were not included in the analysis done by Kitzis et al. [1], and in which both the paternal and the maternal mutations were identified, were included in the present analysis.

The sample of families was further subdivided into two groups: one composed of all families in which both parents were carriers of the ΔF508 mutation [2], and one in which only one parent was a ΔF508 carrier, while the other was a carrier of another known mutation. This subdivision allowed us to investigate the parental origin of the mutation in the second group of families. Results for the first group (both parents ΔF508 carriers) are shown in table 1. There is no deviation from the expected 2:1 ratio of heterozygotes to homozygotes among either the brothers or the sisters of CF patients in this group.

Table 1. Segregation of alleles in families with both parents ΔF508 carriers

	Carriers	Noncarriers	Total
Boys	413 (411.3)	204 (205.7)	617
Girls	431 (428.7)	212 (214.3)	643
Total	844 (840.0)	416 (420.0)	1,260

Expected numbers are given in parentheses.

Results for the second sample are reported in table 2. There were 218 families in which the father was a ΔF508 carrier, and 198 in which the mother was a ΔF508 carrier. Although this is not a significant deviation from a 1:1 ratio, the following analysis was carried out separately in these two groups. The sex ratio among sibs was very close to 1:1 in both groups. Overall, boys were more likely to be carriers of ΔF508 or another mutation and girls were more likely to be noncarriers, independently of whether the ΔF508 mutation was coming from the father or the mother, but none of the observed proportions was significantly different from that expected under Mendelian segregation of the alleles.

In conclusion, there is no statistically significant indication in our sample of a segregation distortion;

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Table 2. Segregation of alleles in families with only one parent a ΔF508 carrier

		ΔF508 carriers	Other carriers	Non-carriers	Total
ΔF508 fathers	boys	59 (56.7)	61 (56.7)	50 (56.7)	170
	girls	57 (55.7)	48 (55.7)	62 (55.7)	167
	total	116 (112.3)	109 (112.3)	112 (112.3)	337
ΔF508 mothers	boys	50 (44.7)	44 (44.7)	40 (44.7)	134
	girls	44 (47.0)	39 (47.0)	58 (47.0)	141
	total	94 (91.7)	83 (91.7)	98 (91.7)	275
Total	boys	109 (101.3)	105 (101.3)	90 (101.3)	304
	girls	101 (102.7)	87 (102.7)	120 (102.7)	308
	total	210 (204.0)	192 (204.0)	210 (204.0)	612

Expected numbers are given in parentheses.

however, it is intriguing that, although not significant, the observed deviation is in the same direction of that observed by Kitzis et al. [1].

Appendix

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