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Linkage Heterogeneity between X-linked Retinitis Pigmentosa and a Map of 10 RFLP Loci

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Summary

In nine families in which X-linked retinitis pigmentosa (XLRP) is segregating, the lod scores of XLRP in a map of 10 RFLP loci were obtained by multipoint linkage analysis. The XLRP locus was located telomeric to DXS7 in seven of the families and centromeric to DXS7 in two of the families. Under the hypothesis of two XLRP loci, a heterogeneity (admixture) test was performed, providing significant evidence of heterogeneity in XLRP ($P < .01$). No correlation was detected between the clinical manifestations of XLRP and the two different disease loci.

Introduction

X-linked retinitis pigmentosa (XLRP) is a degenerative disease of the retina, causing progressive nightblindness, constriction of the visual fields, and a deterioration of visual acuity leading eventually to blindness or severe visual handicap in affected males. Some heterozygous females show similar but milder manifestations, particularly of an older age.

XLRP was previously assumed to be caused by a single gene defect. The XLRP locus was first found closely linked to DXS7 on the proximal short arm of the X chromosome (Bhattacharya et al. 1984). Further linkage studies confirmed the linkage of XLRP to DXS7, but different locations for the XLRP locus were suggested: Nussbaum et al. (1985), Denton et al. (1988), Musarella et al. (1988), and Wirth et al. (1988) suggested that the XLRP locus is telomeric to DXS7, while Friedrich et al. (1985) and Wright et al. (1987) suggested that the XLRP locus is centromeric to DXS7. A location telomeric to DXS7 was also suggested by studies of two boys both of whom had deletions in the Xp21 region: one with Duchenne muscular dystrophy, retinitis pigmentosa (RP), chronic granulomatous disease, and McLeod phenotype (Francke et al. 1985) and the other with RP, chronic granulomatous disease, and McLeod phenotype (de Saint-Basile et al. 1988).

In an attempt to clarify the number and position of the XLRP loci, we report here the results of multipoint linkage analysis including 10 X chromosome marker loci and heterogeneity testing in nine Australian XLRP families. The clinical manifestations of the disease were analyzed in each of the families to detect any possible correlation between gene location and XLRP phenotype.

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Material and Methods

Family Studies

Nine XLRP families (see Appendix) were ascertained through ophthalmological clinics in Sydney, Melbourne, and Perth, and available family members were examined by some of us (families 27, 42, 58, 173, and 240 by F.H., family A by G.K. and P.D., family H and L by P.D., and family P by R.G. and I.C.). All kindreds were of British descent. Two of the families (27 and 240) have previously been published (Chen et al. 1988; Denton et al. 1988; Wirth et al. 1988). The criteria used for identifying affected males and female carriers

were as described elsewhere (Bird 1975; Wright et al. 1983). In brief, diagnosis of the disease in males was based on family history, night blindness, ophthalmoscopical appearances of the retina, the electro-oculogram test, and electroretinography. Males more than 10 years of age and with normal ophthalmological findings were classified as normal. Females who had an affected father or one or more affected offsprings and/or ophthalmological findings compatible with XLRP carriers were classified as heterozygotes. Because of the difficulty of excluding heterozygous status on purely ophthalmological grounds, clinically normal female members were excluded from the linkage analysis.

DNA Analysis

DNA extraction from venous blood and Southern blot analysis were carried out as described elsewhere (Denton et al. 1988). Ten polymorphic X chromosome marker loci—DXS164 (pERT87–8,15), DXS84 (754), DXS141 (pERT145–12), OTC, DXS7 (L1.28), TIMP, DXS146 (TAK8), DXS255 (M27β), DXS14 (58.1), and DXS1 (p8)—were used, their characteristics are shown in table 1.

Multipoint Linkage Analysis

Since there were previous suggestions of genetic heterogeneity, lod scores of two-point linkage analysis that were pooled from these nine families are not presented here. Multipoint linkage analysis for each family was computed using the LINKMAP 3.5 computer program (Lathrop et al. 1984). The genetic distances between the 10 markers were taken from Drayna and White (1985), Goodfellow et al. (1985), and Chen et al. (1989), except for the genetic distances regarding TIMP, DXS146, and DXS255 and the order of DXS146 and DXS255, which were determined arbitrarily. The lod scores of XLRP in the map of 10 marker loci were approximated by using a method modified from Ott et al. (1986). The multipoint lod scores of XLRP in a test interval between two adjacent marker loci were derived from a five-point linkage analysis including two other marker loci. For example, the lod scores of XLRP between DXS84 and DXS141 were obtained by a five-point linkage analysis including DXS164–DXS84–DXS141–OTC, and the lod scores of XLRP between DXS141 and OTC were obtained by a five-point linkage analysis including DXS84–DXS141–OTC–DXS7.

Heterogeneity Testing

The admixture test (Smith 1963) was applied to the present 11-point lod scores in the nine XLRP families to test for the significance of genetic heterogeneity. The admixture test performed by the computer program HOMOG2 allows for two family types, both linked but with different genetic distances for the two types: family type 1 with θ_1 and family type 2 with θ_2 (Ott et al. 1986). This hypothesis of two linked family types is particularly appropriate in the case of XLRP, because the genetic distance between the two potential loci was estimated to be less than 50 cM, the estimated genet-

Table 1

Information on the 10 Marker Loci Used

Locus/Probe	Location	Enzyme	Alleles	Frequencies	Symbol
DXS164/pERT87-15	Xp21.2	*Taq*I	3.3, 3.1	.33, .67	Q, q
DXS164/pERT87-15	Xp21.2	*Bam*HI	9.2, 7.4, 2.5	.34, .66	H, h
DXS164/pERT87-8	XP21.2	*Bst*XI	4.4, 2.2	.64, .36	R, r
DXS84/754	Xp21.1	*Pst*I	12, 9	.62, .38	F, f
DXS141/pERT145-12	XP21.1	*Taq*I	4.8, 3.7	.25, .75	U, u
OTC/pOTC	XP21.1	*Bam*HI	16, 5.4	.75, .25	D, d
OTC/pOTC	Xp21.1	*Msp*I	6.6, 6.2	.61, .39	A, a
DXS7/L1.28	Xp11.3	*Taq*I	12, 9	.68, .32	L, l
TIMP/EPA cDNA	Xp11.3-11.23	*Bgl*II	12, 9.5, 2.5	.66, .34	P, p
DXS146/TAK8	Xp11.2	*Xba*I	5, 3.3	.36, .64	T, t
DXS255/M27β	Xp11.22	*Pst*I/*Bgl*II	hypervariable fragments[a]		M, m, w
DXS14/58-1	Xp11.21	*Msp*I	4, 2.5	.65, .35	E, e
DXS1/p8	Xq11-12.2	*Taq*I	15, 9	.84, .16	B, b

[a] Hypervariable fragments of M27β were recoded to only two or three alleles in each family to serve computation time.

ic distance between Xp21 and the centromere. The HOMOG2 program also calculates the proportion (alpha) of the families belonging to family type 1 and the posterior probability of each family belonging to family type 1.

Results

The segregation patterns of XLRP and the alleles of 10 RFLPs in the nine families are shown in the Appendix. The lod scores of 11-point linkage analysis in each of the nine XLRP families are shown in table 2. The recombination fraction corresponding to the maximum multipoint lod score in a particular family was used to estimate the most likely location for the disease locus, and these values in nine families are shown in table 3.

For the large family, 240, the maximum multipoint lod score was 15.62 at $\theta = .115$, a location for OTC. Five families—27, 173, A, H, and P—had the maximum multipoint lod scores between DXS84 and OTC, consistent with a disease locus between these two markers. For families 58 and A, the multipoint lod scores distributing between DXS164 and OTC are very close to the maximum lod scores, suggesting that the gene location in these two families could be anywhere between DXS164 and OTC; nevertheless, these results are compatible with a gene location telomeric to DXS7. All these seven families had negative lod scores between DXS146 and DXS255, and the estimated location for the other locus at $\theta = .385$ (tables 2, 4). On the other hand, family 42 had a maximum multipoint lod score of 1.81 for DXS146, and family L had a maximum multipoint lod score of 1.20 for DXS1. Although the number of individuals in these two families was low (see the Appendix, figs. 2, 8) and although the maximum multipoint lod scores were less than 2, the positions of the maximum lod scores and of the negative lod scores in the region telomeric to OTC in these two families imply a disease locus centromeric to OTC. In family L, the negative lod scores in the region telomeric to DXS7 and the positive lod scores in the region centromeric to DXS146 imply a gene location centromeric to DXS7. The locations of the two XLRP loci derived from this study are consistent with the two locations, one centromeric and the other telomeric to DXS7, suggested by previous publications (Francke et al. 1985; Friedrich et al. 1985; Nussbaum et al. 1985; Wright et al. 1987; de Saint-Basile et al. 1988; Musarella et al. 1988).

Under the H_2 hypothesis—i.e., that there are two linked family types—the location of one locus ($\theta_1 = .115$) corresponds to a location of OTC, and the location of the other locus ($\theta_2 = .385$) corresponds to a location between DXS7 and DXS1 and close to DXS255 (see tables 2, 4). Families 42 and L had very low posterior probabilities (.059 and <.001, respectively) of being the type 1 family, while the other seven families had a 1.000 posterior probability of being the type 1 family (table 3), suggesting that families 42 and L had a gene location different from that in the other seven families. The estimated alpha, 78% (table 4), corresponds to there being seven type 1 families in the nine families investigated, suggesting that the disease locus close to OTC was more common in the families we have studied. Heterogeneity with two linked family types (hypothesis H_2) is much better supported than homogeneity with one family type (hypothesis H_1), the difference in $\log_e$ likelihood being equal to 4.458, corresponding to a χ^2 value (2 df) of 8.916 ($P = .0058$) (table 5).

Discussion

All previously published linkage analyses on XLRP have been based on the assumption of a single gene defect in all families. Our studies indicate that in the nine XLRP families presented here the disease appeared to be caused by mutations in either of two loci, one telomeric to DXS7 close to OTC and referred to below as the *distal locus* and the other centromeric to DXS7 and referred to below as the *proximal locus*.

Musarella et al. (1988) described a family, family 20, in which two triply informative crossover events implied an XLRP locus between DXS28 and the Duchenne muscular dystrophy locus, which is different from either of the two loci suggested by the present study. However, although a number of deletions in this region have been studied, in no case has a patient with a deletion in this region been reported to have RP (van Ommen et al. 1986; Francke et al. 1987). Moreover, the pedigree of family 20 was shown to consist of a nuclear family with four affected sons (Musarella et al. 1988), and there was insufficient genetic evidence to prove that this family has a bona fide X-linked form of RP and not any other form of RP. If the disease in this family is X linked, then a chromosomal rearrangement could be a possible explanation for an XLRP locus in this region.

In our set of nine families we have found that the distal disease locus is more common than the proximal disease locus. The families in previous publications can be classified as either type 1 families with the distal locus (Nussbaum et al. 1985; Denton et al. 1988;

Table 2

Multipoint Lod Scores at Recombination Fraction (θ) in Nine XLRP Families

Locus and θ	XLRP Family								
	27	42	58	173	240	A	H	L	P
DXS164:									
.00	−∞	−∞	1.63	.901	−∞	4.502	−∞	−∞	−∞
.01	5.391	−2.715	1.625	.836	9.441	4.518	−1.936	−4.816	−1.187
.019	5.871	−2.594	1.622	.743	9.979	4.536	−1.769	−4.465	−.614
.028	6.651	−2.653	1.621	.599	10.358	4.555	−1.778	−4.465	−.291
.037	6.007	−2.894	1.622	.330	10.499	4.576	−1.962	−4.818	−.069
DXS84:									
.045	−∞	−∞	1.624	−∞	−∞	4.599	−∞	−∞	.098
.056	7.570	−.274	1.623	1.696	13.598	4.584	−.568	−1.888	.258
.066	7.864	−.103	1.623	1.960	14.072	4.572	−.277	−1.394	.385
.076	8.036	−.107	1.623	2.100	14.409	4.564	−.111	−1.157	.488
.086	8.160	−.286	1.624	2.187	14.688	4.558	.004	−1.054	.574
DXS141:									
.095	8.295	−∞	1.617	2.280	15.162	4.481	.119	−1.055	.557
.099	8.322	−.631	1.608	2.312	15.434	4.417	.171	−1.092	.465
.103	8.313	−.340	1.611	2.305	15.475	4.427	.193	−1.163	.463
.107	8.304	−.173	1.614	2.300	15.514	4.437	.215	−1.288	.462
.111	8.296	−.056	1.617	2.292	15.552	4.448	.235	−1.542	.460
OTC:									
.115	8.237	.020	1.620	2.193	15.621	4.354	.504	−∞	.509
.154	7.815	.415	1.582	2.064	14.894	4.017	.648	−.952	.487
.188	7.501	.560	1.555	2.117	14.095	3.955	.536	−.827	.387
.217	7.233	.639	1.537	2.164	13.139	3.926	.411	−.868	.238
.242	7.004	.690	1.527	2.209	11.702	3.925	.261	−1.077	−.036
DSX7:									
.265	6.377	1.160	1.366	2.272	−∞	3.779	.102	−∞	−∞
.276	5.829	1.612	1.073	2.271	1.829	3.514	.047	−.713	−1.238
.286	5.705	1.632	.927	2.262	2.314	3.413	−.080	−.442	−1.081
.296	5.572	1.653	.767	2.251	2.134	3.306	−.258	−.296	−1.100
.306	5.426	1.673	.589	2.238	1.360	3.192	−.818	−.199	−1.294
TIMP:									
.315	5.186	1.704	.264	2.214	−∞	2.343	−∞	−.157	−∞
.326	4.964	1.731	.093	1.890	−1.853	1.339	−3.096	−.124	−1.721
.336	4.764	1.750	.007	1.549	−1.760	.990	−2.992	−.079	−1.583
.346	4.462	1.768	−.133	1.088	−2.399	.522	−3.071	−.043	−1.604
.356	3.911	1.787	−.401	.351	−4.008	−.223	−3.344	−.013	−1.731
DXS146:									
.365	−∞	1.806	−∞	−∞	−∞	−∞	−∞	.425	−1.993
.369	−1.871	1.800	−2.560	−7.184	−19.693	−4.990	−4.478	.847	−2.159
.373	−1.518	1.792	−2.387	−6.967	−18.868	−4.764	−4.431	.854	−2.376
.377	−1.516	1.785	−2.390	−7.154	−19.203	−4.940	−4.610	.861	−2.697
.381	−1.866	1.778	−2.569	−7.817	−20.848	−5.594	−5.091	.868	−3.269
DXS255:									
.385	−∞	1.771	−∞	−∞	−∞	−∞	−∞	.875	−∞
.396	2.435	1.738	−.368	−1.272	−14.65	−2.185	−3.326	.90	−2.933
.406	2.922	1.706	−.103	−.721	−12.815	−1.360	−2.865	.916	−2.419
.416	3.161	1.675	.039	−.418	−12.358	−.906	−2.704	.935	−2.156
.426	3.298	1.645	.13	−.216	−12.986	−.603	−2.771	.955	−1.999
DXS14:									
.435	3.38	1.616	.194	−.069	−∞	−.382	−∞	.957	−1.903
.459	3.396	1.548	.294	.171	−7.49	−.040	−3.622	1.022	−1.816
.481	3.30	1.484	.348	.316	−6.747	.163	−3.147	1.069	−1.885
.50	3.111	1.424	.381	.411	−7.133	.296	−2.836	1.115	−2.108
.519	2.77	1.369	.40	.477	−8.831	.389	−2.602	1.16	−2.615
DXS1:									
.535	−∞	1.317	.411	.523	−∞	.456	−2.414	1.204	−∞

Table 3

Maximum Multipoint Lod Score (Z) at Recombination Fraction (θ) and Posterior Probability (w) of Being a Type I Family in the Admixture Test

	Family								
	27	42	58	173	240	A	H	L	P
Z	8.322	1.806	1.630	2.312	15.621	4.599	.648	1.204	.509
θ	.099	.365	.000	.099	.115	.045	.154	.535	.115
w	1.000	.059	1.000	1.000	1.000	1.000	1.000	<.001	1.000

Musarella et al. 1988; Wirth et al. 1988), or as type 2 families with the proximal locus (Friedrich et al. 1985; Wright et al. 1987). An accurate estimate of the proportion of families with either of the two disease loci will not be known until a very large set of families is studied.

The likelihood of there being two different XLRP loci complicates the use of linkage analysis for carrier detection and prenatal diagnosis in XLRP families. In the case of small families linkage analysis data may not be sufficient to establish the gene location. Consequently, an important research aim in this area is to search for any clinical manifestations of the disease that are characteristic of a particular locus, so that gene location or genotype can be inferred from the phenotype. However, to date there is no evidence that either of the XLRP loci is correlated with any particular clinical characteristics. In our own study families 27, 42, 58, 173, and 240 were found by one of us (F.H.) to be phenotypically indistinguishable and to have the typical form of XLRP as described by Wright et al. (1983). However, the XLRP locus in family 42 appeared to be in the proximal location, while in families 27, 58, 173, and 240 the XLRP locus was in the distal location. The tapetal reflex in heterozygotes has been used to distinguish one form of XLRP (McK-30320) from the classic form of XLRP (McK-31360) (McKusick 1986, p. 1337). However, the tapetal reflex was detected in some of the heterozygotes in families 27, 240, and H, who had the distal disease locus, as well as in one heterozygote in a family who had the proximal disease locus (Friedrich et al. 1985). In the case of families 42 and L, both of whom had the proximal disease locus, the disease was much more severe in family L than in family 42. In family L all the four affected males were legally blind by the age of 20 years, while in family 42 the two affected males could read in or beyond their third decade. Variations in clinical manifestations were also reported in the XLRP families studied by Musarella et al. (1988), and all of these families had the distal disease locus.

We have examined only a small series of nine families for genetic heterogeneity, and we have not found evidence for a third XLRP locus. However, evidence for a third XLRP locus has been derived from a recent multipoint linkage analysis study that included data from several research centers in a variety of countries (J. Ott, personal communication).

Table 4

Maximum $\log_e$ Likelihood (M), Estimated Recombination Fractions of the Two Loci (θ_1 and θ_2), and alpha in the Admixture Test

Hypothesis	M	θ_1	θ_2	Alpha
H_2	77.404	.115	.385	.780
H_1	72.946	.154	.154	(1)
H_0: absence of linkage	.0	∞	∞	(0)

Table 5

Components of χ^2 in the Admixture Test

Component	df	χ^2	P
H_2 vs. H_1: heterogeneity	2	8.916	.0058
H_1 vs. H_0: linkage	1	145.892	<.0001

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Appendix

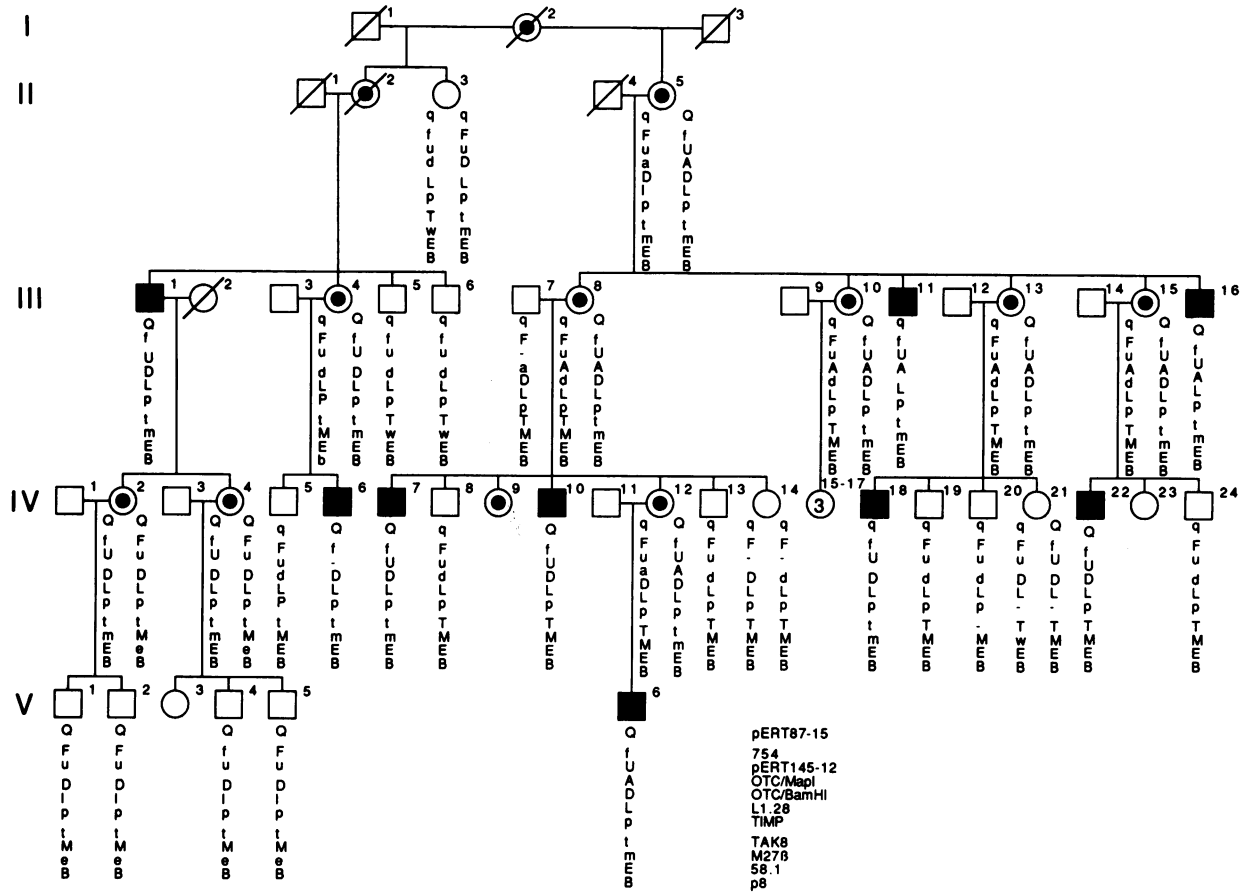

Figure 1 Family 27 segregated with XLRP and RFLP alleles (for details of the RFLP alleles, see table 1)

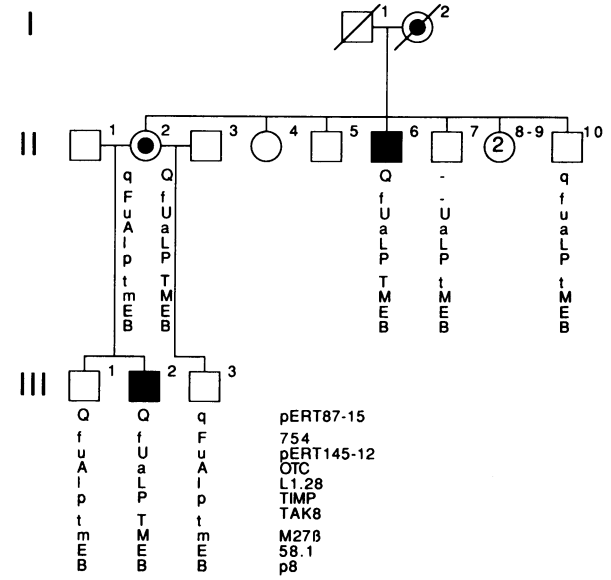

Figure 2 Family 42 segregated with XLRP and RFLP alleles

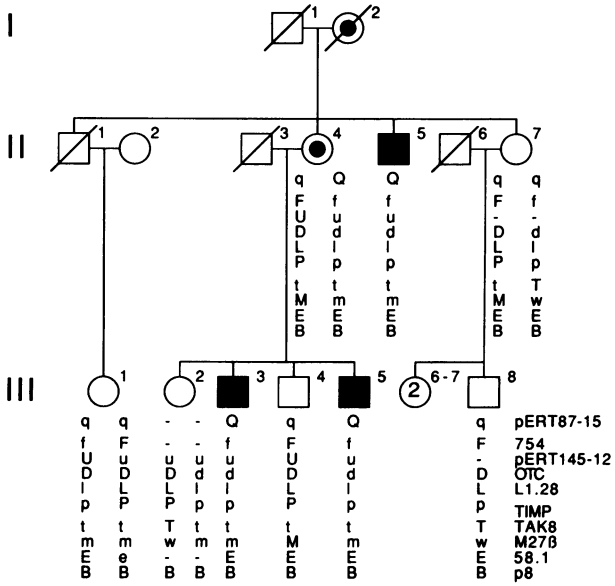

Figure 3 Family 58 segregated with XLRP and RFLP alleles

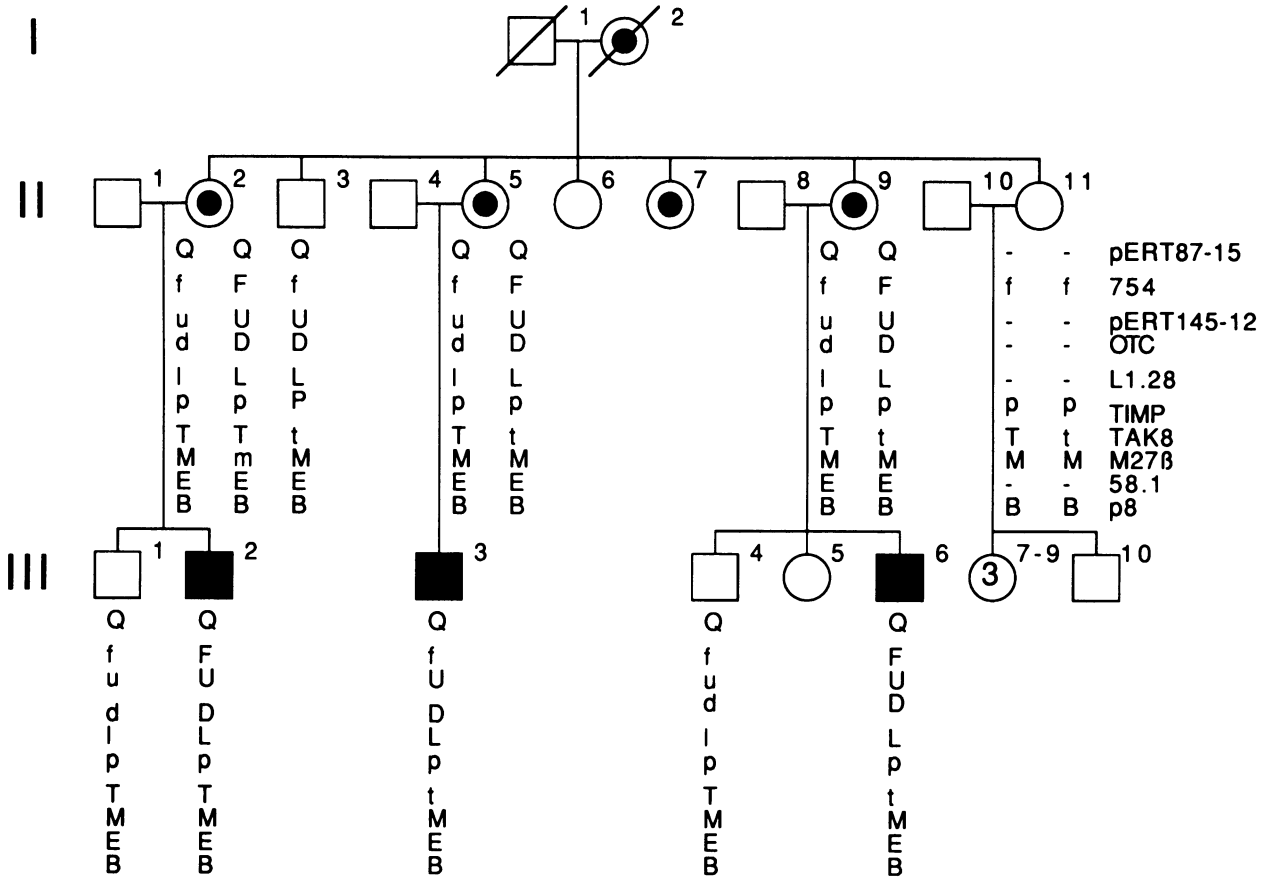

Figure 4 Family 173 segregated with XLRP and RFLP alleles

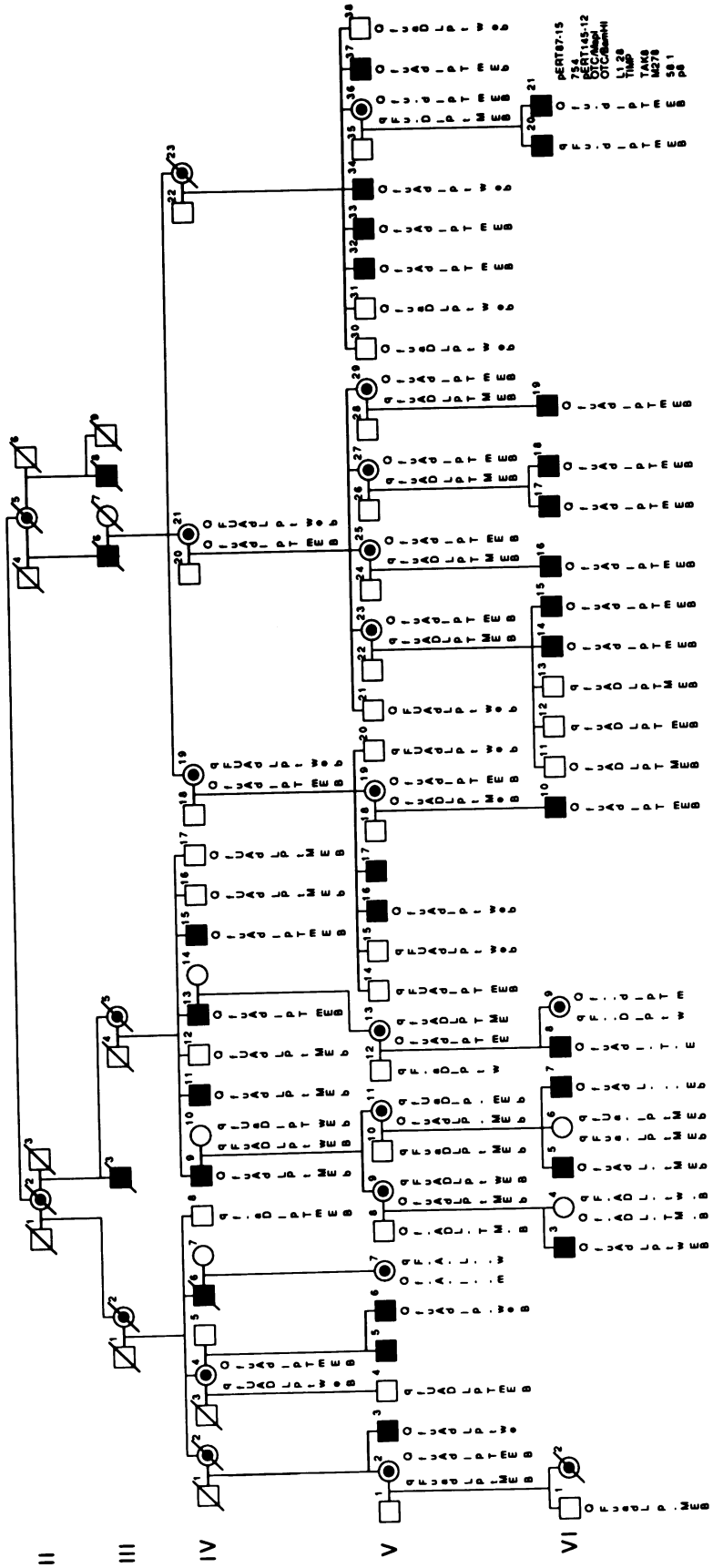

Figure 5 Family 240 segregated with XLRP and RFLP alleles

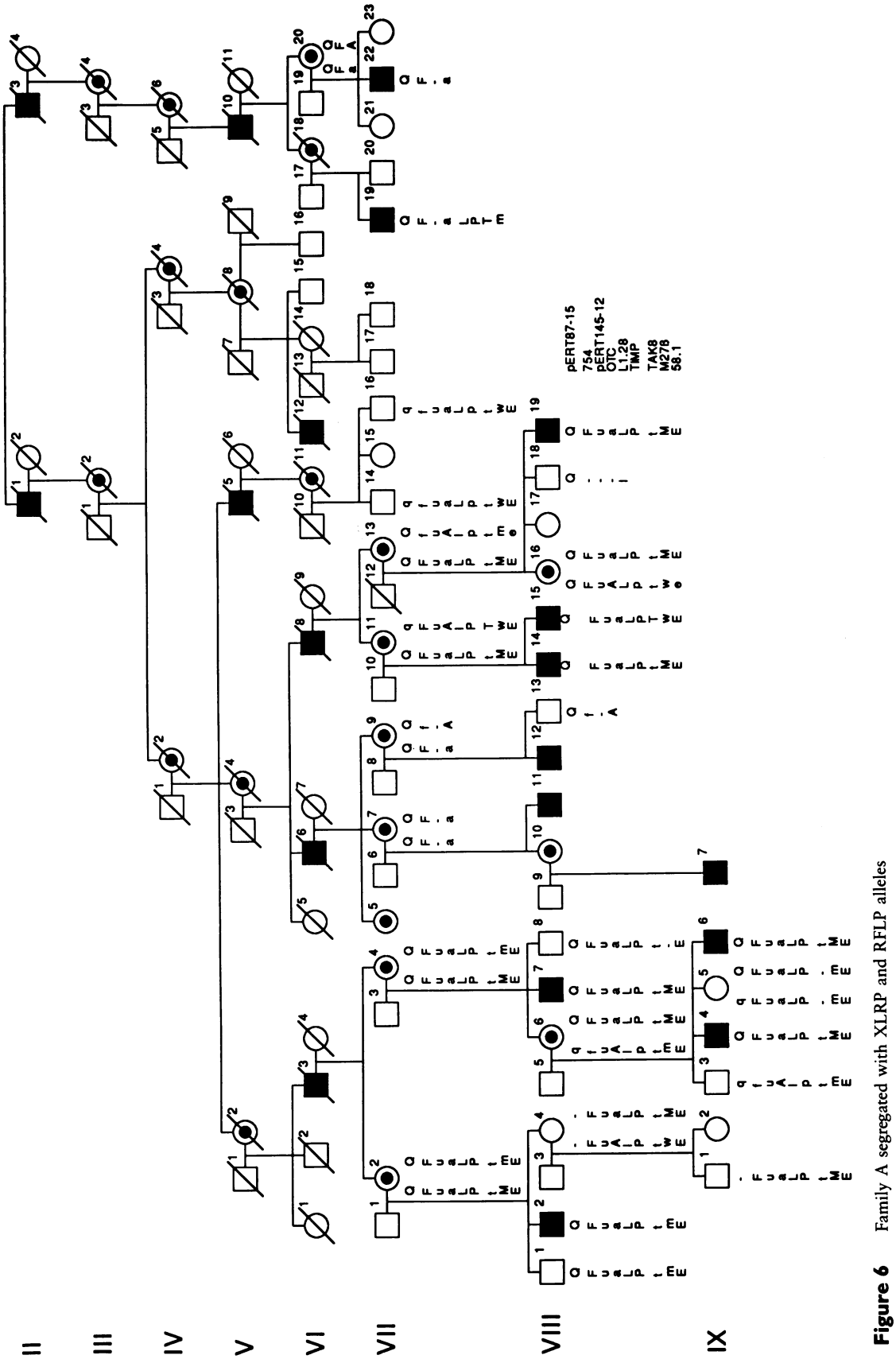

Figure 6 Family A segregated with XLRP and RFLP alleles

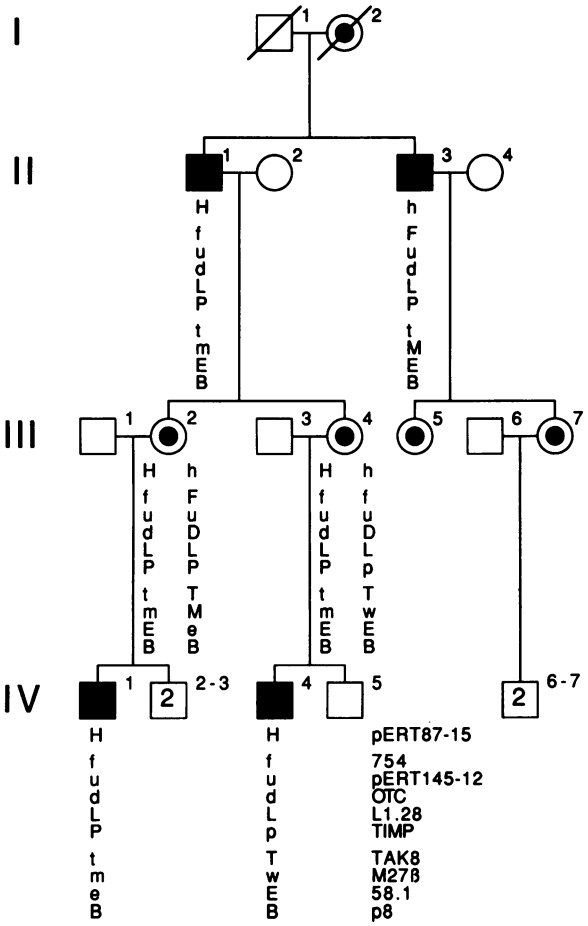

Figure 7 Family H segregated with XLRP and RFLP alleles

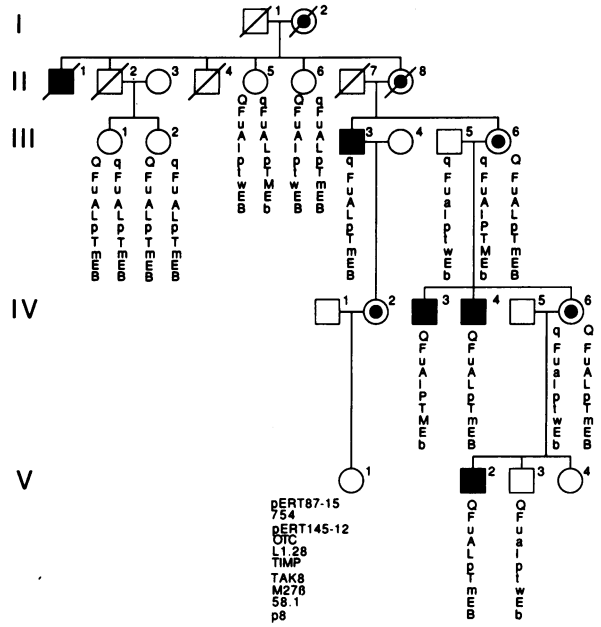

Figure 9 Family P segregated with XLRP and RFLP alleles

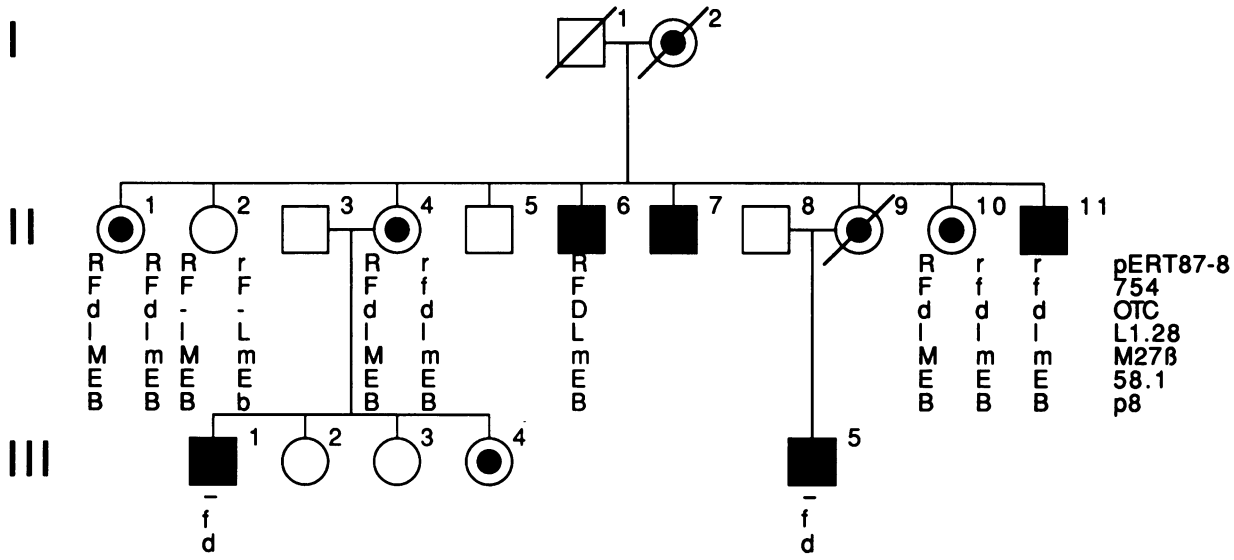

Figure 8 Family L segregated with XLRP and RFLP alleles

References

Bhattacharya SS, Wright AF, Clayton JF, Price WH, Phillips CL, McKeown CME, Jay M, et al (1984) Close genetic linkage between X-linked retinitis pigmentosa and a restriction fragment length polymorphism identified by recombinant DNA probe L1.28. Nature 309:253–255

Bird AC (1975) X-linked retinitis pigmentosa. Br J Ophthalmol 59:177–199

Chen JD, Halliday F, Serravalle S, Denton M (1988) Localization of the X-linked retinitis pigmentosa locus between DXS7 and DXS84 in a family showing tapedal reflex in heterozygotes. Ophthalmic Paediatr Genet 9:143–147

Chen JD, Hejtmencik JF, Romeo G, Lindlof M, Beohm C, Caskey CT, Kress W, et al (1989) A genetic linkage map of five marker loci in and around the Duchenne muscular dystrophy locus. Genomics 4:105–109

Denton MJ, Chen JD, Serravalle S, Colley P, Halliday FB, Donald J (1988) Analysis of linkage relationships of X-linked retinitis pigmentosa with the following Xp loci: L1.28, OTC, 754, XJ-1.1, pERT 87, and C7. Hum Genet 78:60–64

de Saint-Basile G, Bohler MC, Fischer A, Cartron J, Dufier JL, Griscelli C, Orkin SH (1988) Xp21 DNA microdeletion in a patient with chronic granulomatous disease, retinitis pigmentosa, and McLeod phenotype. Hum Genet 80:85–89

Drayna D, White R (1985) The genetic linkage map of the human X chromosome. Science 230:753–758

Francke U, Harper JF, Darras BT, Cowan JM, McCabe ERB, Kohlschütter A, Seltzer WK, et al (1987) Congenital adrenal hypoplasia, myopathy, and glycerol kinase deficiency: molecular genetic evidence for deletions. Am J Hum Genet 40:212–227

Francke U, Ochs HD, de Martinville B, Giacalone J, Lindgren V, Distèche C, Pagon RA, et al (1985) Minor Xp21 chromosome deletion in a male associated with expression of Duchenne muscular dystrophy, chronic granulomatous disease, retinitis pigmentosa, and McLeod syndrome. Am J Hum Genet 37:250–267

Friedrich U, Warburg M, Wieacker P, Wienker TF, Gal A, Ropers HH (1985) X-linked retinitis pigmentosa: linkage with the centromere and a cloned DNA sequence from the proximal short arm of the X chromosome. Hum Genet 71:93–99

Goodfellow PN, Davies KE, Ropers HH (1985) Report of the Committee on Genetic Constitution of the X and Y Chromosomes. Human Gene Mapping 8. Cytogenet Cell Genet 40:296–352

Lathrop GM, Lalouel JM, Julier C, Ott J (1984) Strategies for multipoint linkage analysis in humans. Proc Natl Acad Sci USA 81:3443–3446

McKusick VA (1986) Mendelian inheritance in man. Johns Hopkins University Press, Baltimore

Musarella MA, Burghes A, Anson-Cartwright L, Mahtani MM, Argonza R, Tsui L-C, Worton R (1988) Localization of the gene for X-linked recessive type of retinitis pigmentosa (XLRP) to Xp21 by linkage analysis. Am J Hum Genet 43:484–494

Nussbaum RL, Lewis RA, Lesko JG, Ferrell R (1985) Mapping X-linked ophthalmic diseases. II. Linkage relationship of X-linked retinitis pigmentosa to X chromosomal short arm markers. Hum Genet 70:45–50

Ott J, Mensink EJBM, Thompson A, Schot JDL, Schuurman RKB (1986) Heterogeneity in the map distance between X-linked agammaglobinemia and a map of nine RFLP loci. Hum Genet 74:280–283

Smith CAB (1963) Testing for heterogeneity of recombination fraction values in human genetics. Ann Hum Genet 27:175–182

van Ommen GJB, Verkerk JMH, Hofker MH, Monaco AP, Kunkel LM, Ray P, Worton R, et al (1986) A physical map of 4 million bp around the Duchenne muscular dystrophy gene on the human X-chromosome. Cell 47:499–504

Wirth B, Denton MJ, Chen JD, Neugebauer M, Halliday FB, van Schooneveld M, Donald J, et al (1988) Two different genes for X-linked retinitis pigmentosa. Genomics 2: 263–266

Wright AF, Bhattacharya SS, Clayton JF, Dempster M, Tippett P, McKeown CME, Jay M, et al (1987) Linkage relationships between X-linked retinitis pigmentosa and nine short-arm markers: exclusion of the disease locus from Xp21 and localization to between DXS7 and DXS14. Am J Hum Genet 41:635–644

Wright AF, Bhattacharya SS, Price WH, Phillips CI, McKeown CME, Crews SJ, Jay M, et al (1983) DNA probes in X-linked retinitis pigmentosa. Trans Ophthalmol Soc UK 103: 467–474