A tight linkage cluster, with two new RFLPs (D8S96 and D8S108), in the interval 8cen-q13

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Description, Source and Method: Probes pBS8-46 (locus D8S96) and pBS8-96 (D8S108) are pBS plasmid vectors (Stratagene, Inc.) containing anonymous inserts of 2.9 and 2.0 kb, respectively, isolated from a human, chromosome-8 specific genomic library (1). The inserts are in *HindIII* sites. With either probe, Southern gel blotting of *HindIII*-digested human genomic DNA detects a single fragment if radiolabeled probe is pre-associated with sheared, boiled human placental DNA.

Variation and Other Enzymes: For D8S96, *NsiI* detects a two-allele restriction site polymorphism with fragment sizes and frequencies (in 30 unrelated individuals [2]) of 4.4 kb — 85% and 3.8 kb — 15% (Figure). The expected heterozygosity (and pic) is 26%. Testing a minimum of 7 unrelated Caucasians, pBS8-46 was not polymorphic for *ApaI*, *EcoRI*, *DraI*, *HgiAI*, *SacI* or *SylI*. For D8S108, *SacI* detects a two-allele restriction site polymorphism in the same population with fragment sizes and frequencies of 11.2 kb — 68% and 9.3 kb — 32% (Figure). The expected heterozygosity is 44%. pBS8-96 was not polymorphic for *ApaI*, *BanII*, *BglII*, *DraI*, *EcoRV*, *HgiAI*, *NsiI*, *MboI*, *RsaI*, *ScaI*, *SstII*, *XbaI*, *XhoI* or *XmnI*.

Inheritance and Linkage: Mendelian inheritance was observed in a large, seven-generation family with autosomal dominant retinitis pigmentosa (RP1) (2). The following statistically-significant between-marker linkages were observed (maximum lod score, percent recombinant and 1-lod confidence interval — using LIPED):

	D8S96 vs.		D8S108 vs.
D8S5	4.8 at 15% (8–26%)	D8S5	not significant
D8S41	4.8 at 0% (0–13%)	D8S41	3.0 at 0% (0–12%)
D8S165	7.8 at 0% (0–5%)	D8S165	9.1 at 0% (0–5%)
PENK	19.8 at 0% (0–2%)	PENK	8.6 at 0% (0–5%)

Linkage testing between D8S96 and D8S108 gave a maximum lod score of 2.4 at 0% (0–18%) recombination, a value which is not statistically significant but is consistent with the other distances. The standardized disequilibrium value between D8S96 and D8S108 (Δ), based on haplotypes determined in the 30 unrelated individuals, was not significantly different from zero.

Chromosomal Location: D8S96 and D8S108 have been mapped to 8cen-q13 in a human-rodent somatic cell panel (1). PENK, to which D8S96 and D8S108 are tightly linked, was previously mapped to 8q23–24 (4) but maps to 8cen-q13 in our somatic cell panel (unpublished). D8S41 and D8S165 have not been regionalized. The probes do not cross-hybridize with each other nor do they detect the same polymorphic sites.

Comment: The tight linkage cluster encompassing D8S41, D8S96, D8S108, D8S165 and PENK will be useful in establishing a fine-structure map in the interval 8cen-q13, a region which includes or is close to RP1 (2). Although the between-marker linkages in this cluster are zero in this family, the 1-lod confidence interval may cover as much as 15 mbp of DNA.

Availability: Probes available from Dr. Wagner.

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	D8S41	D8S108 v. D8S165	PENK
0%	3.0	9.1	8.6
1%	3.0	8.9	8.5
5%	2.7	8.1	7.6
10%	2.3	7.0	6.6
20%	1.5	4.9	4.6
30%	0.8	2.8	2.6
40%	0.2	0.9	0.9
θ	0.0%	0.0%	0.0%
$Z_{\max}$	3.0	9.1	8.6
range	0–12%	0–5%	0–5%

	D8S5	D8S41	D8S96 v. D8S165	PENK
0%	— ∞	4.8	7.8	19.8
1%	— 4.1	4.7	7.6	19.4
5%	2.4	4.4	6.8	17.9
10%	4.3	4.0	5.8	15.9
20%	4.5	3.5	4.0	11.7
30%	3.2	2.3	2.2	7.4
40%	1.5	0.9	0.8	3.3
θ	15%	0.0%	0.0%	0.0%
$Z_{\max}$	4.8	4.8	7.8	19.8
range	8–26%	10–13%	0–5%	0–2%

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