Proc. Natl. Acad. Sci. USA
Vol. 89, pp. 4598–4602, May 1992
Medical Sciences

Integration of gene maps: Chromosome 1

(human genome/linkage)

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Contributed by N. E. Morton, February 10, 1992

ABSTRACT **A composite map of 177 loci has been constructed in two steps. The first combined pairwise logarithm-of-odds scores on 127 loci into a comprehensive genetic map. Then this map was projected onto the physical map through cytogenetic assignments, and the small amount of physical data was interpolated for an additional 50 loci each of which had been assigned to an interval of less than 10 megabases. The resulting composite map is on the physical scale with a resolution of 1.5 megabases. In the future these methods may be used to incorporate locations from linkage, contigs, radiation hybrids, restriction fragments, and somatic cell maps. Dense, reliable, and well-documented maps are essential for long-range sequencing and to localize and clone disease genes.**

Chromosome 1 is the largest in man and it provided the first autosomal linkage and physical maps (1) and radiation hybrid map (2). The Centre d'Etude du Polymorphisme Humain (CEPH) consortium map recognized 58 reliably ordered framework loci and an additional 43 locally unordered loci whose regional assignment was indicated (3). A number of loci mapped in other samples are given in the LODSOURCE data base (4). They include blood groups, isozymes, and diseases not represented in the CEPH sample, as well as additional data on other markers. Multipoint analysis neglecting interference and typing errors requires assembly of raw data from hundreds of reports over nearly 40 years, which is clearly not feasible. Here we use multiple pairwise analysis of sex-specific logarithm-of-odds (lod) scores with allowance for interference and typing errors to produce a genetic map of 127 loci, which is then integrated with other data into a composite map of 177 loci, which conveys physical location.

MATERIAL AND METHODS

The LODSOURCE data base accumulates data as standard lod tables for males, females, and unspecified sex. Since the object of linkage analysis in man is to produce sex-specific maps agreeing in order but not distance, we factored bivariate lod scores by sex, $Z(\theta_m, \theta_f) = Z(\theta_m) + Z(\theta_f)$, where $Z(\theta) = \log_{10}[P(\theta)/P(\frac{1}{2})]$. Here Z denotes a lod, θ a recombination fraction, and $P(\theta)$ the probability of a sample as a function of θ, and m and f are males and females, respectively. Lod scores are additive over samples and may be summarized for each pair of loci by no more than six numbers: $\hat{\theta}_m$, $\hat{Z}_m$, $\hat{\theta}_f$, $\hat{Z}_f$, $\hat{\theta}_u$, $\hat{Z}_u$, where the caret indicates a maximum likelihood estimate and u denotes unspecified sex. Bivariate lod scores were calculated for CEPH data (3) by the CRIMAP program (P. Green, personal communication) and factored into male and female entries by the LODS program (5). All sources except CEPH were taken from the LODSOURCE data base, which derives maximum likelihood estimates by interpolation in standard lod tables extracted from the literature. Multiple pairwise analysis of these data was performed by the MAP90 computer program (6), which can estimate an error frequency ε (7) and a mapping parameter p such that map distance w is a function of θ, ε and p (8). It also includes a bootstrap to optimize order and a stepwise elimination of weakly supported loci to identify a conservative set of reliably ordered (framework) markers. The genetic map was combined with other evidence from the literature and the on-line genome data base (GDB) (9) by using the location data base program (*ldb*) (10). This integrates these partial maps into a composite map that conveys both order and physical location. A summary map comprises the ordered loci and composite location together with the genetic map, cytogenetic and other physical data, and any homologies in the mouse (see Table 3). Locus symbols were obtained from GDB (9) and Human Gene Mapping 10.5 (11).

RESULTS

The Framework Map. A map of loci for which order is well supported by linkage is termed a framework map (4). Such a map is useful for interval location of disease loci. A subset of such loci selected through a gene mapping committee as suitable for low-resolution linkage studies are termed reference loci. Twenty-one loci have been designated as reference markers for chromosome 1 (12). They all have heterozygosities >0.50, have been placed in the genetic map by at least two independent studies, and have been physically mapped on hybrid panels or by *in situ* hybridization. They are highly informative and span nearly the whole chromosome. Such gold-star loci have not, however, been useful in other organisms, because high-resolution mapping requires dense markers (10) and technical advances replace one type of hypervariability by another (13). Local support is measured by the lod of the best order against the most likely interchange with an adjacent locus, and interval support is measured by the lod of the best order against the most likely insertion in another interval. Therefore interval support is always less than or equal to local support. Keats *et al.* (4) suggested that a framework map by multipoint analysis should have interval support (and therefore local support) of at least 3, corresponding to odds of 1000:1, which by a posterior probability argument is required to assert significant linkage for two random markers. They recognized that this argument does not apply to two markers known to be on the same chromosome, but they expressed the hope that an extreme significance level could compensate for the sensitivity of multipoint analysis to typing errors. Subsequently, it has been shown that multiple pairwise analysis is less sensitive to typing errors, especially with error filtration as performed by the MAP90 program (7). Accordingly we have used a local support

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Abbreviations: CEPH, Centre d'Etude du Polymorphisme Humain; GDB, genome data base; lod, logarithm of odds; cM, centimorgan(s); Mb, megabase(s).

of at least 1 to define framework loci by multiple pairwise analysis. Framework loci may also be defined on physical evidence (14). To construct a comprehensive genetic map the CEPH consortium map of chromosome 1 was used to provide an initial framework (3); *AMY2B, SPTA1*, and *D1S8* were excluded because, at this stage, the MAP90 program did not support the consortium final order for these loci. The remaining loci were inserted at their most likely locations in this map of 55 loci. A final conservative framework map with a minimum local support of 1 with the inclusion of the 21 reference loci was obtained by using an algorithm for stepwise elimination of loci with the lowest local support. This process gave a map of 49 loci from *D1Z2* to *D1S68* that is in close agreement with the consortium map except in regions where there is a large gap between reference loci. For example, in the 50 centimorgans (cM) that separate *D1S61* and *D1S81* on the male map our algorithm chooses the highly supported loci *D1S65, D1S84*, and *SNRPE* in preference to *F13B* and *D1S53*. Clearly, gold-star loci are not unique and are subject to continual revision by new evidence and/or consensus.

Since order in a comprehensive genetic map is locally unreliable, framework loci should provide better estimates of error frequency, mapping parameter, and sex-specific arm lengths. From replicate typing the error frequency has been estimated as 0.006 (54 discordancies among 4205 duplicate samples) (3). The MAP90 program agrees closely, with an error frequency of 0.008 ± 0.001 (Table 1). The mapping parameter that best fits the whole chromosome is 0.309 ± 0.013, where the standard errors neglect covariances with map distances and are therefore slightly underestimated. The mapping parameter is in fair agreement with the value of 0.351 ± 0.007 from chiasma distributions for metacentric chromosomes in man (8). Failure to allow for typing error inflates the mapping parameter to 0.387 and gives a significantly bad fit (χ^2_1 = 1785.33 − 1760.03 = 25.30). The hypothesis that the female map is proportional to the male map is rejected (χ^2_{47} = 430.89), as are the hypotheses of no interference ($p = 1$, χ^2_1 = 212.56) and Kosambi interference ($p = 0.5$, χ^2_1 = 36.42). When each arm is examined separately (Table 2) the error frequency remains the same, but the mapping parameter and map lengths are reduced, in agreement with evidence from *Drosophila* that paracentric maps have a smaller mapping parameter than pericentric maps (15). The final comprehensive genetic map was obtained by using an error frequency of 0.008 and a mapping parameter of 0.309 with map length scaled to the values in Table 2.

When arms are examined separately the estimate of map length in males is 229 cM. To include the telomeres on the assumption of a uniform distribution the length should be multiplied by $(n + 1)/(n - 1)$, where the number of loci, n, is 49. This gives a length of 238.5 cM. Whether or not this adjustment is made, the genetic map is in excess of the length from chiasmata, which is 201 cM from arms with a terminal chiasma (16) and 194 cM for all arms (17). It seems likely that conservative enumeration of chiasmata omits a fraction that may be as great as 16%, and therefore the distribution of chiasmata along the unbanded meiotic chromosome should be taken as only a rough indication of the genetic map. It remains true that a male map much in excess of the chiasma map raises a suspicion of inadequate allowance for typing errors or interference.

Table 1. Tests of hypothesis on the framework map (parameters fixed by hypothesis in parentheses)

Hypothesis	ε	p	K	Map length, cM		χ^2
				Male	Female	
Sexes separate	(0)	(0.35)	1.68	249.2	419.1	1787.21
	(0)	0.387	1.69	256.5	432.9	1785.33
	0.007	(0.35)	1.68	242.2	406.7	1762.61
	0.008	0.309	1.67	233.7	390.8	1760.03
	0.000	(1)	1.72	416.1	716.0	1972.59
	0.002	(0.5)	1.70	279.4	474.6	1796.45
$w_f = Kw_m$	0.008	0.275	1.70	224.3	381.3	2190.92

ε, Error frequency; p, mapping parameter; K, ratio of genetic map lengths in females and males.

Table 2. Estimates of framework parameters

Arm	ε	p	Map length, cM		K
			Male	Female	
p	0.009	0.236	117.3	210.1	1.79
q	0.007	0.253	111.7	164.5	1.47
p + q	0.008	0.309	233.7	390.8	1.67

ε, Error frequency; p, mapping parameter; K, ratio of genetic map lengths in females and males.

The Composite Map. Chromosome 1 has poor physical information, with few contigs, no long-range restriction fragment map, no standard somatic cell panel defining regions, and no radiation hybrid map since the pioneer work on a few loci (2). However, cytogenetic assignment provides coarse localization that can be used to project the genetic map into the physical map. Therefore this fragmentary evidence may be integrated into a composite map that will converge to a reliable physical map as new data are incorporated (10). Cytogenetic locations were obtained from the on-line GDB (9). Locations in megabases (Mb) for cytogenetic bands were obtained by measurement of chromosome diagrams (18). If the left and right limits of a cytogenetic assignment for the ith locus are l_i, r_i Mb, the point estimate is $c_i = (l_i + r_i)/2$ and the interval is $S_i = r_i - l_i$. Let $\hat{c}_i$ be the projection of the sex-averaged genetic location w_i on the physical map, and let $Y_i = -\ln(c_i - \hat{c}_i)^2$. Then the linear regression $Y = A + BS$ defines a weight $K_i = e^{A+BS_i}$ to be applied to the projection $c_i = f(w_i)$, a polynomial in which the powers of w_i were chosen stepwise. This process converged after a few cycles of iterative least squares to a sigmoid curve which was used to project the genetic map onto a physical scale. Cytogenetic assignments and contigs were then incorporated by the *ldb* program, with highest priority being given to contigs and lowest priority to cytogenetic assignment in the absence of other evidence (10). Each locus was assigned a rank (to indicate reliability of ordering) of 2 for reference loci, 1 for other framework loci reliably ordered by linkage, and 0 for locally unordered loci. Loci having only a cytogenetic assignment to a band width greater than 10 Mb have been omitted in Table 3. There are 177 loci in this map, of which 56 are framework loci. Of these, 21 are designated reference loci, a further 28 were identified by a stepwise elimination algorithm, and 7 (*D1S50, D1S91, ALPL, D1S38, D1S14, TSHB, D1S36*) were identified subsequently as also having interval support of at least 1. All but 2 loci have a cytogenetic assignment, 127 are on the linkage map, and 50 have only a physical assignment. For contigs of known polarity, location in megabases has been estimated by using the linkage map projected onto the physical scale. Loci assigned to a segment of unknown polarity and not believed to be partially homologous are treated as a megalocus, with the same location estimated from linkage as described above. Gene clusters of partially homologous loci are indicated as a single locus with the @ suffix.

Of the 177 loci, 36 have known homologs in the mouse (25). Blocks of genes from mouse chromosomes 1, 3, and 4 are conserved, but there are some conflicts in order; it is not clear how much rearrangement there has been within a block. The human map is fallible, and the mouse map combines heter-

Table 3. Summary map of chromosome 1

Locus	Rank*	Composite map, Mb	Genetic map, cM ♂	Genetic map, cM ♀	Cytogenetic bands Left	Cytogenetic bands Right	Physical map, Mb	Mouse map CH:cM†	Ref.‡
pter	0	0.00	0.0	0.0	ptr	ptr	0.00		
D1Z2	2	0.00	0.0	0.0	p36.3	p36.3			
D1S80	0	0.00	0.0	0.0	p36	p35			
D1S77	2	0.55	0.0	4.4	p36	p34			
D1S76	0	1.07	4.0	4.4	p36	p35			
D1S49	2	1.56	7.6	4.4	p36	p34			
GDH	0	1.56	7.6	4.4	p36	p36			
D1S50	1	2.07	7.6	8.0	p36	p34			
D1S98	0	3.70			p36.3	p36.3			
D1S153	0	3.70			p36.3	p36.3			
D1F35S2	0	3.70			p36.3	p36.3			
D1S43	2	5.12	17.9	16.8	p36	p34			
D1S47	0	5.12	17.9	16.8	p36	p34			
D1S91	1	8.15	25.2	25.5	p36	p35			
PGD	0	8.15	25.2	25.5	p36.3	p36.13		4:65	
ENO1	0	8.15	25.2	25.5	p36	p36	8.15	4:	2
PND	0	8.15	25.2	25.2	p36	p36		4:66	
ERPL1	0	11.67	25.2	47.8	ptr	p36			
D1S97	0	12.35			p36.2	p36.12			
D1S96	0	12.35			p36.2	p36.12			
D1S95	0	12.35			p36.2	p36.12			
D1S71	2	14.64	41.6	47.8	p36	p34			
DNB	0	16.40			p36.12	p36.12			
TSG12	0	16.40			p36.12	p36.12			
D1S94	0	18.65			p36.12	p36.11			
D1S56	2	18.79	45.9	64.0	p36	p34			
EKV	0	19.54	46.0	67.6					
D1S112	0	19.55			p36.11	p36.11			
ALPL	1	19.56	46.0	67.7	p36.1	p34		4:60	
EL1	0	20.00	46.0	69.5	p36	p34			
FUCA1	1	20.49	46.0	71.8	p34	p34	20.49	4:	2
EBVS1	0	24.45			p35	p35			
CMP	0	24.45			p35	p35			
CRTM	0	24.45			p35	p35			
RH	1	24.89	47.2	74.4	p36.2	p34			
CSF3R	0	26.40			p35	p34.3			
HMG17	0	27.67	49.6	74.4	p36.1	p35			
FGR	0	27.67	49.6	74.4	p36.2	p36.1		4.62	
APNH	0	29.58	49.7	76.0	p36.1	p35		4:	
D1S63	2	32.67	50.0	78.2	p35	p32			
D1S7	1	38.27	50.2	82.7	p35	p33			
D1S40	0	41.95	53.2	82.7	p35	p32			
D1S45	1	44.47	55.2	82.7	p35	p32			
BLYM	0	48.05			p32	p32			
FRA1B	0	48.05			p32	p32			
D1S100	0	48.05			p32	p32			
TCL5	0	48.05			p32	p32			
TAL1	0	48.05			p32	p32			
D1S101	0	48.05			p32	p32			
AK2	0	50.45			p34	p34	50.46	4:	2
CLN1	0	52.13	55.3	88.5	p32	p32			
D1S57	2	52.13	55.3	88.5	p35	p32			
MYCL1	1	60.78	55.3	95.2	p32	p32		4:53	
FRA1C	0	62.45			p31.2	p31.2			
GLUT1	0	66.40	57.2	97.5	p35	p31.3			
UMPK	0	71.59	58.3	100.2	p32	p32	71.59		2
D1S41	1	73.26	58.7	103.4	p35	p32			
D1S62	0	74.24	58.7	105.6	p32	p32			
D1S86	0	75.41	58.9	108.1	p32	p22.1			
SC	0	76.04	60.4	108.1	p36.2	p22.1			
RD	0	76.04	60.2	108.1	p36	p22.1			
D1S44	1	76.04	60.4	108.1	p32	p32			
D1S85	0	81.06	60.4	118.8	p32	p22.1			
D1S15	2	81.54	61.2	118.9	p32	p22			
D1S21	1	83.36	61.2	122.8	p32	p22			
D1S17	2	85.79	63.3	125.7	p32	p22			
C8@§	0	86.08	64.0	125.7	p32	p32			
D1S18	0	87.17	64.0	127.9	p32	p22			
D1S19	1	89.17	68.0	127.9	p32	p22			
PGM1	1	94.50	73.6	132.5	p22.1	p22.1	94.50	4:42	2
D1S22	1	95.89	75.8	137.0	p22	p22			
D1S2	0	96.92	78.5	139.2	p22	p22			
ACADM	2	98.14	78.5	144.6	p31	p31			
FRA1E	0	98.95			p21.2	p21.2			
D1S35	0	101.69	78.5	160.5	p22.1	p13			
D1S16	1	102.11	78.5	162.3	p22	p22			
D1S38	1	104.36	88.1	162.3	p22.1	p13			
D1S34	1	105.51	92.9	162.3	p22.1	p13			
F3	0	108.10	92.9	172.9	p22	p21			
D1S20	0	113.51	106.6	180.5	p22	p22			
D1S12	0	114.13	107.4	182.2	p22	p21			
AMY@§	2	115.60	107.4	187.7	p21	p21		3:68	
D1S10	0	115.60	107.5	187.7	p22	p13			
D1S14	1	116.81	108.8	191.0	p21	p13			
D1S64	0	116.81	108.8	191.0	p22.1	p13			
D1S39	0	117.45	111.1	191.1	p22.1	p13			
D1S37	1	117.77	112.3	191.1	p22	p21			
GST1	0	118.79	112.3	195.0	p31	p31			
D1S55	0	118.90	112.5	195.0	p22.1	p13			
D1S73	0	120.14	112.8	199.4	p21	cen			
HSDB3	0	120.50			p13.1	p13.1			
D1S9	0	121.39	113.1	203.7	p22	p13			
D1S11	1	122.71	114.5	207.1	p13	p13			
CD2	0	123.53			p13	p13	123.53	3:66	19
CD58	0	123.53			p13	p13	123.53		19
ATP1A1	0	123.53			p13	p13	123.53	3:67	19
NGFB	0	123.53	114.5	210.1	p13	p13	123.53	3:67	19
TSHB	1	123.53	114.6	210.1	p13	p13	123.53	3:67	19
AMPD1	0	123.53			p13	p13	123.53	3:67	19
NRAS	0	123.53	114.6	210.1	p13	p13		3:63	
GBA	0	123.53	114.6	210.1	q21	q21		3:52	
NEFHL	0	124.30			p12	p12			
D1S36	1	125.20	114.6	216.3	p13	p13			
D1S13	2	126.59	116.9	218.9	p13	p13			
D1Z8	0	128.00			cen	cen			
cen	0	128.00	118.9	221.8	cen	cen	128.00		
D1Z3	0	128.00			cen	cen			
D1Z7	0	128.00			cen	cen			
D1Z5	1	128.00	118.9	221.8	cen	cen			
D1S90	0	132.34	120.1	224.7	cen	qtr			
01QH	0	138.36	121.4	228.9	q12	q12			
D1S67	0	141.98	122.1	231.5	q21	q21			
MUC1	2	144.16	122.1	233.4	q21	q23			
CD1@§	0	148.13			q22	q23	148.13	3:62	20
SPTA1	0	148.13	122.1	237.2	q21	q21	148.13	1:73	21
CRP	1	148.89	124.7	238.0	q21	q23	148.89	1:71	21
APCS	0	149.39	122.1	237.2	q21	q23	149.39	1:72	21
FCER@§	0	149.76			q23	q23	149.76	1:72	21
FY	0	150.59	126.9	240.5	q22	q23			
ATP1A2	1	151.25	128.1	241.5	q21	q23	151.25	1:72	21
CMT1B	0	155.92	129.3	244.6	cen	qtr			
APOA2	2	155.92	129.3	244.6	q21	q23		1:71	
NEM1	0	155.92	129.3	244.6	q21	q23			
CAE	0	162.52	131.8	248.4	q21	q25			
D1S26	0	162.52	131.8	248.4	q12	q23			
D1S104	1	163.39	132.7	248.4	q21	q23			
UGP1	0	164.99			q21	q22	164.99		2
D1S75	0	169.22	132.7	254.5	q22	q23			
D1S66	0	169.93	133.5	254.5	q21	q31			
FCGR@§	0	171.70			q23	q23		1:71	
PBX1	0	171.70			q23	q23			
HOXP	0	171.70			q23	q23			
D1S42	0	172.09	134.2	256.2	q21	q31			
D1S61	2	176.59	139.1	256.2	q21	q31			
F5	0	181.99	139.1	262.2	q21	q25	181.99	1:68	22
GRMP	0	181.99			q22	q25	181.99	1:68	22
LNHR	0	181.99					181.99		22
ELAM1	0	181.99			q22	q25	181.99		22
FRA1G	0	184.50			q25.1	q25.1			
NCF2	0	186.95			q25	q25			
AT3	1	187.57	145.4	262.2	q23	q25.1		1:66	
PEPC	0	216.10	161.8	277.9	q25	q25	216.10	1:49	2

Table 3. (*Continued from previous page.*)

Locus	Rank*	Composite map, Mb	Genetic map, cM ♂	Genetic map, cM ♀	Cytogenetic bands Left	Cytogenetic bands Right	Physical map, Mb	Mouse map CH:cM†	Ref.‡
F13B	0	216.10	161.8	277.9	q31	q32.1	216.10		
LAMB2	1	216.99	163.9	277.9	q31	q31		1:61	
D1S84	1	219.20	168.9	277.9	q31	q32			
D1S65	1	221.03	170.2	280.7	q31	q32			
SNRPE	1	223.45	174.4	282.2	q25	q43			
D1S4	0	223.45	174.4	282.2	p21	qtr			
HF	0	224.74	174.4	285.3	q32	q32	224.74	1:56	
D1S59	0	226.44	174.4	289.1	q21	q31			
VWS	0	226.69	174.4	289.7	q32	q41			
D1S53	0	229.63	174.4	296.7	q31	q32			
D1S52	0	229.87	175.0	296.7	q31	q32			
REN	1	230.70	177.0	296.7	q32	q32	230.70	1:48	23
CTSE	0	230.70			q31	q31	230.70		23
C4BP@§	0	232.33	179.1	298.6	q32	q32	232.33	1:47	24
DAF	0	232.33	179.1	298.6	q32	q32	232.33		24
CR2	1	232.33	179.1	298.6	q32	q32	232.33	1:83	24
CR1@§	0	232.33	179.1	298.6	q32	q32	232.33	1:83	24
MCP	0	232.33			q32	q32	232.33		24
D1S54	0	232.98	179.1	300.3	q32	q32			
D1S58	0	233.05	179.1	300.4	q31	q32			
D1S70	1	234.51	180.9	302.2	q32	q44			
USH2	0	244.14	186.6	322.1	cen	qtr			
FH	0	244.30			q42.1	q42.1	244.30		2
D1S81	2	245.60	187.9	325.0	q32	q44			
FRA1H	0	246.20			q42	q42			
HRES1	0	246.20			q42	q42			
D1S46	0	248.47	194.0	327.5	q32	q44			
D1S48	1	250.48	194.0	334.0	q32	q44			
D1S103	2	252.27	194.0	340.0	q32	q44			
NID	0	254.00			q43	q43			
D1S51	0	256.07	196.7	351.3	q32	q44			
D1S8	0	257.41	198.8	354.8	q42	q43			
D1S74	2	258.00	200.7	355.5	q32	q44			
FRA1I	0	260.10			q44	q44			
D1S102	2	260.66	215.5	377.1	q32	q44			
D1S69	0	263.00	233.7	390.8	q44	q44			
D1S68	2	263.00	233.7	390.8	q32	q44			
qter	0	263.00	233.7	390.8	qtr	qtr	263.00		

*Rank 2, reference locus; 1, (other) framework locus; 0, locally unordered.
†Mouse chromosome number: location in cM.
‡Reference to physical map data.
§Gene clusters as follows: *C8@*(*C8A,C8B*); *AMY@*= (*AMY2B, AMY2A, AMY1A, AMY1B, AMYP1, AMY1C*); *CD1@*= (*CD1D, CD1A, CD1C, CD1B, CD1E*); *FCER@*= (*FCER1A, FCER1G*); *FCGR@*= (*FCGR3B, FCGR2A, FCGR2A1, FCGR3A, FCGR2B*); *C4BP@*= (*C4BPAL1, C4BPA, C4BPB*); *CR1@*= (CR1L, CR1).

ogeneous linkage data from interspecific crosses, both sexes, ovarian teratomas, and crosses of inbred lines by methods that are not entirely objective. As the linkage maps of both species improve and as physical and linkage maps are integrated, many discrepancies in order will be removed. References in Table 3 are to partial physical maps, which give the evidence from which the summary map was constructed.

DISCUSSION

There are some striking discrepancies in the summary map. *ACADM* and *GST1* map proximal to *PGM1* in the genetic map, but the cytogenetic assignment is distal. *GBA* is assigned to the p arm by linkage in a small number of families, but to the q arm by *in situ* hybridization. *CTSE* maps distal to *REN* by high-resolution *in situ* hybridization, but the cytogenetic assignment is proximal. Apparent lack of colinearity with the mouse map has been discussed above.

It would not be surprising if the receptor clusters *FCER@* and *FCGR@*, which are assigned to q23, were tightly linked, since the corresponding structural loci form the *IGHC@* cluster. However, at this point *FCER@* is localized close to *APCS* on a 6-Mb fragment that is not known to contain *FCGR@*, which is therefore localized only to the midpoint of q23. The map contains two inverted orders compared with the CEPH consortium map of 58 loci—namely, the closely linked loci *F13B/LAMB2* and *D1S8/D1S74*.

One reason for presenting Table 3, which represents only part of the *ldb* data base for chromosome 1, is that there is controversy about how physical and linkage maps should be developed (10). Consensus maps that do not convey the evidence on which they were based are a triumph of democracy over science. No chromosome workshop has yet succeeded in producing a publishable summary map, except by omitting all the evidence and a large proportion of the loci. The GDB contains much useful description but has not so far attempted to record location except for cytogenetic assignment and has no algorithms to reconcile partial maps (9). Since much of the information on gene maps is currently wasted or transmitted without authentication, adoption of methods to build composite maps from completely specified partial maps, of which *ldb* is the prototype, is of some urgency. Only a dense composite map is useful in long-range sequencing or to localize and clone a disease gene.

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