Hum Genet (1982) 61:48–49

Human Genetics

Aminolevulinate Dehydratase (E.C. 4.2.1.24): Linkage Analysis

A. Amorim[1], J. Kömpf[2], F. Schunter[3], and H. Ritter[2]

[1] Institute de Antropologia, Faculdade de Ciências, Universidade do Porto, 4000 Porto, Portugal
[2] Institut für Anthropologie und Humangenetik der Universität Tübingen, D-7400 Tübingen, Federal Republic of Germany
[3] Abteilung für Transfusionswesen der Universität Tübingen, D-7400 Tübingen, Federal Republic of Germany

Summary. Linkage data on aminolevulinate dehydratase (ALADH, E.C. 4.2.1.24) and a series of other human genetic markers are presented. One hundred and two families (25 of them being informative) from southwestern Germany were tested. Close linkage ($\theta = 0.05$) between ALADH and the following markers could be excluded: Rh, PGM_1, Fy, ACP1, MNSs, HLA, Bf, GLO, PGM_3, Jk, Pi, PGP, K, GPT. There is some evidence of possible linkage with HPA.

Introduction

Genetic polymorphism of aminolevulinate dehydratase, or porphobilinogen synthase (E.C. 4.2.1.24) was recently described in man (Battistuzzi et al. 1981). These authors reported this enzyme to be under the control of an autosomal locus ALADH with two alleles $ALADH^1$ and $ALADH^2$. In this paper we present the results of our studies on 102 families, 25 of them being informative for linkage.

Materials and Methods

Blood samples were obtained by venipuncture, with or without EDTA as anticoagulant. The samples were used fresh, or stored at −20° C in glycerol medium for up to five years. Hemolysates were prepared after two washings by sonication, followed by treatment with toluene.

Starch gel electrophoresis (15% Connaught-starch) was performed in a discontinuous system (bridge buffer: 1.13 *M* NaOH, 0.4 *M* citric acid, pH 6.0; gel buffer: 12.5 m*M* NaOH, 26 m*M*

Table 1. Lod score values for ALADH and other marker loci

Locus	Segregation information[a]	Recombination fraction					Number of	
		0.05	0.10	0.20	0.30	0.40	Families	Children
Rh	P	[b]	−1.35	−0.51	−0.18	−0.04	6	14
	M	[b]	−1.56	−0.64	−0.24	−0.06	5	12
PGM_1	P	[b]	[b]	−0.97	−0.38	−0.09	4	11
	M	[b]	−1.98	−0.71	−0.22	−0.04	6	19
Fy	P	[b]	[b]	−0.84	−0.32	−0.07	5	14
	M	−0.93	−0.46	−0.12	−0.02	0.00	4	8
ACP1	P	[b]	−1.30	−0.25	0.03	0.04	7	22
	M	[b]	[b]	−1.16	−0.45	−0.11	4	13
MNSs	P	[b]	−1.57	−0.57	−0.19	−0.04	5	16
	M	[b]	−1.56	−0.64	−0.24	−0.06	5	12
Gc	P	−1.09	−0.40	0.07	0.13	0.06	3	12
	M	0.35	0.09	0.07	0.05	0.02	3	8
HLA	P	[b]	[b]	−0.82	−0.27	−0.06	7	23
	M	−1.11	−0.44	0.00	0.07	0.03	6	15
Bf	P	[b]	−1.79	−0.70	−0.25	−0.06	4	14
	M	−0.27	−0.44	−0.19	−0.08	−0.02	1	3
GLO1	P	−0.87	−0.26	−0.09	0.09	0.03	5	16
	M	−1.18	−0.67	−0.25	−0.09	−0.02	3	7
PGM_3	M	[b]	−1.78	−0.78	−0.30	−0.07	2	9
Jk	P	[b]	[b]	−1.22	−0.47	−0.11	5	17

Offprint requests to: A. Amorim

0340-6717/82/0061/0048/$ 01.00

Table 1 (continued)

Locus	Segregation information[a]	Recombination fraction					Number of	
		0.05	0.10	0.20	0.30	0.40	Families	Children
	M	−0.21	−0.01	0.07	0.05	0.02	2	6
AB0	P	−0.20	−0.01	0.07	0.05	0.02	3	6
	M	0.26	0.22	0.13	0.06	0.02	1	2
AK	P	0.52	0.43	0.27	0.13	0.03	2	4
Pi	P	−1.90	−1.12	−0.45	−0.16	−0.04	4	9
	M	−1.18	−0.67	−0.25	−0.09	−0.02	3	7
Gm	P	0.05	0.20	0.21	0.12	0.03	4	8
	M	−1.18	−0.67	−0.25	−0.09	−0.02	3	7
HPA	P	0.89	0.96	0.79	0.49	0.16	3	11
	M	−1.30	−0.69	0.13	0.17	0.06	6	20
PGP	P	−1.65	−0.90	−0.31	−0.10	−0.07	5	10
	M	−0.72	−0.44	−0.19	−0.08	−0.02	1	3
Kk	P	[b]	−1.33	−0.58	−0.23	−0.05	2	7
C3	P	0.52	0.43	0.27	0.13	0.03	2	4
	M	−0.21	−0.01	0.07	0.05	0.02	2	6
GPT	P	−0.72	−0.44	−0.19	−0.08	−0.02	1	2
	M	[b]	−1.10	−0.32	−0.07	−0.01	6	14
ME2	P	−1.44	−0.89	−0.39	−0.15	−0.04	2	5
	M	−0.21	−0.01	0.07	0.05	0.02	2	6

[a] P = paternal; M = maternal
[b] Lod score values at least −2.00

Note added in proof: There was not enough linkage information to be presented here for the following markers: 6-PGD, FucA, UMPK, AMY2, Inv, Gt, EsD, GOT2, PEPA, ADA, CDA

histidine × HCl, pH 6.0) for 16 h at 5 V/cm with cooling (temperature of cooling water was +8° C). Staining was done essentially as described by Battistuzzi et al. (1981), with the addition of Zn^{++} (10 m*M* of zinc acetate) to the staining mixture in order to prevent lead inactivation of the enzyme (Thomasino et al. 1977).

Lod score values were obtained using the tables of Maynard-Smith et al. (1961).

For linkage the following markers were studied: AB0, MNSs, Kk, Fy, Jk, Rh, Gm, Inv, Gc, HPA, C3, AMY_2, Pi, Bf, Tf, ACP1, AK1, ADA, UMPK, GPT, Gz, PGP, EsD, PGM_1, PGM_3, 6-PGD, GLO, FUCA, GOT2, ME2, PEPA, CDA.

Results and Discussion

The segregation of ALADH in the families studied is in agreement with Mendelian expectations and will be published elsewhere. Table 1 shows the linkage relationships between ALADH and other genetic markers. Z-scores are given for each sex.

Linkage with $\theta \leqq 0.10$ can be ruled out between ALADH and the following systems: MNSs, Fy, Jk, Rh, HLA, ACP1, and PGM_1. Close linkage ($\theta \leqq 0.05$) can be excluded for K, Pi, GPT, PGP, PGM_3, GLO, and Bf. Positive lod score values (sexes combined) were obtained especially for the HPA system (0.922 at $\theta \leqq 0.20$). This result suggests linkage between ALADH and HPA. To confirm this more family studies are required.

Acknowledgements. A. Amorim was supported by DAAD and INIC (Portuguese Institute für Scientific Investigation), and J. Kömpf by the Deutsche Forschungsgemeinschaft (Ko 565/5).

References

Battistuzzi G, Petrucci R, Silvagni L, Urbani FR, Caiola S (1981) Delta aminolevulinate dehydrase: A new genetic polymorphism in man. Ann Hum Genet 45:223–229

Maynard-Smith S, Penrose LS, Smith CAB (1961) Mathematical tables for research workers in human genetics. Churchill, London

Thomasino JA, Zuroweste E, Brooks SM, Petering HG, Lerner SJ, Finelli VN (1977) Lead, zinc, and erythrocyte delta-aminolevulinic acid dehydratase: Relationships in lead toxicity. Arch Environ Health 35:244–247

Received March 27, 1982