Coll. Antropol. **26** (2002) 2: 403–410
UDC 572:575.17(497)
Original scientific paper

Allele Frequencies of Alpha-1-Antitrypsin (PI) in the Balkans

H.-G. Scheil[1], S. Schuhen[1], W. Huckenbeck[2] and H. D. Schmidt[3]

[1] Institute of Human Genetics and Anthropology, Heinrich-Heine-University, Düsseldorf, Germany

[2] Institute of Legal Medicine, Heinrich-Heine-University, Düsseldorf, Germany,

[3] Department for Anthropology, University of Ulm, Ulm, Germany

ABSTRACT

*The phenotype and allele frequencies of alpha-1-antitrypsin has been studied by an IEF technique (pH 4.2–4.9) in ten population samples from the Balkans. The allele frequencies varied from 0.6667 to 0.7361 (*M1), 0.1100 to 0.1793 (*M2), 0.0992 to 0.1700 (*M3), 0 to 0.0105 (* S), 0 to 0.0078 (*Z) and 0 to 0.0172 (others). The results were compared with data from South and Middle European populations from the literature. Most of the populations form a cluster with small genetic distances, and a weak relationship to geographical distributions. In contrast, the samples from Southern France, the Iberian Peninsula and Madeira form a clearly separated cluster. The differences are mainly based on high frequencies of PI*S in the latter populations.*

Introduction

In the course of an investigation of the genetics of some populations from Southeastern Europe[1–3], the phenotype and allele frequencies of alpha-1-antitrypsin (PI system) has been studied in ten samples of different populations from the Balkans. The results have been compared with Middle, West and South European population samples from the literature. The results are presented in the following.

Material and Methods

The study comprised the following population samples (Figure 1): Albanians (Tirana, 99 individuals), Greeks (Thracia, 108 ind.), Macedonians (Skopje, 128 ind.) Romanians, Dobruja (Constanta, 145 ind.) and South (Ploiesti, 126 ind.), the Aromun samples: Pindonians (Albania, Andon Poci, 100 ind.), Musequiars (Albania, Dukasi, 101 ind.), Moskopolians (Macedonia, Kruševo, 95 ind.), Gramostians (Macedonia, Stip, 108 ind.), Fraseriots

---

Received for publication September 16, 2002

Fig. 1. Geographical distribution of the population samples studied.
1 = Albania (Tirana), 2 = Greece (Thracia), 3 = Macedonia (Skopje), 4 = Romania, Dobruja (Constanta), 5 = Romania, South (Ploiesti), 6 = Aromuns, Pindonians (Albania, Andon Poci), 7 = Aromuns, Musequiars (Albania, Dukasi), 8 = Aromuns, Moskopolians (Macedonia, Kruševo), 9 = Aromuns, Gramostians (Macedonia, Stip), 10 = Aromuns, Fraseriots (Romania, Kogalniceanu)

(Romania, Kogalniceanu, 91 ind.). For the classification of the Aromun populations see Schmidt et al.[4,5]. The samples originated from the general population except of course the Aromun samples. The individuals have belonged to the corresponding groups over the last three generations.

The samples have been typed by standard methods: Isoelectric focusing using a polyacrylamide gel, pH 4.2–4.9, containing 0.65% ACES. All serum samples were stored at –20 °C, but the samples had been thawed several times. Therefore an aliquot of each sample had been treated with dithiothreitol and iodoacetamide prior to use[6].

For the cluster analysis the UPGMA -method was used based on the Rogers distances modified by Wright[7,8].

Results and Discussion

Table 1 shows the observed and expected phenotype frequencies in the populations studied. There was a good agreement between observed and expected numbers assuming a Hardy-Weinberg equilibrium. Table 2 shows the allele frequencies of the populations studied. The frequencies of PI*M1 vary from 0.6667 (Albanians and Greeks) to 0.7361 (Aromuns, Gramostians), and the frequencies of PI*M2 from 0.1100 (Aromuns, Pindonians) to 0.1793 (Romanians, Dobruja), but the allele frequencies of the populations studied and the cluster analysis did not result in a separation according to the geographical distribution and not a clear separation of the Aromun populations. The two observed clusters in Figure 2 are based on very small genetic distances.

TABLE 1
ALPHA-1-ANTITRYPSIN (PI) – OBSERVED AND EXPECTED PHENOTYPE FREQUENCIES IN THE SAMPLES STUDIED

Phenotype	Albanians (Tirana)		Greeks (Thracia)		Macedonians (Skopje)		Romanians, Dobruja (Constanta)		Romanians, South (Ploiesti)	
	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
PI M1	46	44.00	52	48.00	68	67.57	64	66.23	62	65.00
PI M2	2	2.75	2	3.34	1	2.26	4	4.66	1	3.34
PI M3	4	2.43	4	2.37	2	1.76	2	1.99	2	1.24
PI S	–	–	–	–	0	0.00	0	0.00	–	–
PI Z	–	–	–	–	0	0.01	0	0.01	0	0.00
PI V	0	0.01	0	0.01	0	0.02	1	0.04	0	0.03
PI M1-M2	23	22.00	24	25.33	26	24.70	38	35.15	36	29.45
PI M1-M3	16	20.67	15	21.33	22	21.80	26	22.98	17	17.96
PI M1-S	–	–	–	–	1	0.73	1	0.68	–	–
PI M1-Z	–	–	–	–	0	1.45	2	1.35	1	0.72
PI M1-V	1	1.33	1	1.33	1	2.18	1	3.38	3	2.87
PI M2-M3	6	5.17	9	5.63	4	3.98	4	6.10	3	4.07
PI M2-S	–	–	–	–	0	0.13	0	0.18	–	–
PI M2-Z	–	–	–	–	1	0.27	0	0.36	0	0.16
PI M2-V	0	0.33	1	0.35	1	0.40	2	0.90	0	0.65
PI M3-S	–	–	–	–	0	0.12	0	0.12	–	–
PI M3-Z	–	–	–	–	0	0.23	0	0.23	0	0.10
PI M3-V	1	0.31	0	0.30	0	0.35	0	0.59	1	0.40
PI S-Z	–	–	–	–	0	0.01	0	0.01	–	–
PI S-V	0	0.01	–	–	0	0.01	0	0.02	–	–
PI Z-V	–	–	–	–	1	0.02	0	0.03	0	0.02
N	99	99.01	108	107.99	128	128.00	145	145.01	126	126.01

TABLE 1, continued

Phenotype	Aromuns, Pindonians (Albania, Andon Poci)		Aromuns, Musequiars (Albania, Dukasi)		Aromuns, Moskopolians (Macedonia, Kruševo)		Aromuns, Gramostians (Macedonia, Stip)		Aromuns, Fraseriots (Romania, Kogalniceanu)	
	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
PI M1	51	51.12	56	50.62	44	43.79	58	58.52	40	41.56
PI M2	3	1.21	5	2.38	4	2.70	3	1.82	2	3.56
PI M3	3	2.89	4	1.80	0	1.65	0	1.95	1	1.10
PI S	–	–	–	–	0	0.01	–	–	0	0.00
PI Z	–	–	–	–	0	0.00	–	–	0	0.00
PI V	0	0.00	0	0.00	0	0.00	–	–	0	0.00
PI M1-M2	14	15.73	16	21.95	18	21.73	18	20.61	27	24.33
PI M1-M3	26	24.31	15	19.11	19	16.97	25	21.35	13	13.52
PI M1-S	–	–	–	–	2	1.36	–	–	1	0.68
PI M1-Z	–	–	–	–	1	0.68	–	–	1	0.68
PI M1-V	1	0.72	0	0.71	1	0.68	–	–	1	0.68
PI M2-M3	2	3.74	4	4.14	6	4.21	4	3.76	5	3.96
PI M2-S	–	–	–	–	0	0.34	–	–	0	0.20
PI M2-Z	–	–	–	–	0	0.17	–	–	0	0.20
PI M2-V	0	0.11	1	0.15	0	0.17	–	–	0	0.20
PI M3-S	–	–	–	–	0	0.26	–	–	0	0.11
PI M3-Z	–	–	–	–	0	0.13	–	–	0	0.11
PI M3-V	0	0.17	0	0.13	0	0.13	–	–	0	0.11
PI S-Z	–	–	–	–	0	0.01	–	–	0	0.01
PI S-V	–	–	–	–	0	0.01	–	–	0	0.01
PI Z-V	–	–	–	–	0	0.01	–	–	0	0.01
N	100	100.00	101	100.99	95	95.01	108	108.01	91	91.03

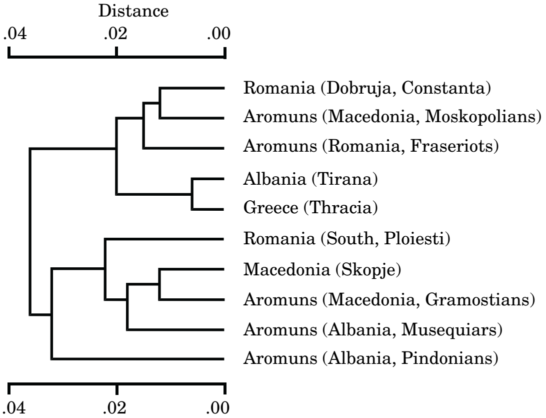

Fig. 2. Alpha-1-antitrypsin – Cluster analysis of the samples studied.

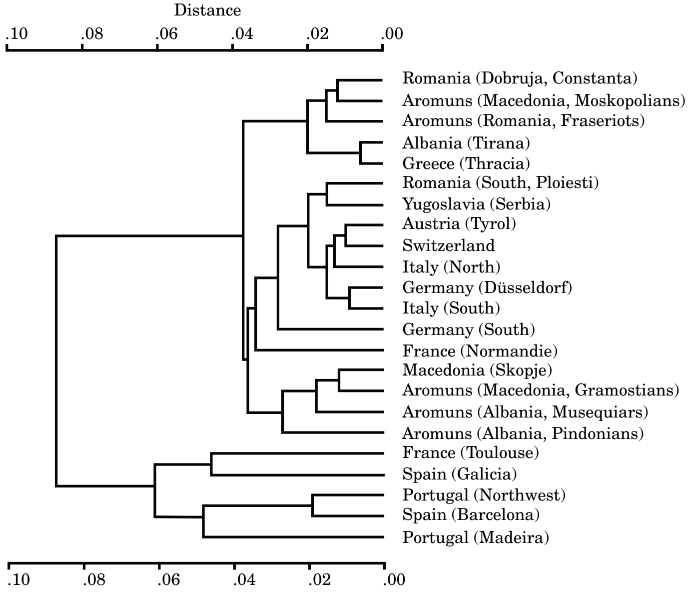

Fig. 3. Alpha-1-antitrypsin – Cluster analysis of Middle and South European populations.

There are only two published data sets for the PI*M subtypes from the Balkans (Yugoslavia)[9, 10]. One of them seems to be based on a selected group[10]. We could compare our results only with data from Yugoslavia and from South, Middle and West Europe. The data from the Balkans cover the range of most of Middle and South European frequencies (Table 3), so, the PI system by itself is not well suited to differentiate between these populations. In contrast, populations of Southern France, the Iberian Peninsula and Madeira show relatively high frequencies

TABLE 2

ALPHA-1-ANTITRYPSIN (PI): ALLELE FREQUENCIES IN THE SAMPLES STUDIED

	Albanians (Tirana)	Greeks (Thracia)	Macedonians (Skopje)	Romanians, Dobruja (Constanta)	Romanians, South (Ploiesti)	Aromuns, Pindonians (Albania, Andon Poci)	Aromuns, Musequiars (Albania, Dukasi)	Aromuns, Moskopolians (Macedonia, Kruševo)	Aromuns, Gramostians (Macedonia, Stip)	Aromuns, Fraseriots (Romania, Kogalniceanu)
PI*M1	0.6667	0.6667	0.7266	0.6759	0.7183	0.7150	0.7079	0.6790	0.7361	0.6758
PI*M2	0.1667	0.1759	0.1328	0.1793	0.1627	0.1100	0.1535	0.1684	0.1296	0.1978
PI*M3	0.1566	0.1482	0.1172	0.1172	0.0992	0.1700	0.1337	0.1316	0.1343	0.1099
PI*S	–	–	0.0039	0.0035	–	–	–	0.0105	–	0.0055
PI*Z	–	–	0.0078	0.0069	0.0040	–	–	0.0053	–	0.0055
PI*VAR	0.0101	0.0093	0.0117	0.0172	0.0159	0.0050	0.0050	0.0053	–	0.0055
N	99	108	128	145	126	100	101	95	108	91

TABLE 3

ALPHA-1-ANTITRYPSIN (PI): ALLELE FREQUENCIES IN SOME MIDDLE AND SOUTH EUROPEAN POPULATIONS

	Austria (Tyrol)	France (Toulouse)	France (Normandie)	Germany (Düsseldorf)	Germany (South)	Italy (North)	Italy (South)	Portugal (Northwest)	Portugal (Madeira)	Spain (Barcelona)	Spain (Galicia)	Switzerland	Yugoslavia (Serbs)
PI*M1	0.7062	0.6258	0.6675	0.6977	0.7500	0.7203	0.7033	0.5726	0.5629	0.6007	0.6600	0.7121	0.7024
PI*M2	0.1480	0.0920	0.1427	0.1602	0.1477	0.1485	0.1700	0.2116	0.1490	0.1908	0.1150	0.1381	0.1825
PI*M3	0.1037	0.1411*	0.1005	0.0907	0.0623	0.0817	0.0800	0.0892*	0.1027	0.0996	0.0600	0.0976	0.0877
PI*S	0.0225	0.1411	0.0631	0.0363	0.0223	0.0297	0.0267	0.1120	0.1821	0.1044	0.1490	0.0383	0.0066
PI*Z	0.0138	–	0.0179	0.0103	0.0121	0.0099	0.0133	0.0083	0.0033	0.0021	0.0090	0.0113	0.0127
PI*VAR	0.0058	–	0.0058	0.0048	0.0056	0.0099	0.0067	0.0062	–	0.0021	0.0060	0.0026	0.0080
N	868	163	1030	827	538	202	150	241	151	938	480	1148	1060
References	12	13	14	15	16	17	17	18	19	20	21	22	9

* = PI*M4 included

of PI*S (Table 3). These relations can be seen too in the cluster analysis (Figure 3). The latter populations form a cluster, clearly separated from the other populations. The remaining South, Southeast and Middle European samples are more or less mingled with relatively low genetic distances. At this time, the reasons for these differences between the two clusters are quite unclear.

Recently, a publication[11] showed the possibility of testing the alleles of the PI system on the DNA level. The results are interesting, especially for defining rare variants and the completion of the PI*M polymorphism.

REFERENCES

1. SCHMIDT, H. D., H.-G. SCHEIL, W. SCHEFFRAHN, The history and genetics of the Aromun populations. In: SUSANNE, C., É. BODZSÁR (Eds.): Human population genetics in Europe. (Biennial Books of EAA, Vol 1, Eötvös University Press, Budapest, 2000). — 2. SCHEIL, H.-G., W. SCHEFFRAHN, H. D. SCHMIDT, W. HUCKENBECK, L. EFREMOVSKA, N. XIROTIRIS, Anthropol. Anz., 59 (2001) 203. — 3. HUCKENBECK, W., H.-G. SCHEIL, H. D. SCHMIDT, L. EFREMOVSKA, N. XIROTIRIS, Anthropol. Anz., 59 (2001) 213. — 4. SCHMIDT, H. D., L. EFREMOVSKA, Z. HANDZISKI, Anthropol. Anz., 59 (2001) 193. — 5. SCHMIDT, H. D., H.-G. SCHEIL, W. HUCKENBECK, W. SCHEFFRAHN, L. EFREMOVSKA, Coll. Antropol., 26 (2002) in press. — 6. THYMANN, M., Hum. Hered., 36 (1986) 19. — 7. ROGERS, J. S., Univ. Texas Publ., 7213 (1972) 145. — 8. WRIGHT, S.: Evolution and the genetics of populations, Vol. 4: Variability within and among natural populations. (University of Chicago Press, Chicago, 1978). — 9. JELIĆ-IVANOVIĆ, Z., V. SPASOJEVIĆ-KALIMANOVSKA, A. TOPIĆ, S. SPASIĆ, V. PETROVIĆ, Gene Geogr., 8 (1994) 129. — 10. TOPIĆ, A., Z. JELIĆ-IVANOVIĆ, V. SPASOJEVIĆ-KALIMANOVSKA, S. SPASIĆ, I. STANKOVIĆ, Acta Paediatr., 91 (2002) 726. — 11. SEIXAS, S., O. GARCIA, M. JESUS TROVOADA, M. TERESA SANTOS, A. AMORIM, J. ROCHA, Hum. Genet., 108 (2001) 20. — 12. BÖHME, A., H. CLEVE, D. SCHÖNITZER, H. REISSIGL, S. KAZDA, W. MÜLLER, Hum. Genet., 63 (1983) 193. — 13. CONSTANS, J., M. VIAU, C. GOUAILLARD, Hum. Genet., 55 (1980) 119. — 14. CHARLIONET, R., R. SESBOÜÉ, C. MORCAMP, F. LEFEBVRE, J. P. MARTIN, Hum. Hered., 31 (1981) 104. — 15. HUCKENBECK, W., P. FREUDENSTEIN, B. ILIE, B. GÜREL, W. BONTE, Adli Tip Derg., 5 (1989) 41. — 16. GENZ, T., J.-P. MARTIN, H. CLEVE, Hum. Genet., 38 (1977) 325. — 17. KLASEN, E. C., Hum. Hered., 31 (1981) 180. — 18. ROCHA, J., A. AMORIM, Adv. Forensic Haemogenet., 5 (1994) 644. — 19. GEADA, H., R. ESPINHEIRA, T. RIBEIRO, L. REYS, Adv. Forensic Haemogenet., 5 (1994) 614. — 20. GENÉ, M., E. HUGUET, A. CARRACEDO, G. ERCILLA, J. CORBELLA, Adv. Forensic Haemogenet., 1 (1986) 235. — 21. CARRACEDO, A., L. CONCHEIRO, Z. Rechtsmed., 90 (1983) 153. — 22. BÄR, W., A. KRATZER, Hum. Hered., 38 (1988) 106.

H.-G. Scheil

Institute for Human Genetics and Anthropology, Heinrich-Heine-University Düsseldorf, POB 101007, D-40001 Düsseldorf, Germany

UČESTALOST ALELA ALPHA-1-ANTITRIPSIN (PI) NA BALKANU

SAŽETAK

Fenotip i frekvencije alela alpha-1-antitripsina istraživane su pomoću IEF tehnike (pH 4.2–4.9) u 10 populacijskih uzoraka s Balkana. Učestalost alela varirala je od 0.6667 do 0.7361 (*M1), 0.1100 do 0.1793 (*M2), 0.0992 do 0.1700 (*M3), 0 do 0.0105 (*S), 0 do 0.0078 (*Z) te od 0 do 0.0172 (drugi). Rezultati su uspoređeni s podacima iz literature o populacijama južne i srednje Europe. Najveći broj populacija formira klaster malih genetskih udaljenosti i slabe povezanosti s zemljopisnom raspodjelom. U suprotnosti s ovim nalazom, uzorci iz južne Francuske, Pirinejskog poluotoka, te Madere formiraju jasno odvojeni klaster. Razlike se većinom temelje na visokoj frekvenciji PI*S u potonjih.