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Genetic studies in Medzev, an isolate in South-Eastern Slovakia. 2. Distribution of blood group genetic markers

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With 16 tables in the text

Summary: Phenotype and gene frequencies of three blood group, four serum protein and seven red cell enzyme polymorphisms were examined in 105 individuals from the population of Medzev, South-Eastern Slovakia. Locus and allele specific tests of homogeneity were calculated in order to obtain the pattern of variation. The results indicate considerable genetic differences between this population and another local population of this region (Chmeľnica) as well as between the Medzev population and the total population of Slovakia. The possible reasons of the genetic heterogeneity within Slovakia are discussed.

Zusammenfassung: An 105 Individuen der Bevölkerung des im Südosten der Slowakei gelegenen Dorfes Medzev wurden für drei Blutgruppen-, vier Serumprotein- und sieben Enzympolymorphismen die Phänotyp- und Genfrequenzen ermittelt. Um die Intensität der genetischen Variabilität zu erfassen, wurden sowohl locus- als auch allelspezifische Homogenitätstests durchgeführt. Die Ergebnisse zeigen beträchtliche genetische Unterschiede zwischen dieser Bevölkerung und einer anderen lokalen Bevölkerung aus dieser Region (Chmeľnica), desgleichen im Vergleich zur slowakischen Gesamtbevölkerung. Die möglichen Ursachen für die genetische Heterogenität innerhalb der Slowakei werden diskutiert.

Introduction

The present paper, the second in the series of genetic studies in Medzev, defines genetic make-up of the population in Medzev on the basis of 14 polymorphic blood group, serum protein and red cell enzyme systems: A1A2B0, MNSs, RHESUS, HP, TF, GC, PI, ACP1, AK1, ADA, GLO1, PGD, ESD and PGM1. According to historical-demographic features and matrimonial patterns this population developed as isolates and practised a high degree of inbreeding (Siváková & Walter 1996). Considering the impact of genetic significance of the changes in the breeding structure, we should analyse and discuss the variation of the above mentioned markers. The frequencies of alleles and haplotypes will be used for estimating patterns of variations. Comparisons will be made with ethnohistorical related population sample of Chmeľnica, from the same region of Slovakia-Spiš (Siváková et al. 1995 b) and with those of the other Slovakian studies (Bernasovský et al. 1976 a, Gáliková & Hrubiško 1980, Kroupová & Mergancová 1985, Kušíková 1975, Siváková et al. 1979, 1994).

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Materials and methods

One hundred and five blood specimens were obtained from male and female individuals in Medzev. The blood specimens were collected by venipuncture in the local Health Care Centre, stored at 4–6 °C until they were transported to Bremen within four days. All typings have been done in Bremen and the laboratory methods were performed according to Spielmann & Kühnl (1982) and Prokop & Göhler (1986). Locus and allele specific tests of homogeneity were calculated according to Rao (1952).

Results and discussion

The phenotype distributions and frequencies observed in three blood groups, four serum proteins and seven red cell enzyme systems are shown in Tables 1–14. Genetic equilibrium can be assumed for all the polymorphic systems under study with the exception of Rhesus system (Table 3). This significant deviation is not easy to explain. Several factors influencing the relationship between observed and expected phenotype numbers could attribute to it, such as sample size, technical factors (though improbable), variation in fitness or changes in breeding structure. One has to take into account also the fact that investigated population sample consists of members sometimes closely related, so this divergence may be due to family rather than population sampling.

Table 15 shows the comparison between Medzev and another isolated population in Chmeľnica regarding allele and haplotype frequencies, respectively, of different serological markers. Genetic differentiation between the two populations clearly emerges when considering the locus and allele specific heterogeneity. They are significantly different for 10 out of 14 loci: 3 erythrocyte antigen loci (A1A2B0, MNSs, RHESUS), however, one or another of the populations shows departure from the Hardy-Weinberg equilibrium either in A1A2B0 or RHESUS system, 3 serum proteins (TF, GC and PI) and 4 erythrocyte enzymes (AK1, ADA, GLO and PGM1). The most remarcable heterogeneity is seen in the following highly significant alleles and haplotypes: *AB0*A, AB0*AX, MNSs*MS, MNSs*Ms, RH*cde, RH*cDE, RH*Cde, TF*C3, PI*S, PGM1*1B, PGM1*2B*. It is worth remembering that apart from the above mentioned differences there are the other features recorded in Chmeľnica, such as rare phenotypes in the Kidd, Duffy and Kell blood group systems (Siváková et al. 1995 b), that underline extent of gene-pool dissimilarities between these populations similar in origin. Thus one can conclude that these two populations have been endogamous enough (Siváková et al. 1995 a, Siváková & Walter 1996) to present significant biological variations, though no increased frequencies of homozygous phenotypes, expected in strongly isolated populations, have been observed.

According to the figures in Table 16 the population of Medzev differs significantly also in the allele and haplotype frequencies, respectively, from the corresponding weighted mean values for Slovakia. Statistical significance is seen for 9 out of 14 loci: A1A2B0, MNSs, RHESUS, TF, ACP1, AK1, ADA, PGD and PGM1. From the particular frequencies and haplotypes contribute to this interpopulation heterogeneity mainly significant variation of the *AB0*A1, AB0*A2* alleles, *MNSs*MS, RH*CDe, RH*cDE* haplotypes and some others – rare (*RH*CDE*) and

Table 1. A1A2B0 phenotype and allele frequencies in Medzev.

Phenotypes	Obs.	Exp.	Alleles	
A1	34	33.22	*AB0*A1*	0.2121
A2	11	10.74	*AB0*A2*	0.0857
B	20	19.54	*AB0*B*	0.1481
A1B	4	6.60	*AB0*0*	0.5541
A2B	3	2.66		1.0000
0	33	32.24		
Total	105	105.00		

$\chi^2_{(2)} = 1.121$; n.s.

Table 2. MNSs phenotype and haplotype frequencies in Medzev.

Phenotypes	Obs.	Exp.	Haplotypes	
MSs	17	18.53	*MS*MS*	0.1716
Mss	21	19.27	*MS* MNS*	0.4284
MNSs	24	20.94	*MS*NS*	0.0725
MNss	26	29.46	*MS*Ns*	0.3275
MMSs	4	5.54		1.0000
MMss	13	11.26		
Total	105	105.00		

$\chi^2_{(2)} = 1.832$; n.s.

Table 3. RHESUS phenotype and haplotype frequencies in Medzev.

Phenotypes	Obs.	Exp.	Haplotypes	
CCD.EE	1	0.07	*RH*cde*	0.3825
CCD.Ee	0	1.96	*RH*Cde*	0.0535
CCD.ee	14	13.68	*RH*cdE*	0.0155
CCddee	1	0.30	*RH*cDe*	0.0240
CcD.EE	2	1.09	*RH*CDe*	0.3115
CcD.Ee	11	17.57	*RH*CDE*	0.0255
ccD.EE	10	4.30	*RH*cDE*	0.1875
ccD.Ee	10	16.09		1.0000
ccddEE	0	0.02		
ccddEe	1	1.24		
CcD.ee	33	26.86		
CcddEe	0	0.17		
Ccddee	4	4.30		
ccD.ee	2	1.9g		
ccddee	16	15.36		
Total	105	105.00		

$\chi^2_{(8)} = 31.014$; $p < 0.001$

Table 4. HP phenotype and allele frequencies in Medzev.

Phenotypes	Obs.	Exp.	Alleles	
HP1	12	11.56	*HP*1*	0.3350
HP2-1	45	45.89	*HP*2*	0.6650
HP2	46	45.55		1.0000
Total	103	103.00		

$\chi^2_{(1)} = 0.038$; n.s.

Table 5. TF phenotype and allele frequencies in Medzev.

Phenotypes	Obs.	Exp.	Alleles	
TF C1	59	60.01	*TF*C1*	0.7596
TF C2-1	25	24.32	*TF*C2*	0.1539
TF C2	2	2.46	*TF*C3*	0.0721
TF C3-1	14	11.39	*TF*D*	0.0144
TF C3-2	1	2.31		1.0000
TF C3	0	0.54		
TF Cl-D	1	2.27		
TF C2-D	2	0.46		
TF C3-D	0	0.22		
TF C-D	0	0.02		
Total	104	104.00		

$\chi^2_{(6)} = 8.107$; n.s.

Table 6. GC phenotype and allele frequencies in Medzev.

Phenotypes	Obs.	Exp.	Alleles	
GC lF	2	0.86	*GC*1F*	0.0905
GC 1F-1S	12	11.40	*GC*1S*	0.6000
GC 1S	34	37.80	*GC*2*	0.3048
GC 2-1F	3	5.79	*GC*Var*	0.0048
GC 2-1S	46	38.40		1.0000
GC 2	7	9.75		
GC 1F-Var	0	0.09		
GC.1S-Var	0	0.60		
GC 2-Var	1	0.31		
GC Var	0	< 0.01		
Total	105	105.00		

$\chi^2_{(6)} = 7.783$; n.s.

Table 7. PI phenotype and allele frequencies in Medzev.

Phenotypes	Obs.	Exp.	Alleles	
PI M1	61	57.01	*PI*M1*	0.7404
PI M2-1	19	21.47	*PI*M2*	0.1394
PI M2	2	2.02	*PI*M3*	0.0914
PI M3-11	9	14.08	*PI*S*	0.0288
PI M3-2	6	2.65		1.0000
PI M3	1	0.87		
PI M1-S	4	4.43		
PI M2-S	0	0.83		
PI M3-S	2	0.55		
PI MS	0	0.09		
Total	104	104.00		

$\chi^2_{(6)} = 11.437$ n.s.

Table 8. ACP 1 phenotype and allele frequencies in Medzev.

Phenotypes	Obs.	Exp.	Alleles	
ACP1 A	11	9.15	*ACP1*A*	0.2952
ACPl AB	34	37.49	*ACP1*B*	0.6048
ACP1 B	39	38.41	*ACP1*C*	0.1000
ACP1.AC	6	6.20		1.0000
ACP1 BC	15	12.70		
ACP1 C	0	1.05		
Total	105	105.00		

$\chi^2_{(3)} = 2.181$;n.s.

Table 9. AK 1 phenotype and allele frequencies in Medzev.

Phenotypes	Obs.	Exp.	Alleles	
AK1 1	92	91.46	*AK1*1*	0.9333
AK1 2-1	12	13.07	*AK1*2*	0.0667
AK1 2	1	0.47		1.0000
Total	105	105.00		

$\chi^2_{(1)} = 0.688$; n.s.

Table 10. ADA phenotype and allele frequencies in Medzev.

Phenotypes	Obs.	Exp.	Alleles	
ADA 1	83	83.26	*ADA*1*	0.8905
ADA2-1	21	20.48	*ADA*2*	0 1095
ADA.2	1	1.26		1.0000
Total	105	105.00		

$\chi^2_{(1)} = 10.068$; n.s.

Table 11. GLO1 phenotype and allele frequencies in Medzev.

Phenotypes	Obs.	Exp.	Alleles	
GLO1 1	20	18.43	*GLO1*1*	0.4190
GLO1 2-1	48	51.13	*GLO1*2*	0.5810
GLO1 2	37	35.44		1.0000
Total	105	105.00		

$\chi^2_{(1)} = 0.393$; n.s.

Table 12. PGD phenotype and allele frequencies in Medzev.

Phenotypes	Obs.	Exp.	Alleles	
PGD A	92	92.41	*PGD*A*	0.9381
PGD AB	13	12.19	*PGD*B*	0.0619
PGB B	0	0.40		1.0000
Total	105	105.00		

$\chi^2_{(1)} = 0.458$; n.s.

Table 13. ESD phenotype and allele frequencies in Medzev.

Phenotypes	Obs.	Exp.	Alleles	
ESD 1	79	78.87	*ESD*1*	0.8667
ESD 2-1	22	20.80	*ESD*2*	0.1143
ESD 2	0	1.37	*ESD*5*	0.0190
ESD 5-1	2	3.46		1.0000
ESD 5-2	2	0.46		
ESD 5	0	0.04		
Total	105	105.00		

$\chi^2_{(3)} = 7.251$; n.s.

Table 14. PGM 1 phenotype and allele frequencies in Medzev.

Phenotypes	Obs.	Exp.	Alleles	
PGM1 1A	33	35.44	*PGM1*1A*	0.5810
PGM1 1A-1B	23	20.92	*PGM1*1B*	0.1714
PGM1 1A-2A	16	19.17	*PGM1*2A*	0.1571
PGM1 1A-2B	17	11.04	*PGM1*2B*	0.0905
PGM1 1B	3	3.08		1.0000
PGM1 2A-1B	6	5.65		
PGM1 1B-2B	1	3.26		
PGM1 2A	5	2.59		
PGM1 2A-2B	1	2.99		
PGM1 2B	0	0.86		
Total	105	105.00		

$\chi^2_{(6)} = 710.136$; n.s

Table 15. The allele frequencies of different genetic markers in Medzev and Chmeľnica, the allele and locus specific test of homogeneity,

Allele/ Haplotype	Medzev	Chmeľnica	Locus specificity	Allele/ haplotype
*AB0*A1*	0.2121	0.2194		n.s.
*AB0*A2*	0.0857	0.0301		**
*AB0*AX*	0.0000	0.0311		***
*AB0*B*	0.1481	0.1548		n.s.
*AB0*0*	0.5541	0.5646		n.s.
	n = 105	n = 87	***	
*MNSs*MS*	0.1716	0.3504		***
*MNSs*Ms*	0.4284	0.3162		**
*MNSs*NS*	0.0725	0.0461		n.s.
*MNSs*Ns*	0.3275	0.2872		n.s.
	n = 105	n = 87	***	
*RH*cde*	0.3825	0.5213		***
*RH*cDe*	0.0240	0.0592		*
*RH*CDe*	0.3115	0.3391		n.s.
*RH*cDE*	0.1875	0.0805		***
*RH*Cde*	0.0535	0.0000		***
*RH*cdE*	0.0155	0.0000		*
*RH*CDE*	0.0255	0.0000		*
	n = 105	n = 87	***	
*HP*1*	0.3350	0.3736		
*HP*2*	0.6650	0.6264		
	n = 103	n = 87	n.s.	
*TF*C1*	0.7596	0.7675		n.s.
*TF*C2*	0.1539	0.2209		*
*TF*C3*	0.0721	0.0116		***
*TF*D*	0.0144	0.0000		*
	n = 104	n = 87	***	
*GC*1F*	0.0905	0.1494		*
*GC*1S*	0.6000	0.5172		*
*GC*2*	0.3048	0.3334		n.s.
*GC*var.*	0.0048	0.0000		n.s.
	n = 105	n = 87	*	
*PI*M1*	0.7404	0.7299		n.s.
*PI*M2*	0.1394	0.1207		n.s.
*PI*M3*	0.0914	0.1494		*
*PI*S*	0.0288	0.0000		**
	n = 104	n = 87	**	
*ACP1*A*	0.2952	0.2931		n.s.
*ACP1*B*	0.6048	0.6035		n.s.
*ACP1*C*	0.1000	0.1034		n.s.
	n = 105	n = 87	n.s.	

Table 15. Continued.

Allele/ Haplotype	Medzev	Chmel˘nica	Locus specificity	Allele/ haplotype
*AK1*1*	0.9333	0.9713		
*AK1*2*	0.0667	0.0287		
	n = 105	n = 87	*	
*ADA*1*	0.8905	0.9655		
*ADA*2*	0.1095	0.0345		
	n =105	n = 87	***	
*GLO1*1*	0.4190	0.4943		
*GLO1*2*	0.5810	0.5057		
	n = 105	n =87	*	
*PGD*A*	0.9381	0.9310		
*PGD*B*	0.0619	0.0690		
	n = 105	n = 87	n.s.	
*ESD*1*	0.8667	0.8965		n.s.
*ESD*2*	0.1143	0.0805		n.s.
*ESD*5*	0.0190	0.0230		n.s.
	n = 105	n = 87	n.s.	
*PGM1*1A*	0.5810	0.5747		n.s.
*PGM1*2A*	0.1714	0.1494		n.s.
*PGM1*1B*	0.1571	0.2529		***
*PGM1*2B*	0.0905	0.0230		***
	n = 105	n = 87	***	

*** = $p < 0.001$; ** = $0.01 > p \geq 0.001$; * = $0.005 > p \geq 0.01$; n.s. = not significant.

Table 16. The allele frequencies of different genetic markers in Medzev and weighted mean values from Slovakia, the allele and locus specific test of homogeneity.

Allele/ Haplotype	Medzev	Slovakia	Locus specific	Allele/ Haplotype
*AB0*A1*	0.2121	0.2751		**
*AB0*A2*	0.0857	0.0280		***
*AB0*B*	0.1481	0.1469		n.s.
*AB0*0*	0.5541	0.5500		n.s.
	n = 105	n = 4052	***	
*MNSs*MS*	0.1716	0.2480		***
*MNSs*Ms*	0.4284	0.3212		***
*MNSs*NS*	0.0725	0.1042		*
*MNSs*Ns*	0.3275	0.3266		n.s.
	n = 105	n = 1546	***	
*RH*cde*	0.3825	0.3874		n.s.
*RH*cDe*	0.0240	0.0420		n.s.
*RH*CDe*	0.3115	0.4159		***
*RH*cDE*	0.1875	0.1185		***
*RH*others*	0.0945	0.0362		***
	n =105	n = 3665	***	
HP 1*	0.3350	0.3684		
*HP*2*	0.6650	0.6316		
	n =103	n = 1520	n. s.	
*TF*C1*	0.7596	0.7898		n.s.
*TF*C2*	0.1539	0.1388		n.s.
*TF*C3*	0.0721	0.0684		n.s.
*TF*others*	0.0144	0.0030		***
	n = 104	n = 1192	**	
*GC*1F*	0.0905	0.0997		n.s.
*GC*1S*	0.6000	0.5838		n.s.
*GC*2*	0.3048	0.3135		n.s.
*GC*others*	0.0048	0.0030		n.s.
	n = 105	n = 1193	n.s.	
*PI*M1*	0.7404	0.7262		n.s.
*PI*M2*	0.1394	0.1556		n.s.
*PI*M3*	0.0914	0.1030		n.s.
*PI*others*	0.0288	0.0152		*
	n = 104	n = 1189	n.s.	
*ACP1*A*	0.2952	0.3664		**
*ACP1*B*	0.6048	0.5992		n.s.
*ACP1*C*	0.1000	0.0344		***
	n = 105	n = 1856	***	
*AK1*1*	0.9333	0.9743		
*AK1*2*	0.0667	0.0257		
	n = 105	n = 1252	***	

Table 16. Continued.

Allele/ Haplotype	Medzev	Slovakia	Locus specific	Allele/ Haplotype
*ADA*1*	0.8905	0.9484		
*ADA*2*	0.1095	0.0516		
	n = 105	n = 407	***	
*GLO1*1*	0.4190	0.4251		
*GLO1*2*	0.5810	0.5749		
	n = 105	n = 407	n.s.	
*PGD*A*	0.9381	0.9730		***
*PGD*B*	0.0619	0.0221		***
*PGD*others*	0.0000	0.0049		n.s.
	n = 105	n = 407	***	
*ESD*1*	0.8667	0.9017		*
*ESD*2*	0.1143	0.0811		*
*ESD*5*	0.0190	0.0172		n.s.
	n =105	n = 407	n.s.	
*PGM1*1A*	0.5810	0.6155		n.s.
*PGM1*2A*	0.1714	0.1966		n.s.
*PGM1*1B*	0.1571	0.1388		n.s.
*PGM1*2B*	0.0905	0.0479		***
*PGM1*others*	0.0000	0.0012		n.s.
	n = 105	n = 407	**	

*** = $p < 0.001$; ** = $0.01 > p \geq 0.001$; * = $0.05 > p \geq 0.01$; ns = not significant.

infrequent (*RH*cdE, RH*Cde*) haplotypes, occurred in Medzev. The other highly significant allele frequencies are: *TF*D, ACP1*C, PGD*A, PGD*B, PGM1*2B*.

It is reasonable to conclude that the sociocultural isolation, derived from historical factors, has influenced the gene pool of this population. This is to be interpreted as indicating that the heterogeneity of the allele frequency distributions is apparently caused by a long-standing, more or less intensive isolation, where founder effect and genetic drift could operate due to the small effective size of the population.

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