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Genetics of the Dombrock Blood Group System

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In April 1965, anti-Do^a, an antibody defining a 'new' red cell antigen, was reported (Swanson, Polesky, Tippett, and Sanger, 1965). The present paper records the results of tests with anti-Do^a on samples received in this unit from October 1964 until April 1966.

Anti-Do^a reacts best by the antiglobulin test on papainized cells, but only a minority of otherwise good antiglobulin sera are suitable. The γ G or γ M reputations of antiglobulin sera have not, so far, provided a guide for finding a suitable reagent. A second example of anti-Do^a (Webb, Lockyer, and Tovey, 1966) behaves in the same way.

Frequencies

The results of testing unrelated people in three populations are given in Table I. The figures for people of Northern European ancestry include 423 reported at Strasbourg (Tippett, Sanger, Swanson, and Polesky, 1967). The gene frequencies are calculated on the assumption that the antigen Do^a is a dominant character. It is seen in Table I that the gene frequencies for the Israelis are very similar to those for the Northern Europeans; on the other hand, 76 Negroes show a lower incidence of the gene *Do^a*, which agrees with the findings of Polesky and Swanson (1966).

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Inheritance

From the Northern European genotype frequencies the expected incidence of the six genotypically and the three phenotypically different matings can be calculated, together with the children expected therefrom (Table II).

In Table III the calculated Northern European phenotype frequencies are applied to the results of testing 201 Northern European families. The agreement between observed and expected children is close, confirming the dominant character of the Do^a antigen.

Because of the wide variation of family size, from 1 to 10 children, Fisher's (1939) method for analysing the blood groups of families was also applied to these data. In Table IV the details of the 201 Northern European families are recorded. Applying Fisher's formulae to the Do(a+) × Do(a+) matings of Table IV the expected number of families of various sizes in which all children are Do(a+) can be calculated; similar analysis is applied to the Do(a+) × Do(a−) matings. A summary of the analysis of these 201 families is given in Table V.

Details of 76 Israeli families with 224 children are given in Table VI, and a summary of their analysis in Table VII.

There is very close agreement between the expected and observed number of families in the four categories, both for the Northern Europeans and for the Israelis. Thus, tests on families show that the anti-

TABLE I

INCIDENCE OF DOMBROCK GROUPS IN UNRELATED PEOPLE

	No. Tested	Phenotypes		Genes		Genotypes		
		Do(a+)	Do(a−)	*Do^a*	*Do*	*Do^{a}Do^a*	*Do^{a}Do*	*DoDo*
Northern-European	755	501 66·36%	254 33·64%	0·420	0·580	0·176	0·487	0·336
Israeli	128	83 64·84%	45 35·16%	0·407	0·593	0·166	0·483	0·351
Negro	76	34 44·74%	42 55·26%	0·257	0·743	0·066	0·382	0·552

TABLE II

EXPECTED DISTRIBUTION OF DOMBROCK GROUPS IN NORTHERN-EUROPEAN PARENTS AND OFFSPRING

Genotypes				
Matings		Children		
Type	Frequency	Do^aDo^a	Do^aDo	$DoDo$
$Do^aDo^a \times Do^aDo^a$	0·0311	0·0311	—	—
$Do^aDo^a \times Do^aDo$	0·1718	0·0859	0·0859	—
$Do^aDo \times Do^aDo$	0·2374	0·05935	0·1187	0·05935
$Do^aDo^a \times DoDo$	0·1187	—	0·1187	—
$Do^aDo \times DoDo$	0·3278	—	0·1639	0·1639
$DoDo \times DoDo$	0·1132	—	—	0·1132
	1·0000			

Phenotypes			
Matings		Proportion of Children from Each Mating	
Type	Frequency	Do(a+)	Do(a−)
Do(a+) × Do(a+)	0·4403	0·8652	0·1348
Do(a+) × Do(a−)	0·4465	0·6329	0·3671
Do(a−) × Do(a−)	0·1132	—	1·0000
	1·0000		

gen Do^a is inherited as an autosomal dominant character. A small number of families from other races also conform: 25 Greek, 11 Sardinians, 4 Polish, 2 Negro, and 2 Japanese.

Genetical Independence of Antigen Do^a. It is easy to show that a new antibody differs in specificity from those already known, but not so easy to show that the antigen which it defines is not a previously unrecognized part of one of the old systems. This has to be done by testing family after family until examples are found in which the antigen can be seen to segregate away from the established systems. Some of the families mentioned in the previous section and some incomplete families, lacking one parent, showed informative segregation.

Genetic recombination in the families shows that the gene Do^a is not sited at the loci for any of the established red cell systems: ABO, MNSs, P, Rh, Lutheran, Kell, Lewis, Duffy, Kidd, Yt, or for the secretor system, and that it is not X- or Y-linked. Recombination also dissociates the locus for Do^a from the loci for the following genetic characters of the blood: haptoglobins, acid phosphatase, phosphoglucomutase, 6-phosphogluconate dehydrogenase, lactate dehydrogenase, serum cholinesterase E_1 and C_5, adenylate kinase.

Do^a has not yet been shown to segregate away from the Auberger genes. Unhappily the few available families known to segregate for Auberger did not segregate for Dombrock. However, the incidence of Do(a+) and Do(a−) within Au(a+) and Au(a−) groups does not differ significantly from that in the general population.

TABLE III

DOMBROCK GROUPS OF 201 NORTHERN-EUROPEAN FAMILIES WITH 573 CHILDREN

Matings				Children				
Type	Number			Total	Do(a+)		Do(a−)	
	Obs.	Exp.	χ^2		Obs.	Exp.	Obs.	Exp.
Do(a+) × Do(a+)	77	88·5	1·49	216	192	186·9	24	29·1
Do(a+) × Do(a−)	98	89·7	0·77	270	177	170·9	93	99·1
Do(a−) × Do(a−)	26	22·8	0·45	87	1*	0	86	87
	201		2·71					

* Presumed extramarital

TABLE IV

DETAILS OF 201 NORTHERN EUROPEAN FAMILIES WITH 573 CHILDREN

Mating			Children		Mating			Children	
Father	Mother	No.	Do(a+)	Do(a−)	Father	Mother	No.	Do(a+)	Do(a−)
Do(a+)	Do(a+)	16	1	0	Do(a+)	Do(a−)	1	0	1
		16	2	0			9	1	1
		14	3	0			1	0	2
		4	4	0			3	1	2
		5	5	0			4	2	1
		1	6	0			2	0	3
		1	7	0			3	2	2
		1	10	0			2	3	1
							2	1	3
Do(a+)	Do(a+)	1	0	1			1	3	2
		9	1	1			1	4	2
		1	0	2			1	2	4
		1	1	2			1	3	5
		3	3	1					
		1	4	1	Do(a−)	Do(a+)	10	0	1
		1	4	3			3	1	1
		1	5	2			3	0	2
		1	6	1			2	1	2
							3	2	1
Do(a+)	Do(a−)	6	1	0			1	2	2
		4	2	0			1	3	1
		3	4	0			3	3	2
		1	5	0			1	2	3
		1	6	0					
					Do(a−)	Do(a−)	5	0	1
Do(a−)	Do(a+)	8	1	0			6	0	2
		9	2	0			3	0	3
		3	3	0			6	0	4
		2	4	0			2	0	5
		1	5	0			1	0	6
		1	9	0			1	0	9
		1	10	0			1	0	11
							1	1*	0

* Presumed extramarital.

Linkage Tests. In the search for linkage between the Dombrock locus and those for other blood group systems and for the biochemical genetic characters of the blood, families with at least one doubly heterozygous parent were analysed by the lod score method of Morton (1955), as instructed by Maynard Smith, Penrose, and Smith (1961).

Renwick and Schulze (1965) and Cook (1965) found evidence that recombination was more frequent in women than in men; therefore, families scored through the father are considered separately from those scored through the mother. The sum of the lod scores, Z (θ') for the doubly heterozygous father and Z (θ) for the doubly heterozygous mother, for each system is given in Table VIII.

Morton (1955) considers linkage to be present when Z (θ', θ) > 3 and that linkage is absent if Z (θ', θ) < −2. The Dombrock locus is therefore not closely linked to the blood group loci for ABO, MNSs, P, Rh, Lutheran, or Kidd, and probably not closely linked to the loci for Kell, Duffy, Yt, ABH in saliva, or Le^a in saliva. Neither is the Dombrock locus closely linked to the loci for any of the other genetical markers investigated: haptoglobins, acid

TABLE V

SUMMARY OF ANALYSIS BY FISHER'S METHOD OF NORTHERN-EUROPEAN FAMILIES

Class of Mating	Class of Family	Number of Families		χ^2	d.f.
		Exp.	Obs.		
Do(a+) × Do(a+)	All children Do(a+)	56·05	58		
	Some children Do(a−)	20·95	19	0·23	1
Do(a+) × Do(a−)	All children Do(a+)	42·93	40		
	Some children Do(a−)	55·07	58	0·15	1
				0·40	2

$p = 0{\cdot}81$

TABLE VI

DETAILS OF 76 ISRAELI FAMILIES WITH 224 CHILDREN

Mating		Children		Mating		Children	
Father	Mother	No.	Do(a+)	Do(a−)	Father	Mother	No.	Do(a+)	Do(a−)
Do(a+)	Do(a+)	7	1	0	Do(a−)	Do(a+)	4	0	1
		6	2	0			1	1	1
		5	3	0			1	0	3
		2	4	0			1	1	2
		1	5	0			2	2	3
							1	2	4
Do(a+)	Do(a+)	1	1	1			1	4	2
		2	2	1			1	4	3
		2	3	1			1	6	1
		1	4	3					
		1	6	1	Do(a−)	Do(a−)	2	0	1
							1	0	2
Do(a+)	Do(a−)	3	1	0			3	0	3
		3	2	0			1	0	4
		3	3	0			1	1*	1
Do(a−)	Do(a+)	1	1	0					
		3	2	0					
		2	5	0					
Do(a+)	Do(a−)	1	0	1					
		3	1	1					
		2	2	1					
		1	1	2					
		1	2	2					
		1	0	5					
		1	2	3					
		1	3	4					
		1	4	4					

* Presumed extramarital.

TABLE VII

SUMMARY OF ANALYSIS BY FISHER'S METHOD OF ISRAELI FAMILIES

Class of Mating	Class of Family	Number of Families		χ^2	d.f.
		Exp.	Obs.		
Do(a+) × Do(a+)	All children Do(a+)	20·42	21	0·06	1
	Some children Do(a−)	7·58	7		
Do(a+) × Do(a−)	All children Do(a+)	16·71	15	0·33	1
	Some children Do(a−)	23·29	25		
				0·39	2

$p = 0{\cdot}82$

TABLE VIII

FAILURE TO DETECT LINKAGE BETWEEN DOMBROCK LOCUS AND LOCI FOR OTHER GENETIC CHARACTERS OF BLOOD: A SUMMARY OF LOD SCORES

Blood Groups	No. of Scoring Families	Paternal Recombination Fraction, θ′					No. of Scoring Families	Maternal Recombination Fraction, θ				
		0·05	0·1	0·2	0·3	0·4		0·05	0·1	0·2	0·3	0·4
ABO	28	−24·250	−14·474	−6·079	−2·454	−0·722	17	−12·407	−7·167	−2·735	−0·952	−0·228
MNSs	30	−11·253	−5·014	−0·559	+0·540	+0·382	23	−13·880	−7·458	−2·256	−0·348	+0·148
P	5	−3·694	−2·110	−0·788	−0·255	−0·048	3	−2·012	−1·006	−0·230	+0·009	+0·027
Rh	27	−13·185	−6·404	−1·418	+0·111	+0·280	21	−12·775	−7·079	−2·429	−0·648	−0·033
Lutheran	3	−3·396	−2·042	−0·858	−0·345	−0·074	1	−0·769	−0·482	−0·216	−0·086	−0·020
Kell	4	−2·307	−1·302	−0·488	−0·167	−0·035	1	−0·658	−0·392	−0·162	−0·061	−0·013
Duffy	12	−1·917	−0·401	+0·486	+0·471	+0·180	14	−9·380	−5·275	−1·892	−0·610	−0·172
Kidd	13	−6·859	−3·790	−1·319	−0·406	−0·101	8	−4·810	−2·932	−1·258	−0·549	−0·170
Yt	2	−2·163	−1·331	−0·582	−0·227	−0·053	1	−1·906	−1·116	−0·448	−0·163	−0·036
Secretion Le[a]	1	−0·769	−0·482	−0·216	−0·086	−0·020	1	−0·769	−0·482	−0·216	−0·086	−0·020
ABH secretion	2	−1·145	−0·635	−0·226	−0·072	−0·015	3	−2·083	−1·083	−0·314	−0·063	−0·003
Other characters												
Hp	8	−11·343	−7·423	−3·077	−1·289	−0·379	9	−5·334	−3·014	−1·000	−0·180	+0·094
C_5	4	−4·165	−2·359	−0·872	−0·281	−0·053	2	−1·785	−1·193	−0·620	−0·311	−0·118
E_1	0						1	−0·464	−0·229	−0·060	−0·011	−0·001
AcPh	11	−5·933	−3·379	−1·338	−0·558	−0·235	8	−3·560	−1·624	−0·207	−0·157	−0·119
PGM	15	−5·696	−2·729	−0·527	+0·073	+0·082	6	−2·574	−1·317	−0·385	−0·115	−0·055
AK	1	−1·906	−1·116	−0·448	−0·163	−0·036	2	−1·301	−0·768	−0·311	−0·114	−0·025
LDH	0						1	−0·483	−0·241	−0·064	−0·012	0·001
6PGD	1	−0·721	−0·444	−0·194	−0·076	−0·018	0					

phosphatase, phosphoglucomutase, 6-phosphogluconate dehydrogenase, lactate dehydrogenase, serum cholinesterase E_1 and C_5, and adenylate kinase.

Summary

Tests with anti-Do^a on 755 unrelated people of Northern European ancestry are reported. The corresponding gene frequencies are:

$$Do^a = 0{\cdot}420$$
$$Do = 0{\cdot}580$$

The antigen Do^a behaved as a dominant character in 201 Northern European families with 573 children and in 76 Israeli families with 224 children.

The locus responsible for the Dombrock system was found not to be closely linked to the loci responsible for the established blood group systems or to those for various biochemical characters of the blood.

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