THE KELL-CELLANO (K-k) GENETIC SYSTEM OF HUMAN BLOOD FACTORS

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A NEW agglutinable factor of human blood was recently discovered with the aid of an antibody, an agglutinin, which is remarkable for its high incidence of positive reactions, 99.8 per cent, in white individuals (U. S. A.). This antibody was found in a mother, Mrs. Cellano, whose infant had a mild form of hemolytic disease. Accordingly, the antibody will be referred to as "anti-Cellano" and its corresponding agglutinogen as "Cellano."

A study of the family of an individual from among the 0.2 per cent Cellano negative group revealed the hereditary nature of the Cellano factor.* Of the eight children, three were Cellano negative. Since both parents were Cellano positive, they were presumed to be heterozygous. Assuming two allelic genes, one determining Cellano positive and the other Cellano negative, the following values for the three genotypes were derived:†

Homozygous Cellano Positive	91.2%
Heterozygous Cellano Positive	8.6%
Homozygous Cellano Negative	0.2%

Because of the possible analogy to the M-N and the three Rh-Hr systems, the authors considered the existence of another genetically related blood property present in the Cellano negative and Cellano heterozygous groups. Thus, this theoretic blood factor should have incidences of about 8.8 per cent. Two types of antibodies giving very similar incidences (anti-Lutheran 8 per cent and anti-Kell 7 per cent) had been observed by Coombs, Mourant, Race and their co-workers.[2,3,4] An analysis of the results with anti-Cellano and two specimens of anti-Kell sera on the above-mentioned family reveals the significant conclusion that the Cellano and Kell antigens are genetic alleles (table 1).

For the sake of uniformity, the letters "*K*" and "*k*", already employed by the British workers for the genes determining Kell positive and Kell negative reactions, respectively, will be retained. The results given in table 1 indicate that the gene *k* can now be considered as indicating the presence of the Cellano factor.

As shown in table 1, both parents are heterozygous (*Kk*) and each is capable of transmitting the genes *K* and *k* to their offspring. Such matings, which occur very rarely, i.e., 8.6 per cent × 8.6 per cent or one in 135, are most useful for analysis of

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* See table 1 and the paper by Levine, et al.[1]

† The incidence of the gene for Cellano negative = $\sqrt{0.002}$ = .045 or 4.5%, while the incidence of the gene for Cellano positive = 1 − .045 = .955 or 95.5%. The three values given above are derived from the equation $(.955 + .045)^2$.

factors which have either very low or very high incidences. Thus, Cellano negatives of genotype *KK* (homozygous Kell) which should occur in 25 per cent of the offspring, were found in three of the eight children in contrast to 0.2 per cent in a random population. Similarly, Kell positive (*KK* and *Kk*) which should occur in 75 per cent of the offspring of heterozygous parents, were found in six of the eight children in contrast to 8.8 per cent in a random population.

Further evidence for the allelic nature of the Kell and Cellano factors was obtained in a study of the five siblings of another Cellano negative individual. Two of the five are Cellano negative and four are Kell positive. These findings are presented in table 2.

TABLE 1

	Anti-Kell Anti-Lazarus	Anti-Cellano	Genotype
Father: Mr. J. Kul, Sr.	+	+	*Kk*
Mother: Mrs. M. Kul	+	+	*Kk*
Children: 1. John	+	+	*Kk*
2. Julian	+	o	*KK*
3. Mrs. A. G.	o	+	*kk*
4. Mrs. I. S.	+	+	*Kk*
5. Mrs. A. V.	+	o	*KK*
6. Frank	+	o	*KK*
7. Andrew	+	+	*Kk*
8. Josephine	o	+	*kk*
Controls: Mrs. Cellano	+	o	*KK*
Mr. Lazarus	+	+	*Kk*
Mrs. Lazarus	o	+	*kk*
Jeffrey Lazarus	o	+	*kk*

As in the Kul family, the parents of the five siblings must be heterozygous for both factors and this was confirmed when their bloods were subsequently tested.

In the first publication of the Kell antigen, its frequency was given as 7 per cent, while the serum studied by Wiener and Sonn reacted on 13 per cent.* Sanger, Race and their co-workers now report a larger series with an incidence of 10.17 per cent positive reactions. The calculated incidences of three genotypes based on the latter value and on the value 99.8 per cent for the Cellano factor are compared in table 3.

The close agreement of these values further supports the view that the genes for the Kell and Cellano factors are allelomorphic to each other. As in the case of the M-N and the three Rh-Hr systems (Dd, Cc, and Ee), the three genotypes resulting from the interaction of these two genes correspond to the three phenotypes identified by parallel tests with the Kell and Cellano antibodies. A type of blood which fails to react with both sera has not been observed.

Sera containing anti-Cellano antibodies are necessarily very rare, while the anti-Kell type of antibody has been observed at least six times. A list of these follow:

* The identification of this antibody as anti-Kell was made by Dr. Race.

1. Kell	Coombs, Mourant and Race[3]
2. Si	Wiener and Sonn[7]
3. Drizen	Sanger and Abelson[8]
4. And	Dunsford[9]
5. Lazarus	Levine, Rauch and Block[6]
6. P. L.	Vogel and Rosenfeld[10]

TABLE 2

	Anti-K (Anti-Lazarus)	Anti-k (Anti-Cellano)	Genotype
Father: Mr. H. Mc.	+	+	*Kk*
Mother: Mrs. L. Mc.	+	+	*Kk*
Children: 1. Mrs. B. M.	+	o	*KK*
2. J. G. Mc	+	+	*Kk*
3. E. V. Mc	o	+	*kk*
4. Mrs. A. R.	+	+	*Kk*
5. Mrs. V. S.	+	o	*KK*

TABLE 3

	Anti-Kell (Anti-K)	Genotype	Anti-Cellano (Anti-k)	
Kell positive	89.83	*kk*	91.2	Cellano positive
	9.90	*Kk*	8.6	
	0.27	*KK*	0.2	

The greater incidence of anti-Kell type of sera is not surprising since incompatible matings for the Kell factor occur in 8.8 × 91.2, or 1:12.5 in contrast to a value of 99.8 × 0.2 or 1:500 for the Cellano factor. Thus, the opportunity for the production of anti-Kell sera is 40 times greater than for anti-Cellano.

Anti-Kell type of antibody may be missed in routine tests for isoimmunization, unless the mother's serum is tested against her husband's cells, suspended in bovine albumin, and with the Coombs technic. These procedures are essential for all instances in which isoimmunization may be brought about by a blood factor characterized by a low incidence in the general population. Anti-Kell may be differentiated from anti-Lutheran since the latter antibody does not give a positive Coombs test and, in contrast to anti-Kell, its reactions are stronger at lower temperatures than at 37 C.

Antibody of the anti-Cellano type may be expected if the serum gives an unusually high incidence of positive reactions. It is important, however, to exclude the anti-e (anti-hr″) antibody which gives about 97 per cent positive reactions, or the coexistence of more than one antibody. The latter possibility may be tested by suitable absorption experiments with carefully selected bloods of known antigenic structure.

Extensive racial and genetic studies will be carried out when larger supplies of these two antibodies become available. Preliminary experiments have shown that the Kell and Cellano factors are not antigenic in rabbits.

Although preliminary data indicate that Kell and Cellano factors are not related to other blood properties, more comprehensive studies are required to exclude the possibility of linkage.

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The tests with anti-Kell were made with the aid of Coombs anti-human serum. Identical results with anti-Lazarus serum were obtained using both the Coombs technic and albumin suspended cells. The test with anti-Cellano were made with saline suspended cells.

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