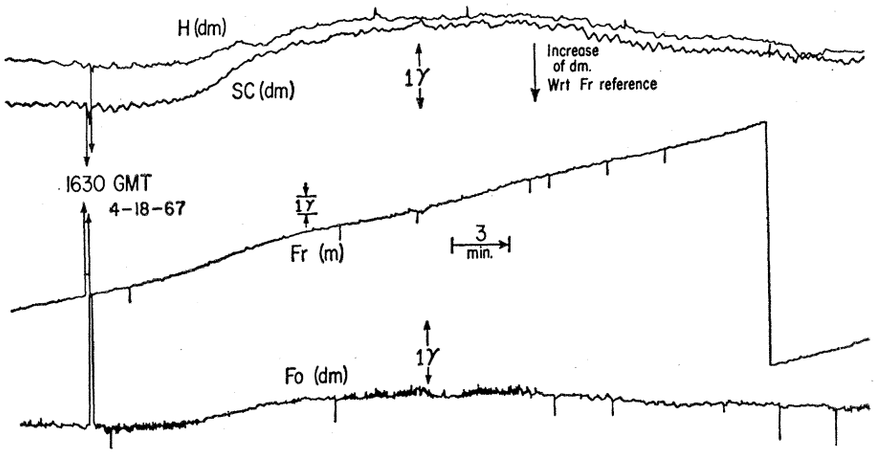

Fig. 4. Local magnetic event observed near Hollister on 18 April 1967 beginning at 1630 hours. Trace moving upward to the right is the reference magnetometer at Franco (*Fr*); the sharp offset is an automatic range adjustment. The other traces are differential magnetometers at the Harris ranch (*H*), Stone Canyon (*SC*), and Forsyth (*Fo*) and represent the amount by which the intensity differs from that at Franco.

San Andreas fault is not available but since the stress change is believed to have occurred at depth, a reasonable magnetic susceptibility would be that of basic rock for which $k \approx 10^{-3}$ cgs unit. Assume a buried sphere tangent to the surface undergoing a stress change of 20 bars. The change in susceptibility in the direction of the applied compressive stress is given by the product of the stress change and the stress sensitivity of the susceptibility (Fig. 1):

$$\Delta k = \frac{-.02}{100 \text{ bars}} \times 10^{-3} \times 20 \text{ bars}$$
$$= -4 \times 10^{-6} \text{ cgs units} \quad (1)$$

The observed anomaly at the surface from a sphere of radius R of uniform magnetization whose center is at a depth d is

$$\Delta F = \frac{\Delta k \, F(4/3\pi R^3)}{d^3} \approx -0.8 \text{ gamma}$$

where $R = d$ and the total intensity F at Hollister is 50,000 gammas.

It has been pointed out by Brace and Orange (*6*) that the electrical resistivity of rocks is dependent on stress. The telluric current field and its small associated magnetic field will also be dependent on stress. However, it can be shown that for a given stress change the piezomagnetic effect is at least an order of magnitude larger. The ultimate source of the stress change cannot of course be determined without other evidence. The source of the observed ferrimagnetic effects cannot be deeper than the Curie isotherm which is estimated to be 22 km in this region. The signature of the observed piezomagnetic effects appears to follow the logarithmic variation of creep behavior of rocks, lending support to a mechanism of creep or plastic deformation.

Other interpretations of this evidence are perhaps possible, but without positive information concerning the distribution of the strain and stress field at depth, we can only speculate. At the very least, it does appear that stress changes can occur at some depth before their effects are expressed at or near the surface.

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References and Notes

1. E. Wilson, *Proc. Roy. Soc. London Ser. A* **101**, 445 (1922); A. G. Kalashnikov and S. P. Kapitsa, *Akad. Nauk SSSR Doklady* **86**, 522 (1952); M. A. Grabovsky and Y. I. Parkhomenko, *Akad. Nauk SSSR Izvestia Ser. Geofiz.* **5**, 405 (1953); A. G. Kalashnikov, *Akad. Nauk SSSR Trudy* **25**, 162 (1954); S. P. Kapitsa, *Akad. Nauk SSSR Izvestia Ser. Geofiz.* **6**, 493 (1955); J. W. Kern, *J. Geophys. Res.* **66**, 3813 (1961); F. D. Stacey, *Phil. Mag.* **7**, 553 (1962).
2. Y. Kato and A. Takagi, *Sci. Rept. Tohoku Univ. Ser. 5 Geophysics* **5**, 67 (1953); T. Yoshimatsu, *Kakioka Mag. Obs. Mem.* **2**, 107 (1962); S. Breiner, *Nature* **202**, 790 (1964); T. Rikitake, Y. Yamazaki, Y. Hagiwara, K. Kawada, M. Sawada, Y. Sasai, T. Watanabe, K. Momose, T. Yoshino, K. Otani, K. Ozawa, Y. Sanzai, *Bull. Earthquake Res. Inst.* **44**, 363 (1966).
3. S. Breiner, *Science* **150**, 185 (1965).
4. D. Tocher, *Bull. Seismol. Soc. Amer.* **50**, 396 (1960).
5. D. Tocher has been most helpful in providing information concerning the ESSA Stone Canyon Seismic Observatory.
6. W. F. Brace and A. S. Orange, *Science* **153**, 1525 (1966).
7. Work supported by NSF grant GP-3603 and by the Environmental Science Services Administration under contract E22-76-67(N). We thank Varian Associates, NASA Ames Research Center, the University of California at Berkeley, and the U.S. Naval Postgraduate School for their generous loan of the rubidium magnetometers.

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Genetic Background and Expressivity of Histocompatibility Genes

Abstract. *A difference in the reactivity of F_1 hybrid female mice to skin grafts from male donors of each of their parental strains suggests that the genetic background can influence the efficacy of the Y antigen to elicit rejection of the graft.*

Although it has been shown that the genetic background of a mouse influences its ability to react against transplantation and other antigens (*1*, *2*), there is as yet no direct evidence that genetic factors, other than the specific determinants of transplantation antigens in a donor, can modify the speed of homograft rejection by influencing the expression of these antigens (*3*). Such an effect could be mediated by the ability of non-H (histocompatibility) genes to alter the amount of cellular antigen produced, the availability of the antigen to the hosts' immune system, or the vulnerability of the graft to immune attack, possibly by influencing the sialomucin content of the connective tissue stroma of the graft (*4*). We now present evidence that non-H genes in a skin graft can influence its survival time by affecting the expression of a specific transplantation antigen.

It is now well established that isografts of skin and other tissues in mice are not always permanently accepted when the donor is a male and the recipient is a female (*5*). In this circumstance, rejections seem to be attributable to the association of a histocompatibility factor with the Y chromosome. Although females of different strains vary considerably in the facility with which they react against male isografts, there has been no evidence of variation in the antigenic specificity of the Y factor (*6*). This interstrain diversity in reactivity is apparently dictated by the genotype of the female recipient which determines her capacity to react against male skin (*2*). However, it is conceivable that another factor also contributes to this variability, namely, a genetically determined difference in the expression of the Y antigen. There would be evidence in support of this premise if it could be shown that there are differences in tempo in the reactivities of F_1 hybrid females to skin grafts from male donors of each of their parental strains and, possibly, from F_1 hybrid males.

Domestically maintained C57BL/6 mice were reciprocally mated with CBA animals, producing F_1 hybrid females with identical genetic constitutions and males which only differed with respect to the origin of their X and Y chromosomes, that is, whether these chromosomes came from the C57BL/6 or CBA parent. In accordance with the genetic laws of transplantation, such hybrid females should be compatible with all of the codominant H genes of both parental strains except that associated with the Y chromosome. Moreover, if this Y antigen does have the same specificity in both parental strains, F_1 hybrid females should reject skin grafts from C57BL/6, CBA, and F_1 hybrid males with the same promptitude, unless their different genetic backgrounds can influence the expression of this factor. Consequently, panels of F_1 hybrid females were challenged, respectively, with C57BL/6 male grafts, CBA male grafts, and F_1 hybrid male skin bearing a C57BL/6 or CBA Y chromosome. This procedure, as well as the exchange of skin grafts between reciprocally produced F_1 hybrid males, was undertaken to provide further evidence that the Y factor has the same specificity in both parental strains (*7*). Finally, male-to-female isografts were also carried out with panels of CBA and C57BL/6 animals.

Donors and recipients were at least 3 months of age at the time of grafting. Full-thickness disks of nonactive trunk skin, about 1 cm in diameter, were transplanted to the right side of the hosts' chests. The operative technique and method of appraisal of the well-being of the grafts were previously described (*8*). Median survival times of grafts were estimated by Litchfield's nomographic method (see *9*).

Table 1. Survival times of skin grafts. Figures in parentheses after recipients represent numbers of recipients. MST, median survival time.

Donor	Recipient	Distribution of graft survival time (days)					MST (days)	S.D. (days)
		15–24	25–50	51–75	76–100	>100		
C57 ♂	C57 ♀ (21)	11	9	1			25.6 ± 4.0	1.39
CBA ♂	CBA ♀ (15)			1	1	13		
C57 ♂	F_1 ♀ (28)	2	9	2	1	14		
CBA ♂	F_1 ♀ (30)	18	11			1	24.2 ± 4.2	1.63
F_1(C57Y) ♂	F_1 ♀ (19)	12	5	1	1		24.0 ± 5.5	1.65
F_1(CBAY) ♂	F_1 ♀ (18)	11	5	1		1	23.0 ± 3.3	1.30
F_1(CBAY) ♂	F_1(C57Y) ♂ (15)					15		
F_1(C57Y) ♂	F_1(CBAY) ♂ (14)					14		

The results (Table 1) indicate that (i) the penetrance and expressivity of the Y factor is much more pronounced in C57BL/6 mice than in the CBA strain. (ii) In spite of this, the survival of C57BL/6 male grafts on F_1 hybrid females is significantly longer (50 percent surviving for more than 100 days) than that of CBA male grafts on similar hosts (these are almost uniformly rejected within 50 days). (iii) There is no difference in the ability of F_1 hybrid females to react against F_1 hybrid male grafts bearing a C57BL/6 or CBA Y chromosome (such grafts are rejected about as promptly as CBA male grafts). (iv) Reciprocal male-to-male F_1 hybrid grafts are uniformly accepted.

In that there is a decisive difference in the ability of C57/CBA F_1 hybrid females to react against CBA and C57BL/6 male grafts, it appears that the genetic background can influence the efficacy of the Y antigen to elicit graft rejection. The alternate explanation, namely, that the difference may be attributed to different Y-linked alleles, seems unlikely from the evidence that reciprocal male hybrid grafts are always accepted and that F_1 hybrid male grafts bearing a C57BL/6 or CBA Y chromosome are similarly rejected by F_1 females. The ability to render C57BL/6 female mice tolerant of male isografts by neonatal exposure to CBA male cells (*7*) is also inconsistent with the allele hypothesis.

The curtailed survival of CBA male grafts on hybrid females contrasts with their almost uniform acceptance by CBA females. In the case of C57BL/6 male grafts, the opposite is true since here the hybrid female displays the diminished reactivity. This indicates that the more pronounced penetrance and expressivity of the Y factor in the C57BL/6 strain is due to the ability of C57BL/6 females to manifest a much stronger response to male isografts than CBA females.

The basis for the discrepancy in the expression of the Y factor in CBA and C57BL/6 mice remains to be determined. However, it is probably related to some endocrinological factor because skin grafts from males which have been castrated at birth, or shortly thereafter, enjoy a prolonged survival on isologous females (*10*). This premise could be tested by determining the survival times of grafts of CBA and C57BL/6 skin from neonatally castrated male donors on F_1 hybrid females.

Our results may also relate to Zeiss' analysis of third-party unresponsiveness in immunologically tolerant rats (*11*). She found that rats of the AS strain, rendered tolerant of strain BS transplantation antigens, also displayed some unresponsiveness to HS grafts, in spite of the fact that (AS × BS) F_1 hosts did not. A similar situation might be expected in CBA females made tolerant with C57BL/6 female cells and in C57/CBA hybrid females. In the former case, CBA male skin is expected to be almost uniformly accepted, whereas in the latter these same grafts are rejected. Bailey's (*3*) failure to demonstrate an effect of genotype on the expression of the Y antigen can probably be attributed to the similarity of the four different genetic backgrounds investigated—they were all derived from the same gene pool.

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References and Notes

1. M. A. Fink and V. A. Quinn, *J. Immunol.* **70**, 61 (1953).
2. E. Klein and O. Linder, *Transplant. Bull.* **27**, 457 (1961).
3. D. W. Bailey, *Transplantation* **3**, 531 (1965).
4. G. A. Currie and K. D. Bagshawe, *Lancet* **1967-I** 708 (1967).
5. E. J. Eichwald and C. R. Silmser, *Transplant. Bull.* **2**, 148 (1955); E. J. Eichwald, C. R. Silmser, I. Weissman, *J. Nat. Cancer Inst.* **20**, 563 (1958); M. Feldman, *Transplant. Bull.* **5**, 15 (1958); L. Sachs and E. Heller, *J. Nat. Cancer Inst.* **20**, 555 (1958); R. F. Gittes and P. S. Russell, *ibid.* **26**, 283 (1961).
6. R. E. Billingham and W. K. Silvers, *Ann. Rev. Microbiol.* **17**, 531 (1963).
7. ———, *J. Immunol.* **85**, 14 (1960).
8. R. E. Billingham, in *Transplantation of Tissues and Cells*, R. E. Billingham and W. K. Silvers, Eds. (Wistar Institute Press, Philadelphia, 1961), pp. 1–26.
9. J. T. Litchfield, *J. Pharmacol. Exp. Therap.* **97**, 399 (1949).
10. M. Vojtíšková and M. Poláčková, *Folia Biol. Prague* **12**, 137 (1966).
11. I. M. Zeiss, *Immunology* **11**, 597 (1966).
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