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### Genetics and Male Sexual Orientation

LETTERS

In their recent study of the genetic origins of at least some expressions of male homosexuality, Dean H. Hamer et al. (Research Article, 16 July, p. 321) join with many (if not most) scholars in acknowledging the complex origins of human sexual behavior (1). Not only do they note that culture, history, and individual experience form part of the puzzle of the development of human sexual desire, but their initial sample, which contains families that do not fit an X-linked pattern of transmission, provides concrete evidence of multiple origins of male homosexuality. We urge researchers to remember that widespread sexual behavior patterns probably represent a multiplicity of pathways leading to a single end point that we in 20th-century Europe and America have named as if it were a unique entity.

Despite our praise for aspects of Hamer et al.'s work, we feel it is also important to recognize some of its weaknesses. The most obvious of these is the lack of an adequate control group. Their study demonstrates cosegregation of a trait (which Hamer et al. have labeled "homosexuality") with X chromosome markers and the trait's concordance in homosexual brothers. This cosegregation is potentially meaningful if the mother is heterozygous for the trait. In this case, segregating chromosomes without the markers should show up in nonhomosexual brothers, but Hamer et al. present no data to that effect. Looking at lack of cosegregation in nonhomosexual siblings would provide a control group that could greatly strengthen Hamer et al.'s contentions about the meaning of their data.

The results of this study also turn out to be highly sensitive to assumptions made about the incidence of male homosexuality (a figure that is difficult to pin down). The statistical significance of their finding of an increased frequency of homosexuality among the maternal male relatives of the homosexual probands depends on the choice of 2% as the base rate for male homosexuality. If instead one chooses a base rate of 4%, three of four significant maternal relative correlations in table 1 of their paper lose significance. This sensitivity to assumptions about background levels makes Hamer *et al.*'s data less robust than the summary in their abstract indicates.

One other component of their method also renders their data less robust than they appear on the surface. Their linkage analysis

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data rest on 40 cases, but for only 15 of these do they have direct measurements of maternal heterozygosity. For the other 62% they used estimates based on known frequencies from available databases. It is difficult to assess the possible bias introduced by using estimates rather than direct measures (2), but it seems prudent to express caution over a data set where a majority of the relevant comparisons have been generated by estimates.

Finally, we wish to emphasize a point with which we are sure Hamer *et al.* would agree: correlation does not necessarily indicate causation. A gene affecting sexual orientation in some segment of the male population might do so very indirectly. For instance, any gene that might increase the tendency of brothers to psychologically identify with one another might influence their similarity in such matters as sexual orientation and would be picked up in the present study.

The scientific debate about the origins of homosexuality is taking place in the midst of a highly political one about the place of gay men and lesbians in our social fabric. Given the increased frequency of hate crimes directed against homosexuals, it is fair and literal to say that lives are at stake. We applaud, therefore, the expression of concern by Hamer and his colleagues for the potential use of their data in the social arena; but we believe that the responsibility of scientists to guard against the misuse of their results goes farther than words: it ultimately must rest in decisions about how and when to publicize preliminary data of the sort produced by these linkage studies. We wonder whether it might not have been prudent for the authors and the editors of Science to have waited until more of the holes in the study had been plugged (or not, as the future will tell).

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### **References and Notes**

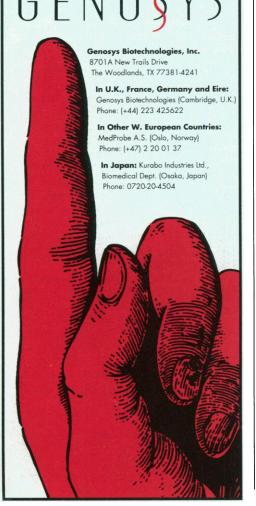
- For one example of the kinds of currently active discussions, see E. Stein, Ed., Forms of Desire: Sexual Orientation and the Social Constructionist Controversy (Routledge, New York, 1992).
- R. Lewontin and D. L. Hartl, Science 254, 1745 (1991); *ibid.* 255, 1054 (1992).

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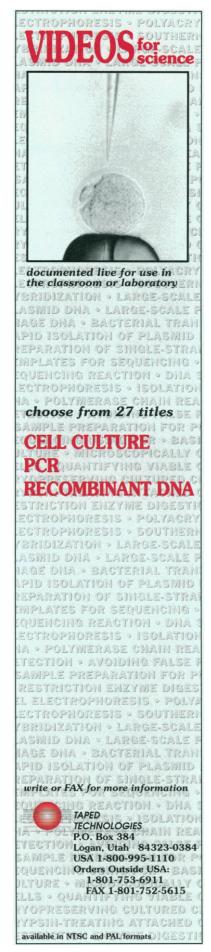
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Our reaction as gay and lesbian scientists to the study by Hamer *et al.* is mixed. On the one hand, we are pleased that there is now scientific evidence that sexual orientation has an immutable component. On the other hand, this work raises the specter of the various possibilities of screening for such components. We, as scientists, feel that now is the time to address the ethical questions surrounding the use of such information in advance, so that the ethics may evolve with the science instead of lagging behind, as often happens.

In the best of all possible worlds, diversity would be valued and this study would be strictly of scientific interest. In our present social environment, however, there are a number of pressing concerns that need to be addressed. One advantage of finding a genetic link to sexual orientation lies mostly in the legislative and legal agenda of obtaining civil rights under current law. For example, the Supreme Court of Hawaii is currently ruling on the legality of gay marriage, not so much on the basis of sex discrimination or the right to privacy, but on the basis of the biological imperative that a genetically immutable trait would have on civil rights protection for a minority group. Hamer's data would strengthen such a case. This information also may abolish society's tendency to seek and establish blame for a person's divergent sexuality.

There are disadvantages to linking a trait to the genome. We are concerned that, in the future, it may be possible to screen fetuses for genetic traits, including homosexuality, allowing for termination of a pregnancy on such a basis. Adults and children could potentially be screened for military recruitment or insurance purposes. We take issue with the possibility that marriage or childbearing might be restricted to genetically desirable people. Unregulated, this genetic information has a potential for great abuse.

NOGLSTP supports the formation of a commission to take up these ethical issues and their implications for public policy, in the areas of national health care reform, civil rights legislation, and the right to privacy. The commission should include scientists, particularly biologists, medical doctors, policy-makers, and ethicists. It could be supported by the National Institutes of Health under its Human Genome Initiative or it could be commissioned by the President or Congress, in a manner similar to the AIDS Commission.

Many may feel that studies addressing the biology of homosexuality are irrelevant to their lives. NOGLSTP supports scientific freedom and the social responsibilities that go along with its discoveries. We believe that basic research, such as Hamer *et al.*'s work, should be pursued in order to further our understanding of how the universe works. However, in the real world we all must be concerned about the ethical and unethical use of genetic information.

### **Rochelle Diamond**

Chair, National Organization of Gay and Lesbian Scientists and Technical Professionals, Inc. (NOGLSTP), Post Office Box 91803, Pasadena, CA 91109

Response: Our study did contain an appropriate control group-142 randomly selected brothers who were typed for Xq28 DNA markers in the CEPH database (1). This group displayed the expected, random segregation of these polymorphisms (see note 28 in our article). We did not include the heterosexual brothers of the gay siblings for two reasons: ascertainment reliability and statistical accuracy. Because homosexuality is a stigmatized trait, individuals who identify themselves as gay are expected to give more reliable information about any homosexual behavior than are those who identify themselves as straight. Moreover, because the penetrance of the Xq28 locus is unknown, including heterosexual brothers would have required solving a single equation in two variables, which is an inherently inaccurate procedure. Thus, including heterosexual brothers might actually

have decreased the accuracy and reliability of our results.

We did not "choose" 2% as the base rate of male homosexuality, we measured it in a comparable population with the use of the same questions, interview format, and definitions as in the present study. Fausto-Sterling and Balaban suggest that we instead use a base rate of 4%, which is apparently based on the 1948 Kinsey studies, in which the study population, interview techniques, and definitions of sexual orientation were different from those we employed. The results of the DNA linkage analysis, which represent the main thrust of our article, are independent of assumptions about the base rate. Varying the frequency of the trait-associated allele between 2% and 10% did not significantly change the lod score (figure 5 of our article).

Marker allele frequencies were not estimated from "available databases," as stated by Fausto-Sterling and Balaban, but from direct measurement of our study population. Furthermore, we used five closely spaced markers with an overall haplotype heterozygosity of more than 99%, making any minor errors in allele frequency estimates irrelevant to our conclusions. Since our paper appeared, we have typed an additional two markers in the Xq28 region and have found no discrepancy with the published results. Thus, further experiments have strengthened rather than weakened our conclusions.

We agree that genetic studies can never, in and of themselves, determine the mechanism by which a locus influences a trait. But such studies can point the way to an understanding of how the gene and its product contribute to a complex and interesting human characteristic.

We concur that attempts to genetically assess or alter normal human characteristics, including sexual orientation, would be unethical, and we endorse initiatives (2) to develop ethical standards for all aspects of human genome research.

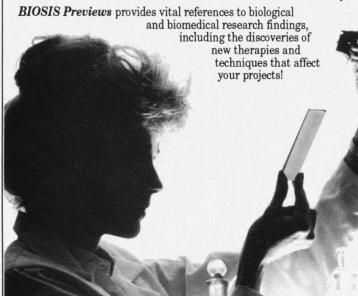
> Dean Hamer Stella Hu Victoria Magnuson Nan Hu Angela Pattatucci Laboratory of Biochemistry, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892

#### **References and Notes**

- CEPH is Centre d'Etude du Polymorphisme Humain, 27 rue Juliette Dodu, 75010 Paris, France.
- For example, the Ethical, Legal, and Social Implications Program of the National Center for Human Genome Research, National Institutes of Health, Bethesda, MD 20892.

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