Letters

Hybridomas Revisited

In your issue of May 16, 1980 (pp. 962-3) you published an article by Nicholas Wade on hybridomas which was accompanied by a column entitled "Inventor of Hybridoma Technique Failed to File for Patent." Certain ambiguities in this material could cause the casual reader to conclude that we, on behalf of The Wistar Institute, obtained patents for monoclonal antibodies in derogation of prior work done by Cesar Milstein and in contravention of an agreement with Dr. Milstein. Any such inferences are wrong.

In that column Nicholas Wade stated

Milstein feels that a patent might be justified for particular clones, even though he asked for all recipients of his mouse plasmacytoma cells not to patent the hybridomas produced from them, but says that he "would feel extremely bad if the rest of the patent is granted, because essentially they are patenting our procedure." Recipients of Milstein's plasmacytoma cells were asked to sign a letter agreeing to the nonpatenting condition. Milstein has searched his files but cannot find such a letter from Koprowski. "I would not like to say he has broken an agreement because I have no proof," notes Milstein.

The fact is that Dr. Koprowski wrote Dr. Milstein on August 5, 1976, informing him that techniques for production of monoclonal antibodies against viruses were already developed at The Wistar Institute and requesting that Dr. Milstein furnish the myeloma cells in order to study further production of such antibodies.

Dr. Milstein replied to this letter on August 26, 1976, telling Dr. Koprowski that he would ship the cells when informed that The Wistar Institute was in a position to receive them. Dr. Milstein was then notified by cable that the Institute was ready to receive the cell line, and it was forwarded.

There was a further exchange of correspondence in November and December of 1976 between Dr. Koprowski and Dr. Milstein, as a result of which Dr. Milstein authorized Dr. Koprowski to pass the cell line on to another scientist at the University of Pennsylvania.

In none of this correspondence is there one word suggesting any restriction on the use of the cell line or on patenting anything produced from these cells.

As a result of research in collaboration with Dr. Gerhard, we filed patent applications for "Method of Producing Viral Antibodies" and "Method of Producing Tumor Antibodies" with the United States Patent and Trademark Office. This was done within the framework of the Institutional Patent Agreement between The Wistar Institute and the National Institutes of Health. Patent applications are filed under these guidelines by approximately 70 major American universities and research institutions in order to generate royalties on inventions at a time when private and governmental support for research has become extremely difficult to obtain.

Prior to the issuance of these patents, we assigned any rights we might have to The Wistar Institute, including any rights to receive royalties from the inventions. This would seem to clearly refute the implication in the column that we "jumped into the [patent] gap" for personal gain.

Lastly, in attributing to Dr. Milstein the statement that "they [the undersigned] are patenting our procedure," the readers of *Science* are again misinformed. The patents which issued to The Wistar Institute deal with the procedures leading to the production of monoclonal antibodies against viral and tumor antigens, a matter which was not addressed in any of the prior Milstein publications. Indeed, the U.S. Patent Office considered the Milstein publications before issuing the Wistar patents.

We enclose for your edification the correspondence which we had with Dr. Milstein, which is referred to above.

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Editor's Note: We think that it is fitting and appropriate to publish this letter on our 16 May article on some of the circumstances surrounding the history and development of hybridomas (monoclonal antibodies).

We have reviewed correspondence between Drs. Milstein and Koprowski which has been made available to us by the Wistar Institute. This correspondence, concerning Dr. Milstein's furnishing the long-lived myeloma cell line to Dr. Koprowski, does not contain any restrictions on the use of the cell line. It is clear, therefore, that the Wistar scientists have not disregarded any wishes or conditions that Dr. Milstein made known to them.

Drs. Milstein, Kohler, Koprowski and Croce have all made significant contributions to the science of monoclonal antibodies.

Africanized Bees

... Citation of a poorly researched Associated Press article (News and Comment, 27 June, p. 1441) leads the reader to the conclusions that Africanized honey bees are no longer spreading rapidly through South America and are no longer causing problems there. Neither of these conclusions is justified; the Africanized bee is continuing to advance through the dry lowlands of northern South America at rates of 150 to 300 miles per year and to disrupt beekeeping and cause minor health problems. The most westerly front of its distribution is about halfway along the northern coast of Colombia near Cartagena. At the present rate bee swarms should reach the Panama-Colombia border sometime in 1981. I anticipate that they will move rapidly through the drier portions of Central America, eventually reaching Mexico and the southern United States.

The claim has often been made in the popular press that the Africanized bees have or will become milder as they hybridize with European bees. However, there is no hard evidence that this has or will ever occur. In fact, the balance of evidence suggests that these bees have changed little since their introduction into South America in 1956. . . .

Unfortunately, the Africanized bee is not fiction nor have the problems associated with this insect lessened through hybridization in the mysterious rain forests of the tropics. The Africanized bee problem is real. It is rich with biological, economic, social, and political complications. It will be with us for a long time.

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Erratum: In the report by John C. Behrendt et al. "Aeromagnetic and radio echo ice-sounding measurements show much greater area of the Dufek Intrusion, Antarctica" (29 Aug., p. 1014), the word "expedition" should have read "exploitation" in line 13 of the first paragraph on page 1014. Also, in line 2 of the next to last paragraph on page 1016, "50 to 60 cm/sec" should have read "50 to 60 (cm/sec²) \times 10 $^{-3}$."