Letters

PCR Amplification of Specific Alleles

Rick Weiss' Research News article "Hot prospect for new gene amplifier" (29 Nov., p. 1292) indicates that ligase chain reaction offers a general method for amplifying specific mutant or polymorphic alleles, while detection of these alleles by polymerase chain reaction (PCR) requires additional steps. He states, "PCR amplifies a stretch of DNA between two primers but tells nothing about the precise sequence of the amplified fragment; to find out exactly what you have amplified, and whether a mutation resides in that stretch, requires restriction enzyme analysis or DNA sequencing." I would like to point out that specific alleles can be selectively amplified by PCR amplification of specific alleles (PASA; also known as allele-specific amplification and ARMS). PASA uses PCR primers whose 3′ end matches a particular allele to specifically amplify that allele. A body of literature now documents the efficacy of PASA [(*1*) and references therein]. Our own experience highlights the generality of PASA; in each of 69 PASA assays attempted, specific amplification was achieved (*2*).

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The Medfly in California

There have been many attempts to explain the 1989–90 discoveries of the Mediterranean fruit fly (medfly) in Southern California. James R. Carey argues (Articles, 20 Sept., p. 1369) that the medfly is established in California. Carey first proposed his theory of medfly establishment while serving as a member of the California Department of Food and Agriculture's Science Advisory Panel (SAP) during the 1989–90 medfly eradication project. His theory was evaluated by the entire SAP and was rejected by the other four members as speculative. Carey's position was also evaluated by a "blue ribbon" committee appointed by the University of California and composed of international researchers in fruit fly biology and statistics. They concluded that (i) the medfly is not endemic, (ii) the 1989–1990 infestation could be linked to the 1988 and possibly to the 1987 West Los Angeles infestations, and (iii) the data currently available do not allow a valid assessment concerning the origin of the medfly before 1987.

Carey has no new experimental data to support his conclusions, but relies heavily on data from the quarantine interceptions of medfly larvae by the U.S. Department of Agriculture (USDA) inspectors. USDA inspectors confiscate hundreds of thousands of pounds of fruit every year and do not cut every fruit to look for larvae. The five interceptions of medfly larvae between 1985 and 1990 cited by Carey represent cases where larvae were found crawling out of fruit and were hence visible without labor-intensive fruit cutting.

The California Department of Food and Agriculture concurs with the majority of expert medfly scientists. We are confident that the appropriate strategies have been applied and that the medfly infestation has been eradicated from California. Fourteen months of high-density trapping in the

highest risk areas of Southern California, over two summers when the medfly was most likely to be present, without any finds, strongly supports the conclusion of the majority. Of course, this does not mean that new introductions and infestations of medfly will not occur in California and other Sunbelt states in the future.

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The hoped for objectivity of science is often strained when scientists confront highly controversial issues. This problem is compounded when an indivdual is perceived as a bearer of bad news. James R. Carey can be proud of what must often be a lonely battle for his point of view. However, his case would be strengthened if he acknowledged the evidence showing that Hawaii may be an important source of the medflies that recurrently invade California. The evidence is mostly indirect, and Carey's call for precise genetic studies is most appropriate.

Carey argues that population mortality factors in the medfly account for its rarity in established areas like Hawaii, but the most important factor determining the overall medfly population levels is more likely to be the succession of host fruits and their availability throughout the year (*1*). Medflies can survive for short periods of time in temperatures that dip below the threshold levels for development (*2*). However, even if most of the yearly climate is highly favorable, a break in available hosts during, say, a period of hot dry weather may make an area unsuitable for sustained colonization. The continued presence of medfly populations in such an area will then depend on the regular influx of migrants. The critical role of host succession has recently been observed on the island of Kauai, where a major increase in coffee plantings filled in a gap in the host cycle that has led to an explosion of the medfly population.

The state of Hawaii is not homogeneous in space or in time. Crops of the highest quality are grown in only one area or on only one or two islands in the state. The movement of papayas from Puna to Oahu and the reverse flow of litchis and mangos to other islands are well-known traditional and thus seasonal events. This transport of fruit (and thus fruit flies) within Hawaii has strong cultural and ethnic roots. Large enclaves of persons with family ties in Hawaii are now living in California, so it is not easy to dismiss fruit mailed from Hawaii to friends and relatives in California as the main source of infestation of our (current) four species of pest tephritid fruit flies.

Host fruit availability and variation in fruit fly populations in Hawaii should be correlated with the interceptions and outbreaks of fruit flies in California. While Carey observes that the rate of interceptions of fruit flies in first-class mail from Hawaii is low, invasions of medflies into California are also rare.

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Response: I first raised the issue of whether the medfly was established in California, not in 1989, but in 1987 at a meeting on an outbreak in Los Angeles shortly after I was asked to join the medfly Scientific Advisory Panel. I repeated this concern the following year in the middle of the 1988 medfly outbreak in Southern California and again early in the 1989–90 eradication program

(*1*). Several panel members who disagreed with my views in 1987 and 1988 were the same persons who advised the California Department of Food and Agriculture (CDFA) on earlier medfly programs and had declared the state free of medflies. For them to have agreed that medflies were not eradicated would have required their concession that their earlier recommendations had been premature. It is unlikely that they would have made such a concession even if they agreed with me because it would have immediately raised questions about the millions of dollars previously spent on medfly eradication by the CDFA and the U.S. Department of Agriculture (USDA). This quandary stemmed partly from the procedure in all California eradication programs for the same persons who advise on operational aspects of the program to also judge the program's ultimate effectiveness and partly from the inevitable political and economic pressures to declare eradication quickly so that quarantine restrictions could be lifted.

Voss incorrectly characterizes the other panel members' current views of my position—not all of them have said that they believe the medfly has been eradicated in California. He correctly notes that one of the conclusions of the University of California (UC) "Blue Ribbon" Committee to investigate the medfly situation in California was that the medfly was not endemic (*2*). However, he does not say that this conclusion was based on a semantic point. The committee's report stated, "Endemic is defined as native or indigenous to an area. The Committee felt that the use of the word endemic was imprecise" (*2*, p. 3). Voss distorts the spirit and intent of that report by quoting part of their statement out of context. I view as highly significant the UC Blue Ribbon committee's major conclusion that the 1989–90 medfly outbreak was linked to the 1988 outbreak, and possibly to the 1987 outbreak, because in both of these years the CDFA declared the medfly eradicated.

Voss implies that the number of medfly interceptions in California airports is low because the USDA inspectors are not looking for them; that the five interceptions were almost coincidental—the result of larvae "crawling out of fruit." This implication is erroneous, as I fully documented in my article. Both Voss and Saul imply that presence of medfly hosts along entry pathways "explains" the recurrent medfly outbreaks. Fruit presence is not an explanation. Rather it is a precondition for the presence of medfly larvae which, in turn, is a precondition for medfly introduction, then for medfly colonization, and so forth. Indeed, successful biological invasions require a multitude of preconditional steps (*3*). Most key pests and their hosts are present at some time along major pathways because of the scope and intensity of world travel (*4*). Therefore to accept the presence of fruit including medfly-infested fruit along an entry pathway as an explanation for repeated, widespread medfly outbreaks in the Los Angeles Basin is to accept a partial and inadequate explanation for an extremely complicated process. Multimillion-dollar eradication programs designed to protect the multibillion-dollar agricultural economy of California must surely be based on answers to questions far more profound than whether fruit is present along entry pathways.

A step toward addressing these more basic questions was taken when the CDFA recently funded a team of geneticists to determine the original geographic source (or sources) of medflies captured in the state. This group recently completed an analysis of mitochondrial DNA variation in 20 medfly populations from the New World, including 10 feral populations from four Hawaiian islands. They concluded that medfly samples collected from Calfornia in 1989 and 1991 were not derived from Hawaiian flies (*5*). These preliminary results provide direct evidence that contradicts Saul's statement that Hawaii is the likely source of medfly infestations in California. While the data are inconclusive regarding the likely origin of California flies, I believe the genetics approach that this group is pioneering will yield important insights into the nature and origin of the California medfly invasion as well as the characteristics of medfly global spread. This type of fundamental investigation must serve as the foundation on which future exclusion and eradication policy is based.

I appreciate the grave concerns of agricultural administrators such as Voss about establishment of the medfly in California. However, the pest cannot be wished away or legislated out of existence. I stand firmly behind the conclusion in my article that the medfly is established in California. The capture of 26 more medflies in Los Angeles County last fall shortly after my article was published and of one early this year in Orange County further substantiates my position (*6*). The majority of the medflies captured in Los Angeles County were within a few blocks of captures made in previous years. The developing medfly crisis in the state must be dealt with directly, immediately, and decisively (*7*). This cannot happen if agriculture policy-makers continue to insist that the medfly problem in California is under control.

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Transmittal of Hepatitis C

A statement in Michelle Hoffman's News & Comment article "Hepatitis A shows promise" that hepatitis C is transmitted largely through blood transfusions (13 Dec., p. 1581) is incorrect. Recent data have demonstrated that only approximately 6% of cases of hepatitis C infection may be attributable to blood transfusion (*1*). Approximately 50% of patients do have a defined parenteral exposure, but the vast majority of cases result from drug use. Interestingly, 40 to 50% of patients have no identifiable source for the infection.

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Erratum: In Richard Stone's News & Comment article " 'Third wave': Roiling the waters" (15 Nov., p. 930), it should have been made clear that Graham W. Gibbs did not make a formal presentation at the conference "The third wave of asbestos disease: Exposure to asbestos in place. Public health control," nor did he write a "forward" to proceedings of the meeting.

Erratum: In Joseph Palca's article "A $9-billion budget for NIH" (News & Comment, 8 Nov., p. 791), the subheading of the graph "NIH's (probable) final budget" should have been "Dollars in millions," not "Dollars in thousands."

Erratum: In the report "Hydroxyl radical photo-production in the sea and its potential impact on marine processes" by K. Mopper and Xianliang Zhou (2 Nov. 1990, p. 661), the range of values represented by the x-axis in Fig. 1A should have been 0 to 7.0×10^{-18} M, not 0 to 2.0×10^{-18} M.