DNA FINGERPRINTING

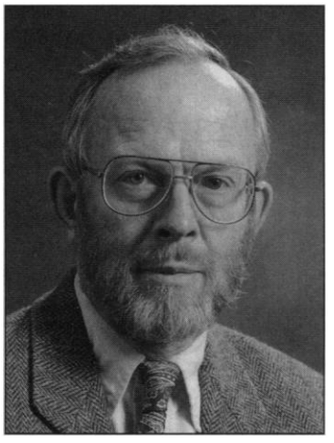
Geneticists Attack NRC Report As Scientifically Flawed

LONDON—Last April, a committee of the U.S. National Academy of Sciences hoped to end a bitter disagreement among population geneticists—one that had already had major consequences far outside the realm of scientific discourse. The dispute revolved around a deceptively simple question: What are the odds that an apparent match between a suspect's DNA and DNA taken from a sample discovered at a crime scene is, in fact, merely the result of pure chance? Because scientists couldn't agree on this question, DNA fingerprinting evidence had been thrown out of court in a handful of cases across the United States. Then came the National Research Council's (NRC) Committee on DNA Technology in Forensic Science, which proposed a way of calculating the answer that it believed would be acceptable not only to the warring factions in the DNA fingerprinting community but also to the courts. "I don't think anyone will fight it," said committee member Eric Lander, the Whitehead Institute mathematician-turned-molecular geneticist, at the time the report was published (*Science*, 17 April 1992, p. 300).

Nine months later, however, it is clear that Lander's judgment was misplaced. At a meeting on forensic DNA typing held here last month,* and in a rash of papers now surfacing in the literature—one of which, by Bernard Devlin, Neil Risch, and Kathryn Roeder of Yale University, appears on page 748 of this issue—the NRC's proposed method is under attack from a coalition of population geneticists and statisticians. They argue that the NRC erred too far on the side of caution in trying to address concerns about DNA evidence raised by population geneticists such as Richard Lewontin and Daniel Hartl, now both at Harvard. Worse, the critics say, the NRC panel's solution, called the "ceiling principle," is built on erroneous assumptions about population genetics. "If I were asked if there is any scientific justification to the ceiling principle," says Risch, "I'd have to say no."

Such an assault in the scientific literature on an NRC report is, to say the least, highly unusual. The critics contend that the report's conclusions are seriously flawed because the NRC panel lacked the necessary expertise: "The major problem is that there was no population geneticist on that panel," says Risch. Although committee members approached by *Science* last week generally defended the ceiling principle on the grounds that it was designed to reduce the controversy over the admissibility of DNA evidence in court, several acknowledged that Risch has a point. "We probably could have done with more representation in that respect," says Johns Hopkins geneticist Victor McKusick, who chaired the committee.

Faulty product? Before the NRC panel stepped into the debate, forensic scientists generally used a method called the "product rule" to calculate the probability that a match between two DNA profiles is due to chance. Under the product rule, crime labs simply calculate the frequency with which each allele from a matching pair of DNA profiles occurs in a reference database—usually consisting of profiles of individuals from the same ethnic group as the suspect. Then they multiply these individual frequencies together to calculate the frequency with which the suspect's profile as a whole is likely to be present in the general population. The answer is typically a vanishingly small number—so small that lawyers, judges, and juries were increasingly respectful of the novel form of evidence.



"Illogical." Newton Morton says the fix doesn't match the problem.

But Lewontin and Hartl (who was then at Washington University in St. Louis) threw the field into an uproar when they argued in court testimony—and in an article in *Science* (20 December 1991, p. 1745)—that the product rule ignores the possibility that particular combinations of alleles may show up more frequently in some subpopulations than in the ethnic group as a whole. The result: The rule could greatly underestimate the probability of a chance match, and so bias evidence against a defendant, they said. More detailed knowledge of the genetics of sub-populations is needed, the duo argued, before probabilities can be calculated with confidence. Most geneticists agreed that it would be nice to have such data, but argued that the chances of a false conviction based on the Lewontin/Hartl concern were negligible.

Enter the NRC panel's ceiling principle. The panel urged the creation of a database consisting of DNA profiles of 100 randomly selected individuals from each of 15 to 20 genetically homogeneous reference populations—such as English, German, Navajo, West African, Vietnamese, and Puerto Rican. Crime labs should determine the highest frequency with which each allele in a suspect's DNA profile occurs in any of these reference populations, the panel said, and these "ceiling" frequencies should be multiplied together to give the matching probability for the profile as a whole. In addition, the report recommended that the minimum figure used in the calculation for any individual allele should be 5%. The NRC panel said it wouldn't take long to assemble such a database, but in the meantime, forensic scientists should use maximum allele frequencies found in each of the four major U.S. ethnic groups—Caucasian, black, Hispanic, and Native American—or 10%, whichever is higher.

But the attempt to find common ground has itself proved controversial. Some critics of the ceiling principle argue that it doesn't even address the potential problem of subpopulations. "They ignore any attempt to describe the substructuring and try to alter the gene frequencies in a way that many of us regard as illogical," says population geneticist Newton Morton of the Cancer Research Campaign's genetic epidemiology unit in Southampton, England. Morton outlines his objections to the NRC report in a forthcoming issue of the *European Journal of Human Genetics*. If the committee simply wanted conservative estimates of match probabilities, says Morton, it could have urged expert witnesses to "move the decimal point a couple of places." Lewontin is not impressed either: "It's just totally irrational," he says, attacking the NRC panel for picking 10% "out of the air" as the minimum allele frequency in the interim version of the ceiling calculation.

Other critics, such as Devlin, contend that the logic that drove the NRC panel to recommend the ceiling principle comes from a single 1972 paper by Lewontin, which suggested that subpopulations within an ethnic group are at least as distinct genetically as are different ethnic groups. The problem, says Devlin, is that the weight of evidence collected since then—but not cited by the NRC—suggests this is not the case. "It's just simply wrong," he says.

Indeed, Devlin, Risch, and Roeder present evidence in their paper that there's no real problem with using the standard product rule. They add that computer simulations

* The Use of DNA Statistics in Crime Cases, organized by the Metropolitan Police Forensic Science Laboratory, 15 and 16 January.

carried out on deliberately substructured databases, made by merging data from different ethnic groups—some of which were presented at the London meeting by statistician Ian Evett of the UK Forensic Science Service—still give adequate results.

Morton isn't prepared to go quite that far. He points out that good defense lawyers will always attack a simple application of the product rule, making it important to account for substructuring. But he argues that there's a population genetic statistic called "kinship," or F_{ST}, that can describe substructuring, and he says it would be easy to correct the probability calculations to account for conservative values of F_{ST}.

Despite the barrage of criticism, Lander vigorously defends the ceiling principle. "The courts were asking whether there was any method that met the legal standard for 'general acceptance by the scientific community,'" says Lander, not a method that would precisely describe population substructuring. Pointing out that the ceiling principle could still give odds of up to 6 million to 1 for a typical matching profile, Lander says: "I realize that there are some statisticians who are convinced that the odds should be 6 billion or 6 trillion to 1, but I can't see the practical point." The goal, he says, was to find a method conservative enough to win over most critics of the product rule, while still providing impressive enough odds to allow convictions.

In that regard, the report has been at least partially successful: Although Lewontin is still critical, his coauthor Hartl is now a strong supporter of the ceiling principle. And even Bruce Budowle, the leading DNA fingerprinting expert with the Federal Bureau of Investigation, concedes that problems with the admissibility of DNA evidence do seem to have eased since the NRC report came out in favor of DNA fingerprinting.

Indeed, some NRC panel members are worried that the current backlash against the report could undermine the progress Budowle describes. "I only worry that renewed controversy about wanting higher odds will confuse the courts into doubting that there is general acceptance that the ceiling principle provides a conservative estimate," says Lander. But Arizona State University law professor David Kaye doubts that defense lawyers would succeed in getting evidence ruled inadmissible because of this latest twist to the forensic DNA typing debate, as "nobody's disputing that some number should be presented." Indeed, Kaye predicts that the scientific criticism of the ceiling principle will eventually cause it to be replaced in the courts by less conservative methods. Maybe so, but it won't die a quiet death. Says Morton: "I don't think [we're] going to quit and forget about this."

–Peter Aldhous

SUPERCONDUCTING SUPER COLLIDER

The Presidential Transition Heightens Uncertainty

After last summer's near-death experience in Congress, when its funding was killed in the House, then revived in the Senate, the $8.3 billion Superconducting Super Collider (SSC) has remained precariously on the critical list. Now, with a new administration in Washington, its fate is more uncertain than ever. Japan—which SSC supporters hope will provide the bulk of the foreign funding for the giant accelerator—is awaiting a signal of Washington's intentions, and Congress is still split on the project's future. A quick cure—or coup de grace—for the beleaguered accelerator will have to come from the Clinton Administration, say physicists and policy makers.

SSC LABORATORY

Digging in. The earth is moving at the SSC site in Texas even though funding is stalled.

Any such cure would require breaking out of what George Brown (D–CA), chairman of the House Science, Space, and Technology Committee, calls the "Catch-22 of foreign funding for the SSC." As Brown described it in a 21 January press release, "Major foreign participation has remained elusive because of uncertainty about the U.S. commitment to the project, yet our own commitment has wavered in large part because of the absence of substantial foreign funding." The Catch-22 intensified in December, when officials in Japan said they would postpone any decision on committing $1 billion or so to the SSC until President Clinton demonstrated his support. All of which adds to the pressure on Clinton to signal his intentions in his March budget request. "If Clinton makes it clear he wants this," says a leading physicist who recently returned from a trip to Japan, "they'll do it. If Clinton waffles, they'll waffle, and if Clinton kills it, they'll be relieved."

The question of foreign participation might have been resolved by now, says a senior staffer on the House science committee, if former President George Bush had been reelected. In that case, he says, the Japanese "wouldn't have had any excuse to say they needed to wait further and take the temperature of Washington. They would have let people know definitively one way or the other before our budget cycle got under way." But with Clinton's arrival, says the staffer, "the Japanese have been let off the hook for a while....Now they have legitimate excuse to wait."

In a 14 January letter to Brown, outgoing Department of Energy (DOE) Secretary James Watkins suggested that the United States take the lead in breaking the impasse. With the Japanese nondecision, he said, DOE could be confident of no more than $400 million in foreign commitments by 1999—far below the $1.7 billion DOE had promised it would raise. Watkins suggested bluntly that the only way to "have any hope of full success in obtaining foreign funding" is by authorizing and appropriating full funding of the SSC up front to ensure that it "be completed on schedule independent of foreign contributions if necessary."

But that would be a tough political sell. An aide to Brown told *Science* that to ask Congress "to vote up or down on $5.5 billion is the most difficult way to frame an SSC vote this year." Even Brown, one of the SSC's strongest supporters in Congress, did not offer his support to Watkins' suggestion, though he did say he personally remained "fully supportive" of the SSC. The SSC's future in Congress is so uncertain, in fact, that the staff of the House Energy Subcommittee, when asked to send a routine background paper on the project to the transition staff,