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Cover: A human breast cancer cell looks vehemently aggressive in this scanning electron micrograph. New research suggests that faulty estrogen receptors in some breast tumors may allow the cancer to proliferate wildly, making the choice of treatment a potentially deadly gamble. Another study offers hope that a compound in soybeans may someday help prevent the seeds of breast cancer from taking root. (Photo: National Cancer Institute)

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# Letters

# Science under scrutiny

"Trouble in the Laboratory" (SN: 3/31/90, p.200) is replete with inaccuracies and innuendo, but I wish to respond to only one point.

Kathy Fackelmann maintains that the central claim of the paper is that "idiotypic mimicry" occurs, supporting Nils Jerne's notion of an idiotype network. It is notable that she bolsters this interpretation by quotes from other scientists but not by quotes from the paper. There is good reason for that: The paper is not about mimicry; that is only one of many possible interpretations of the results.

The paper is basically a description of the surprising behavior of the immune system in these immunoglobulin-transgenic mice. Many points were made in the paper. For me, the most important were:

- 1. The lack of transgene expression in some hybridomas.
- 2. The very high expression of one particular and usually rare variable region gene ( $V_M81\,X$ ).

3. The changed pattern of idiotype expres-

The bases for these phenomena are still under study.

I never believed (and still do not) that idiotype mimicry through "network" interactions was occurring. Dr. Thereza Imanishi-Kari, however, considered this a possibility. So we mentioned the possibility (we called it a "tentative explanation") in the discussion section of the paper. The paper is complete without that suggestion. Anyone who ever heard me lecture on the data will have heard in 1986 about my disbelief of mimicry.

Evidence is building up that the high idiotype levels were due to a (possibly) fortuitous reaction between the  $V_{\rm M}81\,\rm X$  product and the idiotype reagent. If so, the results point to a significant phenomenon not related to mimicry or networks.

David Baltimore Director Whitehead Institute for Biomedical Research Cambridge, Mass.

The 1986 CELL paper authored by David Baltimore, Thereza Imanishi-Kari and their colleagues fails to adequately reflect Baltimore's expressed disbelief that "idiotypic mimicry through 'network' interactions" accounted for the reported findings. On page 256 of the paper, the authors list two possible explanations for the surprising behavior of the immune systems in the transgenic mice they studied. The second explanation, which a careful reading reveals as Jerne's network, is described as "more appropriate in most cases." This statement led many readers to assume the report provided support for Jerne's postulated immune-system network.

If "the changed pattern of idiotype expression" noted by Baltimore in his letter is not idiotypic mimicry, then some very knowledgeable immunologists are terribly confused. Moreover, the three points he cites in his letter as "the most important" are among the issues under investigation by a National Institutes of Health panel

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MAY 12, 1990 291 and a congressional subcommittee.

Kathy Fackelmann reported her article carefully and talked with scientists with the expertise to evaluate the 1986 CELL report. She repeatedly requested an interview with Baltimore to discuss the paper's science, and even provided him a series of written questions to which he could respond in writing. Baltimore rejected all her requests.

— Patrick Young, Editor

"Trouble in the Laboratory" was very troubling to me — not because of the menace at hand, but because Congress is doing things it has no business doing.

Congress is used to situations of political corruption. It is used to facts that happened in the past that can't be reproduced. Therefore, it is critical that congressional investigators reexamine what everyone says, in addition to hearing testimony. Such evidence is subject to corruption, so they have to pounce like a tiger. Congress has to catch everyone who is "guilty" before they manage to cover it up and get elected to even higher government office. This is an imperfect process, as we have all seen.

Science, on the other hand, bounces back from errant researchers and erroneous research with far more resiliency. The proof's in the pudding. If there's any question about the proof, we'll just make more and more pudding until the truth comes out.

Far more money is being spent on this investigation than the original research cost in the first place. It would certainly be cheaper to have the original researchers, in parallel with rival research groups, try to duplicate the experiment or, using some other method, verify or disprove the original hypothesis under question. That's all we care about anyway. We aren't interested in putting anybody behind bars. Having your published results confirmed or contradicted by the majority of related research has its own repercussions.

Allan Bonadio San Francisco, Calif.

What is most disturbing about David Baltimore and Thereza Imanishi-Kari's claim for "idiotypic mimicry" is not the strong possibility that experimental data have been altered. Scientists are people and are as prone to dishonesty as anyone else. In fact, with an increase in corporate involvement and the lure of personal profit, we are likely to see more cheating.

However, in a certain sense, conclusions based on invented data are no different from any other kind of unsupportable finding. The scientific process of duplication and confirmation is supposed to provide sufficient double checking to protect society from the consequences of bad science as well as from fraud.

But the scientific process works only if researchers are willing to critically investigate each other's claims. Just as it is vital to protect the right of a scientist to draw mistaken conclusions, it is also vital to protect the right of a whistle blower to be wrong. Questioning needs to be encouraged, perhaps even rewarded.

And herein lies the most dangerous and revealing aspect of this case. Dr. Baltimore is a famous and powerful man. He carries enormous weight in the immunology research community. The person who challenged his results, Dr. Margot O'Toole, was a post-doctoral student. Despite the significance of the charges against him, Baltimore was consid-

ered for the presidency of MIT and has been rewarded with the presidency of the Rockefeller University. His associate, Dr. Imanishi-Kari, is safely employed at Tufts University with NIH funding. But the person who took the greatest personal risk by questioning her own supervisor's data, Dr. O'Toole, has been unable to find a job in her field of immunology for the past four years.

I assume that future whistle blowers will think twice before publicly questioning a powerful person's evidence. And we all will bear the consequences.

Steven E. Miller Cambridge, Mass.

It would seem that much of the controversy surrounding the 1986 paper by Imanishi-Kari and Baltimore could have been avoided if Cell's editors and referees had done their job properly. I am amazed that the editors of such a prestigious journal would agree to publish a paper whose major conclusion rests on data that the authors did not show and apparently did not collect. I wonder if the names and institutional affiliations of the authors had anything to do with the paper's acceptance.

Wade Hazel Reelsville, Ind.

"Trouble in the Laboratory" was the best account I've read of that controversy, and the first I've encountered that didn't treat the science as too complex for mere mortals to comprehend. I'm grateful that you took the time to go beyond personalities and policy issues to present an account of the scientific claims and the data on which they were based.

Jeffrey J. Wine

Professor Cystic Fibrosis Research Laboratory Stanford University Stanford, Calif.

For this academic reader, the most depressing part of your coverage of the "idiotypic mimicry" controversy was its confirmation of the rather vicious and self-serving personal politics of the academic establishment. Your reporter quotes Harvard's Walter Gilbert as saying that "scientists are not suspicious of human behavior." Perhaps that is because their behavior often can't stand much scrutiny. The power structure of academe is still perfectly feudal, with advancement dependent on apprenticeships, and approval dependent on "loyalty" — not to the truth but to one's superiors.

Margot O'Toole's career has been efficiently destroyed by those whom she was forced to accuse in her pusuit of truth. Just as the engineer who warned of the defective O-ring before the Challenger disaster was not only fired but blacklisted in the industry, O'Toole may never work again in her specialty. Increasingly it seems that conscience and a regard for truth are liabilities in academe.

I am a mere humanist with a penchant for science, but even in my own field I have watched the effective destruction of those who dare to question the system. When a student discovers that a professor has plagiarized, who gets the ax? The student, of course. The professor suffers a bit of embarrassment but no loss of money or position.

That's why I have no sympathy for David Baltimore or Thereza Imanishi-Kari – they are the power structure, and obviously taking good care of themselves. But there ought to be

some kind of hall of fame to honor martyrs like O'Toole.

I am being perfectly frank because I am quite sure you won't print my letter. You, too, depend on the good will of the scientific establishment, and will think twice before allowing me to offend them.

> Robert A. Collins Professor of English Florida Atlantic University Boca Raton, Fla.

## Colorful history

It was with great interest that I read your report on oscillating raindrops and the letters responding to it ("Shaking Raindrops Wash Out Rainbows," SN: 1/6/90, p.4; Letters, SN: 3/24/90, p.179). I have been lecturing on rainbows for several years now, and have found that the history of the study of rainbow optics is fascinating in the way theories of increasing sophistication arise to account for features unexplained by previous theories.

The issue of white fogbows, mentioned in the letter from Derham Giuliani, is one of these. It cannot be explained by the Descartes-Newton geometrical optics theory of the rainbow, nor is it due to oscillating drops. To explain it one needs the physical optics explanation begun by Thomas Young and perfected by George Biddell Airy in the 19th century. In essence, what happens is that the interference maxima for all colors become so broadened that they almost entirely overlap, recombining into white light.

In his Nature of Light & Colour in the Open Air (1984, Dover), M. Minnaert describes this effect and also mentions the odd effects of lightning on the rainbow – which he suggests might be due to electrostatic effects or to the merging of drops. I have long felt that the shimmering of the rainbow observed coincident with the arrival of the thunder must be due to oscillations in the raindrops, as Adolph Schaller's letter suggests. Since the rainbow can form anywhere there are raindrops along a line 138° from the sun, it is possible that some of these drops will be far from the eye - yet close to the lightning - and affected before the thunder reaches the observer, as in Schaller's case. On the other hand, if the drops responsible for the rainbow are close to the observer. then the thunder will arrive at the same time as the shimmering. There is no need to invoke unknown electrical disturbances.

Stephen R. Wilk Senior Scientist, Avco Research Laboratory Everett. Mass.

# Typographical eclipse

Regarding "Japanese satellite begins orbiting moon" (SN: 3/31/90, p.198):

The orbit described as an ellipse
Slips wistfully from astronomers' lips.
Alas! The "l" has been eclipsed,
Left from "elliptical" by "printer's lisp."

Victoria Duers
Storrs, Conn.

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