LETTERS

Construction of Human Tumor Viruses?

A by-product of experiments that have already been conducted in several laboratories may be new viruses capable of producing malignant diseases in humans. Our concern has been initiated by a description of the work of S. S. Kalter and his colleagues (*1*). It appears that an extract derived from the cocultivation of cells containing a murine sarcoma virus and cells persistently infected with a baboon type C RNA virus is capable of producing tumors in dogs, marmosets, monkeys, and chimpanzees. Neither the murine virus (a mouse virus with an exceptional efficiency for inducing "malignant transformation" in culture) nor the baboon virus alone is capable of causing tumors in these animals. The production of malignant tumors in such a variety of primate species suggests the possibility of creating viruses that are oncogenic for humans. Given the perilous consequences, we see no compensating scientific justification for these experiments.

We recognize that at present there is no conclusive evidence for a viral causation of any human malignancy. However, it has been clearly demonstrated in all animal species so far examined that viruses manufactured in the laboratory can be oncogenic. It seems only reasonable to assume that humans may be similarly affected. Indeed, it is important to make sure that current experiments do not prove this assumption to be correct.

Informed officials at the National Cancer Institute have stated that the above experiments were carried out in appropriate facilities. We ask whether any facility is adequate to meet the possibility, even if remote, of containing an artificially created virus that is potentially a human tumor virus.

Concern has been expressed in the scientific community about the safety of the construction of DNA's involving bacterial plasmids and segments of mammalian genomes. In this case, the danger rests on the possibility of inadvertently picking up and amplifying unwanted genetic information that might alter in some way the natural bacterial flora in man and somehow be transmitted into human cells. We believe that the biohazards resulting from such bacterial cloning experiments are minimal when compared to the apparent success in selecting for oncogenic viruses capable of producing tumors in a wide spectrum of primates. Therefore, we urge that all experiments involving cocultivation of known oncogenic viruses with primate viruses be immediately halted until the safety of such experiments are extensively evaluated.

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Government Talk

I always enjoy Philip H. Abelson's editorials, but "More laws, more complexity" (25 June, p. 1291) was a highlight. Abelson opens by quoting the inscription on the front of the National Archives building, "What is past is prologue." I add the story of the Washington cabbie who was asked by his tourist passenger what that meant. He answered, "Lady, that's government talk for 'You ain't seen nothin yet!' "

So true. And so government of the people, by the lawyers, for the lawyers progresses to the end, described by T. S. Eliot as coming "not with a bang but a whimper."

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The Ames Assay

The issues raised by Gina Bari Kolata (News and Comment, 18 June, p. 1215), Harry Rubin and Bruce N. Ames (Letters, 23 Jan., p. 241), and Bridges (*1*) with respect to the use of microbial mutagenesis assays for detection of chemical carcinogens invite further discussion. There is no question that the measurement of backmutation frequencies in certain bacterial strains has value as a component of testing programs seeking to identify substances potentially harmful to humans. What can be seriously questioned is the implication that either a frameshift or base-pair substitution mutation in a haploid prokaryote has any equivalency with the multistep, multifactorial process of carcinogenesis in eukaryotic organisms.

As one justification for the use of the microbial assay for chemical carcinogen identification, Ames claims that "carcinogenicity and mutagenicity results for the polycyclic hydrocarbons show an excellent correlation," although it is not clear whether this correlation is qualitative or quantitative, or both. While many carcinogens show some degree of mutagenic activity in various test systems, even a cursory examination of the quantitative experimental data does not support the proposed correlation (Table 1). A large number of studies subsequent to Iball's (*2*) have provided ample support for his ranking of aromatic hydrocarbon carcinogenicity.

Moreover, if a group of direct-acting agents, which should not be influenced by the vagaries of metabolic activation, are similarly considered, the absence of a correlation is again evident (Table 2).

Over and above the difficulties presented by this lack of correlation between microbial mutagenicity and rodent carcinogenicity results is the conceptual problem in the overly simplified view of cancer induction as resulting from a point mutation. While there is very likely a genetic component in the collection of diseases subsumed by the designation cancer (*3*), the progressive and evolving nature of these diseases in humans, as well as in laboratory animals, appears to be the factor of critical importance. Although many chemical carcinogens may exhibit mutagenic activity in certain assay procedures, the mutational origin of cancers remains an unproven hypothesis, with a substantial body of evidence in support of other mechanisms (*4*).

Finally, there is the matter of perspective with respect to the design of experiments. The salmonella strains widely used for mutagenesis assays at the present time have been constructed by genetic manipulation with the specific goal of showing that chemicals that are carcinogenic in various mammalian test systems will be mutagenic in these bacteria. The conscious selection of those strains whose response supports a preconceived notion is self-fulfilling and not a true test of correlation of the mutagenic and carcinogenic action of chemicals. While one can share the social concerns of most investigators with respect to the potential human risk from exposure to chemicals in the environment, the means to identify agents which exhibit biological activity (mutagenesis, carcinogenesis) and to establish mechanistic relationships must remain unbiased. In a *Science* editorial (30 Jan., p. 341), Alvin M. Weinberg considers the problem of working at the interface between the laboratory and the public arena, and his cautions regarding the carry-over to scientific analysis of the less rigorous standards of validation acceptable in public forums are worthy of reflection.

Table 1. Carcinogenicity (Iball's index) (*5*) and mutagenicity (revertants per nanomole) (*6*) of polycyclic aromatic hydrocarbons. Marginal activity is indicated by ±.

Chemical	Carcinogenicity	Mutagenicity
7,12-Dimethylbenz[*a*]-anthracene	151	19
3-Methylcholanthrene	80	58
Benzo[*a*]pyrene	75	121
Dibenz[*a*,*h*]anthracene	26	11
Benz[*a*]anthracene	±	11
Dibenz[*a*,*c*]anthracene	±	175
Chrysene	±	38
Benzo[*e*]pyrene	0	0.6

Table 2. Carcinogenicity (percentage of mice with tumors) and mutagenicity (revertants per nanomole) (*6*) of direct-acting agents.

Chemical	Dose (mg)*	Carcinogenicity	Mutagenicity
Dimethylcarbamoyl chloride	5.0	70	0.04
β-Propiolactone	0.73	60	4.1
Proprane sultone	0.3	42	6.6
Diepoxybutane	1.1	17	
	0.1	14	0.12
Glycidaldehyde	3.3	24	
	0.1	6	19

*Subcutaneous injection in mice once weekly (*7*).

The Ames assay will continue to be useful as one of a battery of first-step prescreens for chemical agents that may have the potential for interacting with cellular genomes. However, the implication that positive results in this microbial mutagenesis system will correspond to carcinogenicity in experimental animals or in humans does not appear, at present, to be substantiated.

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Not the least benefit from possible eventual reliance on "quick" bacterial tests for chemical carcinogens will be a reduction in the number of animals presently used. Antivivisectionists will not be totally satisfied, but informed citizens who recognize the need for animal-based research will be encouraged if scientists find that the "quick" tests are as good as or better than animal tests for routine screening of chemicals.

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Paper Mills and Campus Ethics

Amitai Etzioni's editorial on paper mills (23 Apr., p. 325) focuses on only the latest result of the degradation of intellectual integrity in our universities. The phrase "publish or perish" of the 1960's has now been replaced by the requirement of "accrue overhead." The corporate model applied to the university requires a profit, and the source of that profit is the research grant. Is it any wonder that students cheat in an environment where the classroom responsibilities of faculty are so openly degraded and discouraged?

The situation is ludicrous. The most dangerous act a nontenured faculty member can perform is to receive recognition as an outstanding teacher. Tenured faculty who devote too much time to the students are denied salary increments and promotion. The rewards are clear—money and release time for success in obtaining funding. If no funds, then more classes, more students, and denial of monetary reward. Merit is equated solely with money in grants, and publications which result from activity that does not generate overhead is criticized. The value of a publication to the scientific or intellectual community is of little consequence.

The student is not to blame. His teachers spend their time trying to second-guess who will give money for what. In the classroom, the faculty are preoccupied with survival problems. The faculty know it, the students know it, and in case anyone misses the point, the administrations state it in very clear terms: administrative reward for grants, departmental recognition for teaching. The salesman gets the money, the teacher gets the pen-and-pencil set.

Etzioni proposes symposia and workshops on the subject of cheating. I suggest we first remove the corruption which permeates our universities. Why not a workshop on hiring part-time instructors for our large classes, instructors who work cheap but still generate the student credit hours? Why not a symposium on how overhead monies have had a net harmful effect on academic quality? Why not a convention on how recognition can be afforded to those who meet professional standards, and on how the "for sale" tag on promotion and tenure can be removed?

Higher education is under attack, and because we have been corrupted we just may not survive with all the freedoms we now enjoy, and indeed require, for the free pursuit of what we call truth. But don't blame the student. He is only modeling.

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Etzioni skirts the real reasons for the continuing success of paper mills on many campuses and focuses incorrectly on student responsibility. The actual culprits are the faculty members.

Graduate students who submit ghost-written or researched theses are responding to the professorial practice of claiming major or total credit in published papers for work done by student assistants. Undergraduates are able to pass off phoney term papers as their own to professors who are, by and large, unable or unwilling to discover students' real research and writing capabilities. The paper mill business will continue to thrive until these and other corrupt practices and deficiencies within the "academic community," of which students are now keenly aware, are eliminated.

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Noting Etzioni's editorial on paper mills, I propose (i) that undergraduate students be passed or failed on the basis of daily laboratory performance and occasional examinations; and (ii) that just as every ethical physician makes a daily visit, at least, to patients in the hospital, so should every ethical professor make a daily visit to each graduate student. Both the physician and the professor should spend enough time and make enough observations to know whether or not progress is being made. The physician or the professor should not accept the responsibility for more people than can be effectively observed.

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Etzioni's editorial is a cry of anguish about, and a call for action on, the practice of purchasing term papers, theses, and dissertations. The ethics of the problem are the major point, but the major question is not how to stop it or detect it or punish it. The real question is, Who is cheated? The student has the opportunity to learn through research or he can purchase and be thus assumed to know ever after. Those who slide through their course work by any method (cheating, cribbing, purchasing term papers, or whatever) will find themselves passed over when it comes to finding that uniquely interesting job or that highly desired promotion, simply through lack of preparation. Ignorance is easily betrayed, long remembered, and seldom rewarded.

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The obvious answer to Etzioni's question "What is to be done about students who, in effect, purchase their degrees . . .?" is simply for employers to stop using degrees as a basis for hiring and promotion.

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Briefly, in response to the points made by Hudson and Steffey, whatever is wrong with "the system"—and there is indeed much which ought to be corrected—ultimate responsibility for unethical conduct nonetheless must rest with the acting individual. Nor can we allow individuals to disclaim responsibility for or excuse their unethical conduct on the grounds that others get away with—or are even rewarded for—unethical behavior.

At the same time, it surely is true that setting an example is one of the most persuasive modes of moral education. Walker's suggestion that professors not accept responsibility for more students than they can effectively give supervision, guidance, and attention to provides such a means for professors to demonstrate that they do take their responsibilities seriously—hopefully inspiring students to do the same and nudging the system toward reform.