Basic Science and Public Policy*

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I would like to address my attention to the Cancer Program as seen by the basic science community, not so much in terms of dollars and cents but of the objectives; i.e., where and how the basic sciences should fit and what role they have been asked to play in the Program. I am not going to deal with specifics of appropriation from the NCI budget, nor with the scientific basis of cancer control.

Whatever position one takes with respect to the proper balance of effort in the Cancer Program toward basic and clinical initiatives, we must recognize that cancer is a by-product of our technologic society. We are faced with an overwhelming exposure throughout life to a growing battery of chemicals. Some estimates are that perhaps 20,000 new compounds are introduced into potential contact with human beings each year. The individual compounds would themselves pose a serious threat of recognition and detection. What then can we take to be the prospects for discerning the limits or effects of the interaction of a multitude of chemicals that we breathe, smoke, eat, drink, wash ourselves with, clothe ourselves in? There is no doubt that 5, 10, 15 or 30 years of post-World War II life has made of all of us chemical reaction flasks in which the reagents at work are largely unknown or if the reagents are known, the reactions in which they are critically involved cannot be specified. As important as the detection and elimination of these carcinogens from the environment are and must be, the diagnosis and treatment of cancer as well as prevention aimed at more than the study of chemical carcinogens must be pursued with unrelenting vigor. Cancer is already occurring via these chemicals and intervention looms as the principal instrument of effective modulation for some decades to come for all those already subjected to these carcinogens.

Malignancies of all classes share in common the basic property that the malignant cells have lost contact with control devices in the host animal. Those devices serve to achieve the balanced functioning of the body. Malignant cells grow without respect for the limits set by the body for organ size or production of hormones or other pharmacologically active molecules by specific cells. The invasion of adjacent tissues, attachment to set up a focus of new growth in distant organs and vessels, special products which are released from the tumor cells, and the unequal competition for nutrients established by the colony of malignant cells are the features that constitute the threat and the ultimate destructive force of a cancer or malignant tumor.

Investigators in the biomedical sciences who have dedicated their lives to the most fundamental studies of biologic phenomena, which have led to the development of current anti-tumor therapy and newer methods of detection of chemical carcinogens, fear that the Cancer Program has focused on the transmission of existing knowledge

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to patient care at the expense of research aimed at understanding the problem itself. Part of that fear is engendered by the awareness of scientists throughout the country in all scientific disciplines that the highest echelons of government seem to have accepted the notion that managerial initiatives can solve any problem. Scientists recognize that money can buy impressive tables of organization with a body at every desk without making serious strides toward even the recognition of the real state of knowledge. Every effort must therefore be made to expose the inner workings of a program to scrutiny by the several publics including the scientists. These internal administrative and managerial issues have been carefully and effectively planned for in the Cancer Program and it is the most critical assignment of the Panel, the Advisory Board, and the Director of NCI to address these problems.

Biomedical science has as its ultimate objective clarification (in the most finite detail) of the normal functioning of cells, much of which is understood through abnormal conditions. Mutations, used to delete a normal enzyme or other product, thus creating an abnormal state, provided one of the principal biologic tools for the study of normal DNA synthesis, protein synthesis, vitamin utilization and energy production. Abnormal conditions occurring spontaneously in nature have proved equally important for the study of normal processes, e.g., diabetes and normal sugar metabolism, hemoglobin abnormalities and protein structure and genetics. Basic scientists working in the biological and biomedical sciences have no quarrel with the ultimate objective of early recognition of the abnormal by understanding of the normal. Beyond that they are also concerned with prevention, cure, or arresting the progress of abnormal conditions. What the basic scientist fears most is that a program based upon false assumptions will apply the long range goal unwisely to the immediate project in which he is engaged. Such application imposes justifications, requires proof of legitimacy, preselects the observation the investigator can pursue, and determines to what degree those observations may be pursued. Thus the long range goal—prevention and cure—can become a corrosive criterion undermining the most fertile initiatives for lack of program relevance.

All investigators in the biological sciences are agreed that serendipity is their most valuable ally. What emerges unexpectedly in experiments is often the most critical information obtained in the experiment and those findings are especially pertinent to new directions in approach and understanding, throwing new light on old questions. It is imperative that the state of mind of the investigator be such as to perceive the unexpected for what it may ultimately be worth. Program relevance dictates a selection in registering of observations that may categorize as worse than useless a contradictory finding.

The Cancer Program as such came into being from recognition by national figures with a long-term interest in the cancer problem that much of what was being accomplished in experimental laboratories around the world did not reach clinicians and was unlikely to benefit cancer patients in the near future unless a special national effort were mounted. The proponents of this plan were no doubt correct in their appraisal. And it must be admitted that the basic scientists were not prominent among those who were aware of the dilemma nor among those who spearheaded presentations before the Congress. In fact, many are agreed that the timing was astute; the Cancer Program was conceived and its backers strongly influenced by the insights into biologic regulation and control produced between 1945 and 1970 by molecular biologists and geneticists the world over. Who would have disagreed that the time was ripe for applying that fundamental knowledge to a problem defined as one of regulation or control gone haywire, cancer?
Unfortunately, the specific events leading to malignant behavior on the part of a cell are not yet in any fundamental way understood. What we do know is that radiation, chemicals and viruses with varying degrees of complicity can cause cancer in experimental animals. It is probable that the final trigger is the same though that is by no means certain. Many naturally occurring cancers in man come to the final malignant state only after 15 to 20 years of recognizable premalignant state. Everywhere there are thresholds but no threshold has yet been crossed and there is no indication at present what is likely to prove crucial. Therefore, the Program must be basic in its conception of what objectives are to be applied and where none are to be assigned.

The Cancer Program has, in my opinion, demonstrated from its inception a commitment to supporting the research proposals of investigators of the highest quality without reference to relevance by a program-limited definition of relevance. With the encouragement of the Cancer Panel headed by Mr. Schmidt and the Advisory Board chaired by Dr. Rhoads, greater emphasis has been directed to investigator-initiated research, as witnessed by an increasing proportion of allotted funds being spent and to be spent in projected budgets for fiscal '78, '79, and '80 on investigator-initiated proposals. Perhaps equally as significant, the definition and management of basic research accomplished by contract agreement have been liberalized to allow freedom of pursuit by the investigator. Of equal importance, measures have been initiated in all Divisions of NCI to implement stricter peer review in all contract agreements for basic research. No one involved in policy decisions in the Cancer Program would deny that the problem of the support of basic research in the total Health Program remains unresolved. In my opinion, solutions involve increased fund allotments in the total Health Program for untargeted research. The current state of our ignorance of fundamental human biological processes should make evident that this reality cannot be denied.

The Cancer Program has proposed and increasingly supported the most basic of research program projects and research grants in immunology, virology, cell biology, bacterial metabolism, DNA synthesis, bacteriophage assembly, protein structure, carbohydrate chemistry and biochemistry. It has sought to enlist the most perceptive and creative biological, biophysical, and biochemical minds in areas of fundamental cancer biology. It is my hope to convince our most gifted and productive scientists, of all levels of experience, to devote some fraction of their time to the intriguing and vexing problems of the induction of malignancy, its early detection, its prevention and therapy. The program from the start envisaged a fundamental role for basic science going even so far as to create basic science centers as specialized centers and making mandatory a basic science component of every Comprehensive Center. The basic sciences have been and are still being asked to play a focal role in the Program and in advising all segments of the Program at the level of the science they could and should undertake. It is perhaps the diversity of the basic science involvement, with the lack of an identifiable basic science program segment, that has misled the basic science community into believing that its role is limited and secondary.

Because the Cancer Program's commitment to basic research is long standing and explicit and has developed as a model for future initiatives, new and imaginative steps are in order. It is essential that every encouragement be given to worthy new ideas, no matter how unconventional they may be. The criteria of scientific competence and originality should warrant a significant thrust toward the support of exciting proposals with a high risk factor. To accomplish this, I would propose a specific program to fund "high excitement ideas" of broadly defined merit. These would have task force
status and be screened after primary study section review by a Scientific Review Committee of NCI with funding authority.

There is a second critical need as I see it in the basic science area. It is for a modest number of 5- to 10-year grants to talented young investigators to allow them to attack problems of major scientific and program value that will not necessarily yield the required number of research papers per year at the outset. Too much pressure is put on the young to choose research areas of high data yield. The progress of work on these grants—of a sum sufficient to permit serious research—would be followed by a special committee, with a view to assisting wherever possible the investigator in the resolution of difficult areas of his project. If basic science is to maintain its importance as the frontier of unexplored domains, breakpoint funds for the calculated adventure must be assured. An understanding of the biology of diseases long in the making in an ecologic sense, will require a burst of new and radical ideas that we cannot hope to generate without inviting our most gifted individuals to the freest inquiry.

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