a repeating unit of two each of F2A1, F3, F2A2, and F2B and about 200 base pairs of DNA.

2) A chromatin fiber consists of many such units forming a flexibly jointed chain.

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units where nuclease action is rapid, and sites within the repeating units where nu-clease action is slow. Brief digestion would be expected to convert most of the chro-matin to pieces of about 200 base pairs of DNA with associated protein (the result quoted in the text). Further digestion would result be expected to involve breakdown of some of the 200 base pair pieces and binding of the histones that are released to the remain-ing pieces. The digestion should continue until the binding of extra histone completely pro-tects the pieces that remain. This limit should be reached when about half of the pieces remain (the result of Clark and Felsenfeld) since roughly twice the amount of histone naturally occurring in chromatin is required to neutralize all the negative charge on the DNA (on the basis of the amino acid com-positions of the histones and relative amounts in chromatin of histones and DNA). 9. E. W. Johns, *Biochem. J.* 104, 78 (1967).

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- of types with respect to base sequence.
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- I thank Drs. A. Klug, F. H. C. Crick, and M. S. Bretscher for helpful discussions and Drs. F. H. C. Crick, A. Klug, and S. Brenner for criticism of the manuscript.

## **Budget and the National Cancer** Program

National Cancer Institute funding through grants and contracts for 1972 to 1974 is presented and discussed.

#### Frank J. Rauscher, Jr.

Since its creation in 1937, the National Cancer Institute (NCI) has been the primary agency through which the federal government has supported cancer research. The National Cancer Act of 1971 gave the NCI responsibility for conducting a much broader National Cancer Program with the goal of bringing cancer under control. The act specifically directs the director of

the institute to "plan and develop an expanded, intensified, and coordinated cancer research program encompassing the programs of the National Cancer Institute, related programs of the research institutes, and other Federal and non-Federal programs." This mandate includes support for cancer research in industry and in countries outside the United States.

The purpose of this article is to present accurate information on funding from the NCI for fiscal years 1972, 1973, and 1974, and, in particular, to compare dollars allocated through the grant and contract mechanisms for these years. All figures for 1972 and 1973 are actual obligations, whereas those for 1974 are estimates. Because of the lateness of the present fiscal year and the concomitant firmness of spending plans these estimated 1974 figures, with the possible exception of those for training grants, will vary only slightly.

The National Cancer Act was signed into law by the President in December 1971. In fiscal year 1971, prior to this enactment, the total budget available to the NCI was \$233 million. In 1972 this was increased by \$145 million to \$378 million. In 1973 the Congress authorized \$492 million but the NCI was permitted to spend no more than \$432 million in accordance with the Administration's overall spending plan. Recently, the President decided to spend

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Table 1. National Cancer Institute comparison of grants and contracts.

Item	1972 actual (10 <sup>3</sup> dollars	5)	1973 actual (10 <sup>3</sup> dolla	urs)	1974 operating level* (10 <sup>3</sup> dollars)		
·	ŀ	Research gr	ants				
Regular research	69,309		86,203		115,653		
Cancer centers	50,203		67,510		91,075		
Task forces	638		3,950		11,003		
Total research grants	120,150	(50%)	157,663	(54%)	217,731	(55%)	
Re	esearch and	research s	upport contr	acts			
Total research contracts	49,544	(20%)	69,296	(23%)	95,000	(24%)	
Total research support							
contracts	72,505	(30%)	66,865	(23%)	80,809	(21%)	
Total research and research							
support contracts	122,049	(50%)	136,161	(46%)	175,809	(45%)	
Total grants and contracts	242,199†	(100%)	293,824†	(100%)	393,540†	(100%)	

\* Including release of impounded funds and congressional increase. † These amounts do not encompass the total NCI budget. Excluded are fellowships and training grants, NCI intramural research, NCI management and NIH management fund, cancer control and construction.

up to the maximum amounts provided in the continuing resolution, which released approximately \$60 million to the NCI. In the present fiscal year (1974) the President proposed a budget of \$500 million for the NCI. The Labor/HEW appropriations bill passed by the House of Representatives included \$522 million for the NCI, and the Senate bill included \$580 million. The House and Senate agreed on \$551 million for the NCI in the final Labor/ HEW bill which was sent to the President. As the dollar amount in this bill was significantly over the President's request, the Congress allowed the President an option to reduce the total Labor/HEW bill by \$400 million, but further stated that if this option were exercised no individual program could be cut by more than 5 percent. It is now understood that the President will cut the total bill by \$400 million. This would provide for NCI a budget of \$527 million, plus impounded funds of \$58.9 million and other adjustments, for a total 1974 operating level of \$589.2 million. The impounded funds, as well as guidelines for their use, have now been received by NCI. The NCI operating level, therefore, has been increased from \$432 million in 1973 to \$589.2 million in 1974, an increase of \$157 million. The total budget, with the exception of up to \$25 million, must be obligated prior to 30 June 1974. Authority is included in the NCI appropriation to carry up to \$25 million forward to 1975. This can be used for construction projects and other grants and contracts where negotiations are not complete by the end of the fiscal year. The NCI's spending plan is based largely on the National Cancer Plan and has been endorsed by the President's Cancer Panel and by the National Cancer Advisory Board. All agree that these funds can be spent effectively and are necessary for taking full advantage of new research opportunities.

# Funds for Research Grants and Contracts

The data in Table 1 compare the two principal funding mechanisms by which support is provided to non-NCI investigators for research. Figures for support contracts are included for further comparison with grant and contract research dollars. It will be seen that funds for total research grants including cancer centers and off-campus task forces increased from 50 percent in 1972 to 55 percent of grant and contract funds in 1974. Research contracts increased from 20 percent in 1972 to 24 percent of grant and contract funds in 1974. During the same period, funds for support contracts increased, but as a percentage of total budget for research and research support grants and contracts, there was an actual decrease of 9 percent for support contracts.

Support contracts are those with academic and commercial organizations that devise and perform tests for environmental carcinogens; toxicologic and pharmacologic studies of drugs; and standardization and production of animals, cell lines, drugs, viruses, antiserums, other diagnostic reagents and procedures, and the like. A major proportion of these resources is provided to grantees at no cost to their individual grants. The figure of \$217.7 million for research grants in 1974 does not include all dollars funded through the grant mechanism. Additional grant funds are included with other cancer activities. These funds consist of approximately \$25.6 million for training, \$7 million for cancer control, and \$35.9 million for construction.

Table 2 presents this budgetary information in more detail, and reflects part of grants other than research to include planning grants and core grants. The third column shows how the funds would have been obligated at a budget level of \$500 million. Figures in the fourth column show how the funds will be utilized at the new budget of \$589.2 million. In item 1 of Table 2, a 1974 obligation of \$64.5 million is incurred by the NCI as a moral or "locked in" commitment to fund noncompeting regular research grants. The first year of award is usually followed by two additional years of support. The funding of competing regular research grants (new and competing renewals) depends on new dollars which between 1973 and 1974 were increased by approximately \$19.6 million. Item 3 shows that, in 1974, of all dollars for research, excluding intramural research, 67 percent will be funded through grants and 33 percent through contracts. Of the latter amount \$46 million of \$95 million allocated through research contracts will be awarded to universities. Item 4 shows the percentages of regular research grants (including cooperative clinical trials) and traditional project grants, approved by the National Cancer Advisory Board, that the NCI anticipates being able to pay in 1974. The percent payability of these competing grants is, of course, influenced by factors other than the amount of new money received each year, or moral commitments of noncompeting regular research grants. The change in percentage is also caused by the variation in the number of domestic and foreign applications approved and the increasing amount of money per application. The NCI now actively encourages dual assignments of cancerrelated applications from other institutes. These applications, which cannot be paid by the institute of prime assignment, retain their original priority scores and compete within the NCI along with proposals initially assigned to the institute for payability. During the past 3 years NCI has provided \$3.6 million to fund 53 projects of this type.

#### Uses of the Contract Mechanism

Funds for the contract mechanism have also increased, although at a rate less rapid than for grants during the period 1972 to 1974. It may be helpful to describe historical and current aspects of this mechanism, particularly as now used within the NCI. The contract mechanism has been used by the NCI to fund projects including those of "basic" research for the following reasons.

1) In 1962 a decision was made by the NIH director, Dr. James A. Shannon, to exclude commercial "for profit" organizations from competition for grants. Support for some of these organizations was continued through the contract mechanism after recompetition and reassessment of relevance, need, and priority as well as merit of the project. This action therefore established a major part of the funding base for contracts within the NCI.

2) The NCI has long believed that basic or fundamental research within a developmental or "planned program" can be supported by the contract mechanism under certain circumstances. Specifically, if the knowledge gap in moving from point A to point B is basic or fundamental in nature—and the problem is not being investigated with research supported by the grant mechanism—then a contract can be used to support efforts to fill in the information gap. This in no way precludes funding of original ideas from young (or old) investigators who choose not to conduct research within the framework of a "planned program."

3) Beginning in the 1950's the contract mechanism was used to stimulate research and development in fields such as chemotherapy and viral oncology. Although the institute and its consultants thought these fields merited more emphasis, they were not popular with many investigators for various reasons, and understandably could not survive study section review of innovative and meritorious science. This was especially true for the development, production, and distribution of drugs and research reagents.

4) In the late 1960's decisions were made that precluded the support of most foreign projects through the grant mechanism. The contract mechanism was therefore used to support research and development projects outside of the United States, which were of high priority in terms of merit but which also had mandatory prerequisites of uniqueness and a reasonable probability of accruing benefit to Americans, as well as to people of those nations in which the projects were conducted.

5) In a mechanistic and time sense, contracts were used to get things started more quickly. About 3 years ago the average contract could be awarded within 5 or 6 months of solicited or unsolicited submission. Now, the average time to process a new contract, from development of project plan to award date, is about 9 months because additional reviews, advertisement, and competitive negotiations are necessary.

6) The contract mechanism with ad hoc or standing peer committees capable of multidisciplinary program review of relevance, need, and priority was thought to be a better way to review, implement, and monitor end-resultoriented programs than was the grant mechanism with its predominant tradition of review for merit by disciplineoriented study sections of projects. I recognize that these and other assumptions are subjects of much concern to the scientific communities and are, therefore, being reevaluated.

7) Projects supported by the NCI through other federal agencies must be paid by interagency agreements and contracts.

8) Finally, together with the above, there are other reasonable and realistic influences that determine how funds can be spent, including instructions from the Congress and the Office of Management and Budget. Nonetheless, the principal decisions of how funds are spent remain with the NCI. These decisions in turn are influenced greatly by concerns and advice from the scientific communities of this country. I believe that data on funding trends presented in this article show responsiveness to these concerns and advice. In this regard, it is important to emphasize that a deflection of 1 percent within a

Table 2. National Cancer Institute comparisor	n of	research	grants	and	research	contracts.	

Item	1972 actual (10 <sup>3</sup> dollars)	1973 actual (10 <sup>3</sup> dollars)	1974 President's budget (10 <sup>3</sup> dollars)	1974 operating level <sup>*</sup> (10 <sup>°</sup> dollars)	
Noncompeting	36,417	Grants			
Competing	32,892	54,688 31,515	64,532 33,568	64,532 51,121	
Total regular research grants	69,309	86,203	98,100	115,653	
Cancer centers	50,203	67,510	84,065	91.075	
Task forces	638	3,950	10,000	11,003	
Total grants	120,150	157,663	192,165	217,731	
Research	113,893 (95%)	139,373 (88%)	168,453 (88%)	101 721 (99.0/)	
Nonresearch	6,257 (5%)	18,290 (12%)	23,712 (12%)	191,731 (88%) 26,000 (12%)	
_		Contracts			
Research	49,544 (41%)	69,296 (51%)	86,968 (54%)	95,000 (54%)	
Nonresearch	72,505 (59%)	66,865 (49%)	73,942 (46%)	80,809 (46%)	
Total	122,049	136,161	160,910	175,809	
		Summary			
Research grants	113,893 (70%)	139,373 (67%)	168,453 (66%)	191,731 (67%)	
(universities)	(66,782)	(92,963)	(113,000)	(128,000)	
Research contracts	49,544 (30%)	69,296 (33%)	86,968 (34%)	95,000 (33%)	
(universities)	(20,265)	(33,134)	(42,000)	(46,000)	
Total	163,437 (100%)	208.669 (100%)	255,421 (100%)	286,731 (100%)	
<b>D</b>	Percent of grants funded from	n National Cancer Advisory	Board approvals		
Research grants funded	66%	55%	33%	54%	
Traditional grants only	62%	52%	26%	50%	

\* Including impounded funds and congressional increase.

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budget of \$589.2 million represents a change of nearly \$6 million. For example, a variation of one percentage point of the total budget could mean that we would or would not fund 106 regular project grants at an average of \$56,000 per grant. It is also important to understand that the federal budgetary process is such that most major changes cannot be made in less than 12 months. I hope that the NCI, along with the scientific community, will first determine the projects and programs that need to be done and then determine the best funding mechanism to get the jobs done.

#### Funding by Mechanism

The data in Table 3 summarize actual and estimated obligations for the total budget for three fiscal years by mechanism and organizational programs of funding. Several points of explanation and clarification follow. The figure of \$217.7 million for "Total Research Grants" does not include approximately \$25.6 million for training, \$7 million for cancer control, and \$35.9 million for construction obligated through the grant mechanism. Also it does not include approximately \$7.1 million from NCI for the grant mechanism part of the NCI management and NIH management fund for consultants, review, approval, and direct salaries, and the like. All told, NCI funding of grant supported activities represents nearly 50 percent of the total operating funds for 1974.

The \$25.6 million for training in 1974 includes continuation of moral obligations for the past traditional program plus about \$5.5 million of new authority for the fellowship program as recently announced by the Secretary of Health, Education, and Welfare.

### **Cancer Control Program**

Cancer control is a program for which NCI had no mandate or au-

Table 3. National Cancer Institute funding by mechanism.

Item	1972 actual (10 <sup>3</sup> dollars)	1973 actual (10 <sup>3</sup> dollars)	1974 operating level* (10 <sup>3</sup> dollars)
Total research grants	120,150	157,663	217,731
Total research and research support contracts	122,049	136,161	175,809
Fellowships and training grants			
(including research career programs)	20,421	15,706	25,598
Cancer control		5,222	34,055
Construction	51,003	38,804	45,033
NCI intramural research	25,696	33,032	39,000
NCI management and NIH management			
fund	33,246	38,819	51,929
Total NCI	372,565	425,407	589,155

\* Including impounded funds and congressional increase.

Table 4. National Cancer Institute program structure.

Item	1972 actual (10 <sup>3</sup> dollars)	1973 actual (10 <sup>3</sup> dollars)	1974 operating level (10 <sup>3</sup> dollars)	
Research thrust*				
Cause and prevention research	99,682	115,277	145,778	
Detection and diagnosis research	19,200	26,973	40,264	
Treatment research	119,338	144,741	193,862	
Cancer biology† Subtotal	52,705 290,925	63,781 350,772	84,798 464,702	
Resource development				
Cancer centers support <sup>‡</sup>	11,788	15,840	20,334	
Research manpower development	18,582	14,132	24,180	
Construction Subtotal	51,270 81,640	39,151 69,123	45,340 89,854	
Cancer control Total NCI	372,565	5,512 425,407	34,599 589,155	

\* Includes research in cancer centers. † Includes research that cannot reasonably be classified in any one of the other research thrusts, but where output has potential application to all thrusts. ‡ Planning and core support of centers. thority immediately prior to the Cancer Act of 1971. I believe it is the most important new component of the National Cancer Program. Significantly, Congress and the Office of Management and Budget provided new funding for cancer control, which was not at the expense of funds for basic, fundamental research. This is the program that attempts to deliver research results and opportunities to people. I have told the Congress and the Executive that NCI and the cancer community place priority on doing all that can be done now with existing information to benefit cancer patients and to prevent cancer in the population at large. This program must receive the highest priority while we strive for continuing funding of basic research that will fill the major information gaps needed to prevent and treat cancers in man more effectively

Funds for "NCI Intramural Research" support research and development activities primarily at Bethesda and at the Frederick Cancer Research Center (Fort Detrick). The major component of this support is for about 1000 people within NCI at Bethesda, and includes salaries and operational costs. In addition, another 750 persons at NCI are engaged in management and coordination of the total National Cancer Program, which is funded mainly through grants and contracts.

Funds for NCI management and NIH management fund are for grants and contracts management, consultant honoraria, travel, planning, communications, budgeting, personnel, and central management and services of NIH.

Table 4 presents data on the total budget for three fiscal years—by research thrust, resource development, and cancer control. The research thrust designations are identical with those of the National Cancer Plan and the relation of programs to funding levels are virtually identical to those recommended by the 250 non-NCI consultants who helped develop this edition of the plan. These figures are not identical with those in Table 3 because Table 4 includes a distribution of NCI management and NIH management funds to each program.

#### Summary—Fiscal Year 1974

Table 5 presents summary data on how NCI funds will be obligated in fiscal year 1974 by mechanism of support (intramural NCI, grants, contracts,

Table 5. Summary of fiscal year 1974 budget. Dollar values are in millions.

Fiscal year 1974	Intramural NCI			Extramural funds						Total NCI		
			Grants		Contracts		Interagency agreements		Dol-	Per- cent	Per- cent	
	Dol- lars	Per- cent	Dol- lars	Per- cent	Dol- lars	Per- cent	Dol- lars	Per- cent	lars	of line item	of total funds	
Extramural funds	0	0	286.2	57.4	200.3	40.2	11.8	2.4	498.3	100.0	84.6	
Intramural NCI NCI/NIH management	39.0	100.0	0	0	0	0	0	0	39.0	100.0	6.6	
costs	33.1	63.8	7.1	13.7	11.5	22.1	0.2	0.4	51.9	100.0	8.8	
Total funds	72.1	12.2	293.3	49.8	211.8	36.0	12.0	2.0	589.2	100.0	100.0	

and interagency agreements). Extramural funds are those spent for "off campus" activities. Intramural NCI funds are those spent for research activities performed on the NIH campus. Management costs for NCI/NIH are the proportionate costs of management, coordination activities, and support for all mechanisms (including \$17 million for the NIH management fund). Of the total NCI/NIH management costs of \$51.9 million, \$33.1 million (or 5.6 percent of the total NCI budget) supports intramural research. The total intramural research of \$39 million, consisting of salaries and operational costs of research performed at the NCI, represents 6.6 percent of the total NCI budget.

Approximately 57.4 percent (\$286.2 million) of all funds to support "off campus" activities will be obligated through the grant mechanism. These funds support activities that include traditional project grants and cooperative clinical trials (\$115.6 million), cancer centers (\$91.1 million including \$20.3 million for planning and core support of centers), task force grants (\$11 million), training activities (\$25.6 million), construction (\$35.9 million), and cancer control and demonstration projects (\$7 million). Approximately 40.2 percent (\$200.3 million) of "off campus" funds will be obligated through the contract mechanism to nonfederal organizations. In addition to research in academic and nonacademic institutions (\$84.7 million), these activities include research resource procurement (\$79.4 million), construction (\$9.1 million), and cancer control and demonstration projects (27.1 million). The contract total includes \$12.5 million to support the Frederick Cancer Research Center (Fort Detrick). About 2.4 percent (\$11.8 million) will be obligated for interagency agreements including research and support activities at the Atomic Energy Commission, the Veterans' Administration, the National Clearinghouse on Smoking and Health, the Department of Defense, and the National Bureau of Standards.

#### Conclusion

The budget picture for the NCI is presented for your information and evaluation-evaluation in the sense that I need and would appreciate your comments. A major issue of course is balance, in terms of clinic versus laboratory; short-term versus long-term; academic versus commercial; targeted versus nontargeted; grants versus contracts versus intramural; national versus international, and the like. It must be recognized that within a program of this emotion, visibility, and importance scientific findings and other considerations will dictate changes on at least a monthly basis. Things other than science contribute to this balance. On any given day we live within the impact of at least three budget years (what we received and did last year, what we will receive and do this year, and what this will allow us to receive and do next

year). The federal budgetary process as well as the priority-setting processes of science are such that new directions cannot be taken as quickly as would be optimal.

Priorities must be set in cancer at least in their broad sense; for in addition to other areas of biomedical research, there are other compelling demands for the limited federal dollar. There will never be enough resources to do all that can be done or needs to be done in cancer research. That probably is as it should be. In this regard it is heartening that operating funds for the institutes at NIH other than NCI will increase by \$264 million in 1974. It is as true that information from research in other disciplines and categorical diseases will provide leads to cancer, as well as the reverse. And certainly, virtually no one wants to see resources for cancer increased at the expense of other important tasks and opportunities.

This article is not an attempt to justify or to defend the spending plan of the National Cancer Program. It is to let you know what's going on and to seek further advice on how to do it better. Articles on other aspects of the program will be published in journals including Science, Cancer Research, and the Journal of the National Cancer Institute.

#### **References and Notes**

 I thank Earle Browning, Financial Management Officer, and Calvin Baldwin, Executive Officer of the National Cancer Institute, for tabulation and verification of much of the fiscal information presented in this article.