

422 * * * PRESENTATION BY DR. ROBERT POLLACK * * *

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425 DR. POLLACK: Thank you, Dr. Amos, Dr.
426 Hammer, Dr. DeVita. I would like to speak on matters
427 of NCI policy toward basic research.

428 It is my belief that the National Cancer
429 Institute should structure its policies for research,
430 for technology, and for political strategy so as to
431 understand the underlying causes of the disease as
432 well as to treat its victims.

433 I believe this is the only known path to
434 eventual control of any life-threatening disease. I
435 will outline my suggestions for actions in the next
436 decade in each of these three strategic domains.

437 First, research. The mechanism of growth
438 control of cells of the body is not yet well
439 understood. This remains the second half of the great
440 war against cancer in which the NCI has enlisted the
441 commitment of so many physicians and scientists.

442 The first half of the war, the discovery of
443 the genetic elements necessary and sufficient to
444 derange a cell and the demonstration that some of
445 these are encapsidated in viruses is well underway
446 and deserves continued support; however, the second

447 part of the war is where the victory will be most
448 quickly felt on the homefront when it comes.

449 Novel pharmacologic intervention will
450 require knowledge of the cellular molecules with
451 which these cancer genes and their products interact.

452 So, specifically, I recommend that the
453 following three points be taken into consideration
454 for policy in the next decade on basic research.

455 First, regulatory elements, regulatory
456 genes are well understood in prokaryotes. The great
457 prerequisite advance in genetics that lead to this
458 detailed knowledge of their structure and function
459 was the Pardee-^{Jacob-Monod}~~Jacques Monod~~ study of a single mutant
460 regulatory gene's activity in a set of different
461 genetic backgrounds by mating of bacteria.

462 The discovery of the mechanism of the first
463 regulatory gene, the I gene of beta galactosides
464 depended on this technology. It is now possible to do
465 the same sort of study in mammalian cells.

466 The technology of DNA transfection is a
467 rapidly growing one and deficiencies of DNA transfer
468 approach unity. This technology should provide
469 selective systems for studying and for isolating
470 genetic elements capable of regulating normal
471 mammalian cell growth.

472 Second, some cellular molecules must
473 interact in solution with the molecules encoded by
474 the set of onc genes defined by transfection.

475 The study of these cellular molecules and
476 the genes that encode and regulate their expression
477 is the best step outward from what is known to what
478 must be learned about cancer at the cellular level.

479 Third, DNA moves. This fact, first
480 described at the macro level of resolution by Barbara
481 McClintock, has now been confirmed and extended to
482 the resolution of single base pairs.

483 Indeed, we now know that as much as ten
484 percent of the DNA in the cells of the fruit fly,
485 Drosophila melanogaster, can move from place to place
486 in the genome.

487 The role of such movement in the rapidity
488 of evolutionary change is one of the most exciting
489 new problems in biology, joining molecular,
490 macroscopic and behavioral biologists for the first
491 time in a common body of answerable questions, but,
492 for our purposes, the elucidation of DNA movement in
493 somatic cells is central insofar as it offers one
494 easy resolution of the two problems I have mentioned
495 above.

496 That is, the position of a given stretch of

497 DNA in the genome can, in some cases, be responsible
498 for its capacity to express its information so that
499 DNA movement itself has potential to be a regulatory
500 element in normal and cancerous cell growth.

501 Second, I would like to discuss for a
502 moment technological development in cancer research.
503 The technology of biology has lead to the capacity to
504 manipulate larger and larger macromolecular arrays
505 and to preserve the nativity of weaker and weaker
506 bonds.

507 Two technological restrictions currently
508 block further experimentation. The current analytical
509 threshold for solubility and nativity is about ten
510 million molecular weight for protein arrays.

511 Second, the demands of solubility destroy
512 arrays that anchor in or through cell membranes.
513 These two limitations destroy information, negative
514 entropy, that is stored as the position of protein
515 ensembles in the cell membrane and at least two major
516 cell-cell events are therefore not now available to
517 molecular analysis. These are cell-cell contact and
518 hormone receptor function.

519 So, work to expand our capacity to handle
520 large macromolecular arrays and work on
521 hydrophobic-hydrophilic reconstruction systems

522 deserve new and vigorous support in the next decade
523 in my opinion.

524 Finally, I would like to discuss for a
525 moment the politics of cancer research as I
526 understand it. Prognostication is a very delicate
527 art.

528 When linked to the awarding of funds, it
529 can be a profound and effective art. The NCI should
530 be proud of the many scientists in-house and
531 extramural who have put in their time to read and
532 review grant applications, as well as the ones who
533 have, in fact, carried out the research.

534 National and local politics ought to have
535 no place in this process. Recently, I have begun to
536 hear fairly reproducible horror stories of peer
537 review bent beyond recognition by the severe cutting
538 of funds available for competitive grants.

539 At the same time, I have received calls
540 from many of my favorite scientists, both inside and
541 out the NCI, who describe in graphic detail a decline
542 in morale as people leave academic jobs for
543 industrial ones, government ones for academic ones
544 under conditions where replacement is difficult or
545 forbidden.

546 Peer review works best when it fosters

547 creativity in science. It degrades into farce, in my
548 opinion, when money is so abruptly cut back that
549 priority scores fall below grade at the slightest
550 hesitation from even one panel member.

551 This is now commonplace on some study
552 sections. Of course, without any doubt, the worst
553 fate that could come to the NCI would be that of
554 other government agencies in recent times to have the
555 executive branch of the government scan potential
556 peer reviewers for their political credentials while
557 cutting funds available for support.

558 So, I believe the most immediate political
559 obligation you have is to assure the continued
560 availability of money for the initiation and
561 continuation of grants for basic research.

562 Thank you. That is my prepared remarks. I
563 will be glad to answer questions as well.

564 (Applause.)

565 DR. AMOS: Now, it is with a certain
566 hesitation that I open these remarks for discussion.
567 I wonder if the chairman cannot assume an arbitrary
568 role here to say that the politics was not a part of
569 this evening's discussion.

570 Are there comments or questions on the
571 other two-thirds of Dr. Pollack's presentation from

572 the Panel members or from the members of the so far
573 non-participating audience? Dr. Gallo?

574 DR. GALLO: May I just say something to put
575 a little perspective on one point that Bob Pollack
576 made. I don't think anybody could disagree with the
577 major comments of supporting basic cancer research. I
578 think that is obvious and no one could take a
579 position against it.

580 But I think the argument that a lot of
581 people who are your favorite scientists have left
582 academia to go into industry whether from the
583 government or from universities, in my view, is
584 probably not the target. I think they didn't go in
585 because they couldn't get funded. I think they went
586 in because of other gains.

587 DR. POLLACK: Harold, what are the
588 groundrules? Shall I let that go by or shall I answer
589 it? It is up to you.

590 DR. AMOS: I think, Bob, since you have
591 been attacked, we should give you at least --

592 DR. POLLACK: In the briefest terms, it
593 doesn't really do well to say we are all for basic
594 research. As I understand basic research and as I was
595 taught to be a scientist, it requires absolute
596 openness and the combination of the decreasing

597 availability of competitive funds for basic research
598 in extramural program, when measured in inflated
599 dollars, and the availability of alternate ways to do
600 research which are not quite as open or as public has
601 lead people to make the final decision to go into
602 other forms of research.

603 I don't believe them to be in the nation's
604 best interests, insofar as they have no replicative
605 function. No one in a company trains a graduate
606 student to be a scientist and, in that sense, I think
607 the country is eating its seed corn and that is a
608 mistake.

609 DR. GALLO: I truly don't disagree with you
610 one iota. I just meant to emphasize a point that some
611 of the visible laboratories or visible individuals
612 who leave academia to go into industry are sometimes
613 motivated not by lack of funding or lack of a large
614 lab intramural NIH or outside.

615 There is a new development and industry is
616 paying a lot of money and I think that is a major
617 factor.

618 DR. AMOS: I think that some of the points
619 that Dr. Pollack has made in his presentation will
620 probably be revisited by one or two other speakers.
621 Therefore, I would like to move on to Dr. Margaret

622 Kripke who will -- before Dr. Kripke begins, there
623 are one or two seats up front. Can you look around to
624 see if there are seats. There are quite a few people
625 standing in back. There are two or three seats up in
626 front, if you would like to come forward.

627 Can we take just a minute to seat the few
628 people, if they would like to be seated. Would anyone
629 hold up their hand beside an empty seat. There are
630 three seats right up here. If no one wants to move,
631 we will proceed then with Dr. Kripke.