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Biochemistry at Stanford: A Case Study in the Formation of an Entrepreneurial Culture
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The Terman Model at the Stanford Medical School

A unique entrepreneurial culture has evolved at Stanford. While he was not the only person responsible for its development, Fred Terman was a key figure in creating the institutional mechanisms that supported Stanford's entrepreneurial culture. A general hypothesis I have been exploring is that in the early 1950s Fred Terman created a model for financing the growth of technology-oriented departments by focusing on building Ph.D. research programs in engineering science using a mix of federal grants and contracts to finance the hiring of new high-quality faculty. The ability of faculty to receive federal funding to support their work was a key measure of success from Terman's perspective. In addition Terman encouraged the development of consulting relations with industrial firms needing scientific research for the new directions in the competitive electronics industry. He also built a variety of other bridges between the new programs he was launching and industry, such as the honors cooperative program for improving the skills and knowledge of workers in technology firms in the area, and in the late 1950s the first industrial affiliates programs in which select industrial partners could obtain closer ties to the innovative new research in the Electrical Engineering Department. His objective was to create cooperative relationships that would provide avenues for hiring Stanford Ph.D.s as well as ways of getting Stanford innovations developed into mainstream technology. An additional interest was to draw upon advanced research in industry to stimulate work at Stanford. No less important were the financial opportunities such relations afforded through gifts and other forms of sponsored research. While strategies for faculty and program development Terman pioneered were intended for growing engineering programs, they could be and were adapted to building other parts of the university. Perhaps the most notable area was the development of the Medical School.

In the immediate post-WWII years the financial condition of the University bordered on a crisis situation. The financial situation facing the Medical School in those years was even worse, indeed, positively desperate. The physical plant of the Medical School, located in San Francisco, was in need of renovation and expansion. The School ran a deficit of approximately $400,000 per year, which had to be financed out of University funds. In 1950 President Sterling and the Board of Trustees appointed a Committee on Future Plans of the Medical School, headed by Professor Henry Kaplan, the Director of Radiology. Between 1951-1952 the Committee interviewed and corresponded with faculty from the Medical School in addition to undertaking interviews with 20 medical leaders at other institutions. The work of the committee was distilled into a voluminous report. The most urgent needs the Committee identified were for major replacement and refurbishing of the Medical School physical plant and for annual financial support. They estimated that rebuilding the physical plant would cost ten to fifteen million dollars. To prevent the bleeding of general funds of the University for the annual Medical School operations would require new endowment of an additional fifteen million dollars. In plant funds and endowment, the total need was estimated at $30,000,000. The magnitude of the needed sum evoked the question: Would it be wiser to modernize and add to the existing Medical School facilities in San Francisco or to build anew on an alternative site? After more than a year of study the conclusion reached was embodied in the Board of Trustees' decision of July 15, 1953 to move the Medical School to the University campus.

As President Sterling commented in his foreword to the collection of speeches at the dedication ceremony of the new Medical Center in 1959 the basic reasoning given for this decision was that the future progress of the medical sciences would be inextricably linked with progress in the basic physical and biological sciences, and increasingly with the social sciences, such as psychology and sociology; therefore, Sterling concluded, “This key relationship of medical education and science to other scientific fields can best be strengthened and advanced by bringing the Medical School into the closest possible physical and intellectual relationship to the whole university.”[1]

The move of the Medical School to the main campus was accompanied by a complete revision of the medical curriculum in which more basic science was introduced. The Stanford Program, as it was called, lengthened the period of medical education from four to five years and included substantial work in basic science as well as a significant exposure to laboratory training. In addition, the medical faculty became a so-called “full-time” faculty, shifting its base of support from clinical fees to funds provided by the University. Thus in moving to the main campus the Medical School faculty became essentially university faculty just like faculty in the Engineering School or in Humanities and Sciences, and along with this the emphasis of the new Medical Center was to shift in the direction of scientific medical research.

Sterling used the attention generated by the new science-based curriculum and the move to the Stanford campus to launch a major public relations campaign and fund-raising drive for the new Medical Center. In addition to a public fund-raising drive, a key part of this effort was Sterling’s lobbying effort with Congress to get the Hill-Burton Act of 1947, which supported the expansion of American medical programs, to include the financing of buildings and other capital expenses. This new Hill-Burton Act was passed in 1956. Stanford was a major beneficiary of the new federal funding. Along with a large influx of federal funds to support the new initiative, Sterling was also successful in obtaining major Ford Foundation funding to support the transition of the faculty to full-time and the hiring of additional faculty for the new expanded Medical Center. Indeed, in a step signaling that the new Medical Center was heading in new directions, Sterling demanded that all heads of departments resign with the move to the main campus.[2] Two new departments were to be created in the move, the Department of Biochemistry and the Department of Genetics.

In the midst of this major transition of the Medical School, Fred Terman became Provost in 1955. Terman’s style of encouraging entrepreneurial activity meshed well with the initiatives already begun by Sterling, Alway, and Kaplan in reshaping the Medical School. Terman wasted no time in encouraging Medical School faculty to adopt his strategies for building programs with government funds. His advice to William Walter Greulich was typical. Greulich, concerned with the low level of Stanford salaries, wanted to increase salaries of faculty by adding compensation to the faculty member from grant and contract funds for supporting his or her normal teaching and research activity. Greulich assured Terman that he had clarified the acceptability of this notion with NIH grants officers and there seemed to be no objection. Terman, however, saw this as inappropriate: such a shift could create a bad impression with other federal granting agencies who wanted contract funds to support exclusively the work under contract. Terman wanted a consistent policy in dealing with all federal agencies. Beyond that Terman felt it undercut the primacy of research. As he told Greulich, permitting staff members to receive additional compensation during the academic year for work done on research contracts would "encourage (and reward) faculty to seek research contracts for the sole purpose of obtaining a substantial bonus on their salary rather than because of a desire to do the particular research involved":

> In searching for a means to improve the finances for the Medical School so that the salary scale can be improved, I would suggest that you keep alert to the possibility of charging government contracts, research grants, and funds with at least some of the regular salary of the faculty members who contribute research services. When the government is paying for research it desires to have done in the national interest, it would seem not unreasonable for the government to pay all of the direct expenses, rather than expect free services from senior research people. The government can afford to pay for what it is receiving, and I do not believe that it needs support from the Stanford endowment and from the tuition fees of our students to get its work done. [3]

More importantly Terman thought an opportunity was being missed for expanding Medical School research faculty through government funds in just the same way he had built the Department of Electrical Engineering and other parts of the Engineering School:

> When in my office, you stated that teaching duties in the Medical School normally took about half the time of a faculty member, and that the other half of his time was available for research. If one could have 50% of this research time charged against research contracts and grants, rather than carried by the regular budget, it would free enough salary money in the Medical School budget to raise all salaries by 33%. If all of the research time could be charged to research contracts (which is probably an impossibility although nearly true in Engineering) it would free enough salary money to double salaries.
>
> Since the idea of having the government or foundation pay for the services that it receives credit for would seem entirely legitimate and is certainly not immoral, I suggest this method of aiding the finances of the Medical School be taken advantage of whenever possible. [4]

As Provost, Terman encouraged faculty to be aggressive in their pursuit of federal funding and scrupulous in accounting for the research-related costs of their work.[5] He held frequent meetings with deans and other University administrators explaining the elements of his “recipe for distinction” and his strategies for using salary-splitting and gift funds from corporate sponsors to expand the research faculty. The initial efforts were not easy. Terman encountered resistance by some faculty who thought federal funding should be avoided in order to remain independent, and his policies were opposed by critics concerned that the primary occupants of the Industrial Park were companies funded by military contracts. He sought to disarm such critics by seeking to attract companies in biomedical sciences into the research park. But Terman’s most important strategy for building an environment that supported entrepreneurial activity was in hiring faculty with similar incentives as his own to build a powerful infrastructure to support their research programs. Perhaps the most striking success of Terman's efforts at building an entrepreneurial culture during his Provost years was in building the new science departments of the Medical School.

Acting on the advice of Henry Kaplan, Terman's first move in expanding the new research orientation of the Medical School was in hiring Arthur Kornberg.[6] Negotiations began with Kornberg in 1957. Kornberg was the Director of the Department of Microbiology at Washington University, St. Louis, where he had been since 1953 following a move from the NIH. At Washington University Kornberg had already assembled a stellar cast of young biochemists and molecular biologists, including Paul Berg, David Hogness, Robert Lehman, Melvin Cohn, and Dale Kaiser. Kornberg and his colleagues also had an extremely impressive track record of Public Health Service grants for supporting their research. Kornberg negotiated with Terman and Alway to move the entire department to Stanford beginning in 1959. This was a major coup for the new Medical School, for in the months following his initial acceptance of the Stanford offer, Kornberg received the Nobel Prize for his work on the replication of DNA. Kornberg not only moved most of his staff to Stanford but was also successful in being awarded more than $500,000 in Public Health Service grants to equip his new laboratories at Stanford.

As part of his negotiations for building biochemistry, Terman encouraged Kornberg to propose potential faculty for other departments that would complement the strengths in biochemistry, and he invited Kornberg to serve on the search committee for the chairmanship of the Chemistry Department. Kornberg immediately proposed bringing Joshua Lederberg to Stanford. Lederberg, who had been awarded the Nobel Prize in 1958, accepted the offer and left Wisconsin to form the new Genetics Department at the Stanford Medical Center in 1959. At Stanford Lederberg wasted no time in building a program in molecular medicine with matching grants of $1Mil each from the Rockefeller and the Kennedy Foundations to support construction of facilities for the Kennedy Center for Molecular Medicine in 1962. Lederberg also received a $500,000 grant from NASA in support of work on planetary biology that year, a project that eventuated in the ACME computing facility and then the SUMEX computing facility.

From their inception the Departments of Biochemistry and Genetics have been hotbeds of innovation in the field of molecular genetics and molecular medicine, and they have been major sources of the biotech revolution in the Bay Area from the 1980s to the present. This movement has been so important that is worth considering it a new phenomenon parallel to the Silicon Valley phenomenon that we might call "Biotech Valley." Aggressive pursuit of federal funding combined with careful cultivation of relationships to industry have been key elements of the entrepreneurial strategy of both departments. Federal grant awards to the Biochemistry Department were approximately $582,000 in 1966. In 1975 they topped $1mil, and reached $2.24mil in 1982, $3mil in 1987, and $4mil in 1993. The Genetics Department enjoyed even greater success in this same time period: Federal grants to Genetics totaled approximately $740,000 in 1966, surpassing the $1mil mark to $1.75mil in 1974, $2mil in 1978, $3mil in 1990 and due to the influx of funding from the Human Genome Initiative exceeded $6mil in 1993 (budget sources in Stanford Annual Reports are unavailable past 1993). In 1974 and 1975 these two departments combined accounted for 20% of the federal grant dollars received by the Medical School, and on average during the period 1966-1993 these two departments have accounted annually for 6.6% (Biochemistry) and 7.6% (Genetics) of the federal grant dollars awarded to the Medical School.

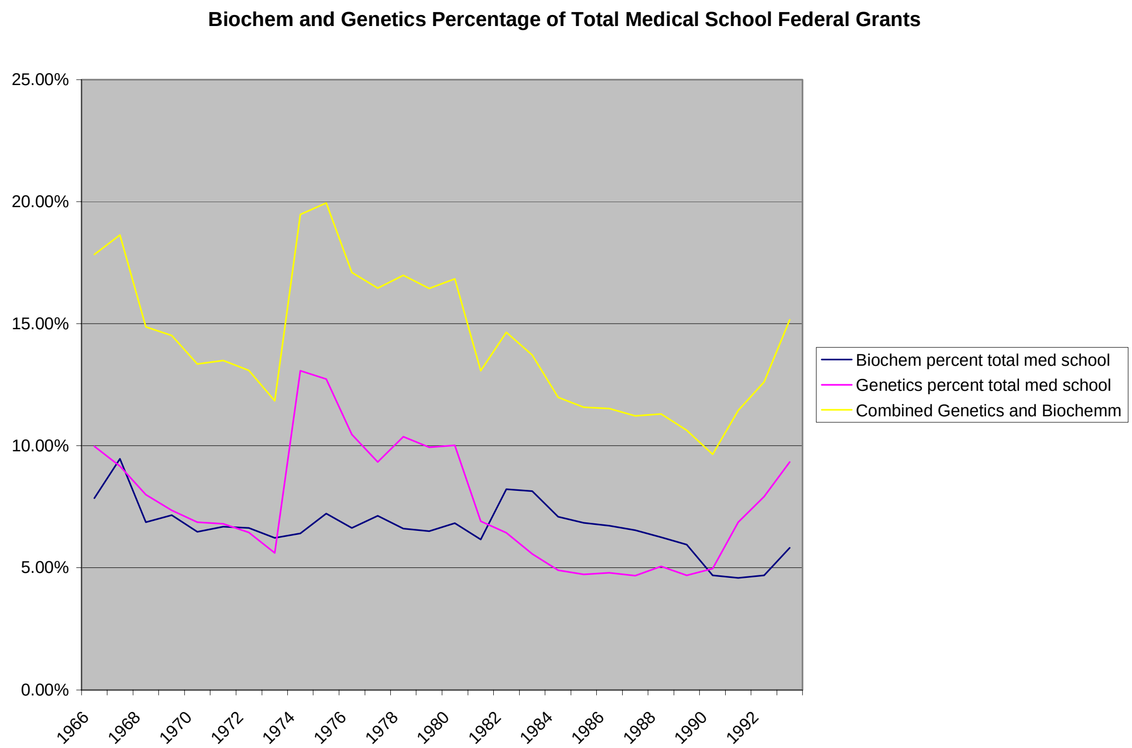

Figure 1: Success in obtaining federal funding.
The chart illustrates the annual percentage contributions of federal grants awarded to Biochemistry and Genetics faculty in the overall total of federal grants to the Stanford Medical School.
Source: Stanford Annual Reports

Success in obtaining federal funding provides only one index of the enormous success of these two groups of Stanford academic entrepreneurs. The Department of Biochemistry, of course, is home to two Nobelists, Arthur Kornberg and Paul Berg. But other faculty members have been recipients of major prestigious awards as well, which is why the department has been rated the top biochemistry department in the US numerous times and is always in the top 5. The Department of Genetics is similarly distinguished with Lederberg as founder, and an illustrious faculty including Len and Leonore Herzenberg, Luca Cavalli-Sforza, Stanley N. Cohen, David Botstein, Ron Davis, and several others.

I have only begun to document the commercial aspects of work in Biochemistry and Genetics, but the productivity of the Genetics faculty in patenting and commercializing aspects of their work is, of course, the stuff of legend. Among the many important developments: Herzenberg’s fluorescence activated cell sorter (FACS) technology and Cohen’s (and Herb Boyer from UCSF) patent on cloning genetically engineered molecules in foreign cells were extraordinary sources of revenue for their department and for the University. The Cohen-Boyer patent has been justly described as launching the biotechnology industry in the Bay Area with the founding of Genentech and a host of biological products. As the accompanying chart demonstrates, the Cohen-Boyer patent was first filed in 1974 but did not begin to generate notable revenue until 1982. Once it took off, however, from 1982-1990 that patent accounted for more than 50% of OTL patent royalties in some years and averaged around 38% of OTL revenues. Moreover, the Cohen-Boyer patent was not the only biotechnology related patent in the OTL stable at that time.

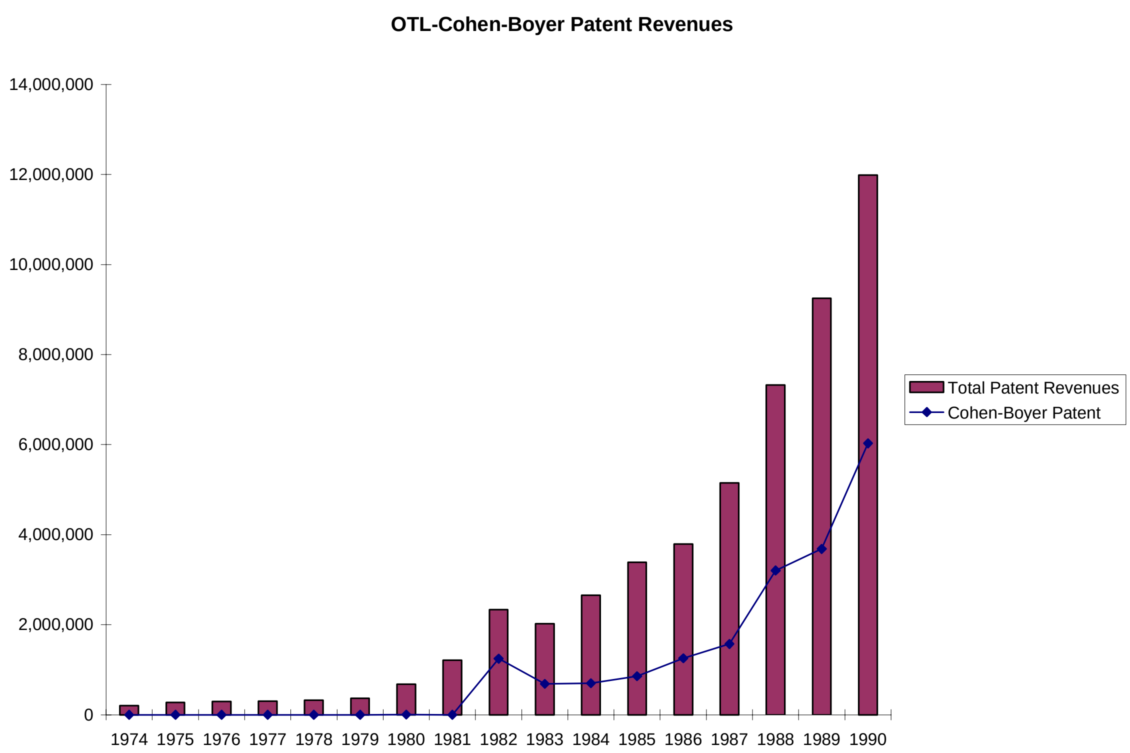

Figure 2: Revenues Generated by the Cohen-Boyer Patent
Source: Stanford Annual Reports

Stanford Biochemistry: A Case Study in Academic Entrepreneurship
What factors have contributed to the explosive innovation of these two departments? Discussions recorded in faculty meeting minutes and faculty I have interviewed point to a number of organizational and stylistic features as salient to the innovative character of the Biochemistry Department.

- Focus almost exclusively on problems of molecular biology related to human genetics
  One of the distinctive features of the Stanford Biochemistry Department has been its exclusive focus on research related to human genetics with application to molecular medicine. In contrast to most biochemistry departments which have a broad spectrum of research areas represented, the Stanford group has focused their work in ways that interact with one another in attacking issues related to human genetics. Certainly the fact that the core group of the department was assembled

by Kornberg at an early stage of their careers has facilitated this focusing of effort. In addition the links to other departments, such as Genetics and Structural and Cell Biology have all succeeded in strengthening this focus on human genetics, in many ways the fulfillment of a vision outlined by Kornberg and Lederberg in their correspondence in 1958-59 on the directions to pursue in building the new programs at Stanford.[7]

- Limited group size
  The Biochemistry Department restricted research group size to five graduate students working with a single faculty member. Despite opportunities for growth, the faculty chose to limit their numbers to a maximum of ten faculty members. The need to monitor group size is a topic frequently revisited in faculty meetings in the late 1970s and 1980s. It was felt that groups of this size promote maximal productivity and communication. When a group got too large to fit this model, as in the case of Ron Davis's genomics group, it was spun off as a separate entity, in this case as the Stanford Genome Center.[8]

- Sharing capital assets from grant resources
  One of the most striking aspects of the Stanford Biochemistry Department is the per capita use of lab space and equipment. Due to the concentration on molecular medicine it was not necessary for each lab group to replicate the equipment of other groups. But more than just a resource conserving measure, this policy was actually intended to increase innovation and the sharing of ideas. Similar to Linvill's and Terman's ideas about the importance of training Ph.D.'s and postdocs for advancing the research agenda of a program, the faculty of the Biochemistry Department all agreed that students sharing equipment and tacit knowledge about the various techniques being pioneered in the lab was the best means for different aspects of the research programs to interact with one another. This was perhaps the most sacred of the principles about how to foster innovation shared by the group.

- Positive but cautious attitude toward industrial cooperation
  From the beginnings of the Biochemistry and Genetics Departments several faculty were consultants to pharmaceutical firms, most notably Cetus, Schering and Syntex, and several served on company boards of directors. Throughout the 1960s and 1970s, however, they were not interested in getting involved in spinning off companies from their research, even after Cohen and Boyer launched Genentech. Stanford, in contrast to Harvard and UCSF faculty, were relatively late in considering closer connections with industry. Several members of the Stanford Biochemistry faculty strongly opposed any industrial affiliations with their academic program. In 1979-80 this became a major topic of discussion in department faculty meetings. The first commercial venture by a member of the Biochemistry Department was the startup of DNAX by Kornberg, Berg, Charles Yanofsky, and Alex Zaffaroni in 1981.

The following excerpt from a letter of Joshua Lederberg to historian Susan Wright recalls the interest in but skepticism about joining industrial ventures in 50s, 60s and early 1970s:

> I don't know what was in other people's minds. Some microbiologists like myself, and in the tradition of the U. of Wisc., were consulting with industry—e.g. for antibiotics development, as I did with Schering and with Bristol Labs. and Syntex in the 50's and 60's—and were sensitive to industrial applications of microbiology. I doubt that this was true for the DNA biochemists who made such great strides, before about 1974. Even at Asilomar (1975) there was great skepticism and naiveté about such possibilities. (Hence the broadside I circulated and revised to publish in "Prism"). But I may be unaware of other parallel interests in the 60's.

> I am pretty sure Stan Cohen was not thinking "industrially" before I introduced him to Cetus; but you should get more reliable (direct) information before quoting this.
>
> My motive in joining Cetus was the expectation that they could organize "far out" efforts in applying microbial genetics to pharmaceutical problems, as the other companies had balked at doing. (I do ask you not to identify them by name.)
>
> The time scale I projected was just about what has happened. (But I in no way anticipated the Wall Street Fever part of it!)
>
> Cetus management was sympathetic but they did not have much money and it took a few years to get other financial partners to provide the resources — eventually, mainly, Standard of Calif., Natl. Distillers, and Standard of Indiana — and really build up the foundations. I don't have the Cetus company documents on these matters and it would be difficult for me to substantiate dates on many decisions where my own participation was only verbal. Contrary to some attributions, I was never a director of Cetus and (alas) was not a founding member, since they were originally organized with somewhat different objectives than my own interest in seeking applications of microbial genetics.
>
> Ron Cape, Cetus CEO, at (415) 549-3300 is the one you should address on these matters.
>
> I wish I could remember just when Stan Cohen told me of his staph/E.coli expt. (I met him in the parking lot at Stanford, and it was the first I knew he was working on "hololigation") — a month or two before it was published, I am sure. I was quite confident then that (a) he had won the race (with me, not knowing I was a contestant) and (b) that the rest would follow, both scientifically and industrially (since I had been thinking in those directions for several years.)
>
> Many other people made a lot of fuss at that time about not (yet) getting faithful expression of eukaryote DNA in bacteria — and that seriously hindered getting financial support for Cetus; I was sure that would soon be surmounted (and without minimizing the ingenuity needed for that, it was). The keys were a) to use c-DNA reverse-transcribed from messenger-RNA; b) the recognition of the introns; c) a better handle on promoters.
>
> As far as my own laboratory work around 1968-72 was concerned, in retrospect, I have to say that my chief shortfall was that I never had an efficient assay for success, as Stan had devised with the cut psc-101 plasmid ; one graduate student I had initially working on this problem (Irene Majerfeld) was also looking at a variety of other DNA-linkers, besides using DNA-ligase tricks, with some uncertain hints they might be working. Her husband got a job in England, and she left with him and completed her dissertation there, mainly on the interaction of aldehydes with DNA.
>
> Some time later, Vittorio Sgaramella joined my lab as a post-doc., and continued to make some important contributions on the action of restriction endonucleases: that they did not generally leave blunt-ended DNA. His final success with dimerizing P-22 phage was completed after the priority-winning papers you know about. Stan Cohen has compiled the chronology of some of the milestone publications in the enclosed statement; I have no quarrel with any of it, but have not attempted a searching criticism.[9]

Arthur Kornberg, trained originally as an M.D., but attracted more by the research side of medicine than the prospects of a potentially lucrative career,[10] has described his own cautious approach to industry connections during the 1960s and 1970s in terms similar to Lederberg's:

> Because the techniques of the biotechnology explosion were created entirely by academic scientists, virtually all biotech ventures in the United States include biologists and biochemists as founders, managers, or advisors. In most vigorous university departments of the medical and

> biologic sciences, prominent faculty members have one or several industrial connections. I never thought that, in 1968, after more than 25 years of full-time academic research in biochemistry, having avoided all commercial associations, I would become advisor to a new biotech venture. Nor did I believe that in the next 25 years, I would be a founder, advisor, or director of half a dozen more. Such affiliations entail advantages and threats to the progress of science and the betterment of human welfare that must be analyzed in order to be understood, and be understood in order to guide our actions.
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> …
>
> On the DNAX side, the entrepreneurial drive came from Alex Zaffaroni. Trained in biochemistry and endocrinology, and with extensive pharmaceutical experience in the applications of scientific discoveries to medical uses, he saw an industrial potential for developments in molecular biology in the 1960s and 1970s. Paul Berg, Charles Yanofsky, and I, who had contributed significantly to these developments, had been turned off by overtures from venture capitalists, but we felt that, with Zaffaroni, we could create an enterprise in which pursuit of basic research with a communal focus could be linked to the development of drugs for treating disease.[11]

Given this reticence to pursue a substantial financial relation with industry, and if at all, mainly in the role of advisors and consultants, what factors led Kornberg, Berg, and other members of the biochemistry faculty to rethink this relationship? Discussions recorded in the minutes of faculty meetings from the late 1970s suggest two considerations as paramount. The first and probably most immediate source was the major cutback in funding from the NIH, particularly for graduate research support, in the late 1970s. Dean Clayton Rich had already sounded the alarm in his report to the directors of departments and centers of the Medical School in 1974. Rich projected an increasing rate of deficit for the Medical School and voiced concern about being able to cover it through endowment and expansion of externally funded sponsored projects. Based on inflation and what he described as expected economic depression, combined with expected cut-backs in federal funding for research Rich projected serious financial problems within the next five years.[12] Having experienced 25 golden years of federal funding for medical research, and having based the expansion and much of the operation of the Stanford Medical Center on available federal funding for medical research and training, it was clear that new sources would need to be sought.

As early as 1976 cutbacks in postdoctoral training programs at the NIH began to have an impact on the Biochemistry Department, and faculty were encouraged to seek additional outside sources to fund their postdoc programs and graduate research programs. By 1979 the department was struggling to avoid monthly departmental deficits, and cutbacks in federal funding prompted a search for solutions. These problems continued on into the 1980s with additional cuts each year, including a 13% cutback from the NIH in graduate funding in 1981-82. A memo from Dale Kaiser to the faculty pointed out some of the issues:

> As a consequence of the announced budget rescission, previously recommended funds amounting to $44,125 for the year 07/01/81 to 06/30/82 and similar amounts each future year would be cut from our predoctoral training grant. These funds would have been used for consumable supplies to support, in part, the research of our graduate students.....
>
> …
>
> In addition the extinction of the NSF predoctoral fellowships will have a major impact on our program. Because of the high quality of our students, we have been able to count on significant support from this source and currently 5 of our 25 students are receiving NSF support. Each future year without NSF fellowships would produce a deficit of $70,100 in tuition ($9520) and stipends

> ($4500), assuming 5 students and 1981-82 tuition rates. It would be reasonable to consider these students research assistants to support them in the future from a project grant.[13]

On top of these cutbacks the NIH decided to increase the stipends of graduate students without adding funds to offset the increase.

As I have argued, the training of graduate students was central to the research mission of the biochemistry faculty. Any cutbacks in the support programs for students affected the overall research goals of the group. To address these issues Dale Kaiser, who was the chair of the department in 1979, solicited suggestions from his colleagues about strategies to meet the crisis. Paul Berg and Arthur Kornberg both proposed creating an industrial affiliates program.[14]

> You asked me to think about the future funding of the department and to share these ideas at a faculty meeting. …
>
> 1. Our traditional pattern of sharing funds and resources has been successful. It accounts in part for the spirit and quality of the department. This pattern can also be defended for its economies in large equipment, expendables, space and technical staff. The scientific interactions generated by this sharing are a priceless dividend.
> 2. The sharing pattern has been of crucial importance to faculty members getting started and has relieved anxieties about working on important problems that seemed to be less fashionable and therefore less fundable. The pattern has also made possible a greater flexibility in the size and operations of a research group from an ebb, say, during a sabbatical period to a surge when a "breakthrough" comes.
> 3. However, all patterns in our affairs must be continually adapted to the variety of external and internal chances that affect us. (Evolution is essential for survival.) For this reason, I agree that it is appropriate to consider the recent changes imposed on us, our responses to them, and how we should prepare for the future.
> 4. The practical external changes are the sharp declines in funding sources (federal, foundation, Stanford) and the resultant greater efforts needed to get the money and to account for it. The principal internal change is the maturity of virtually all our research groups as expressed in size and fundability.
> 5. We have adjusted to strains in the past by urging some faculty members to apply for more money than they thought they needed or could get gracefully. These adjustments included: obsolescence in equipment, prolonged need for some faculty members to apply for more money than they need or can easily account for, hardships in providing assured postdoctoral stipends, and constraints on individual venturesome-ness (e.g. expansions in group size and operations).

Kornberg suggested several moves that might improve the financial situation of the department without distorting its traditional patterns and culture. Among these were even more aggressive attempts to apply for federal and foundation funds, applying for large program grants that the NIH had recently begun funding, and economies in departmental operations. Foremost on his list, however, was the creation of an industrial affiliates program:

> c. Seek new support, as from an Industrial Affiliates Program. Paul has already discussed and should soon again bring up the merits and problems of such a venture. I think we should consider this a top priority item and do it soon if we do it at all. We're already a little late in getting into this kind of venture and it may soon become too competitive to make it attractive.[15]

The Biochemistry Industrial Affiliates Program was launched in 1980 with 11 member companies at a cost of $12,000 per year each. The price of membership eventually rose to $16,000. In the period between 1980-1990 the average income from the program was approximately $160,000 per year. These funds were used as unrestricted departmental gift funds to support the graduate program and other parts of Biochemistry operations.

The discussion of an industrial affiliates program opened the door to even closer ties to companies. The immediate occasion for addressing this issue was an overture made to the department in 1981 by Smith Kline Pharmaceutical Company. Dale Kaiser, who was still the chair at that point, asked faculty to compose memoranda discussing their views on whether a close affiliation with commercial companies would be desirable to pursue. Kaiser's own memorandum, entitled "Creation of a Substantial Financial Relation with a Company," dated 4 December 1981, expressed his own views, but generally represented the viewpoints of the other faculty. Kaiser objected to a financial connection to a company on the following grounds:

1) A substantial commercial connection will reduce our ability to obtain federal funding in the future. Study sections and fellowship review committees will factor it into their decisions with negative effect on us. I cannot imagine, for example, our being awarded the aging program grand had we a million dollar commercial contract in place at the time of our application.
2) A substantial commercial connection will change the reputation of independence which I think our Department presently enjoys. In so doing it will make us less attractive to the best students and postdocs.
3) Stability of commercial support is unknown. Although a five year contract might be written, it could be abruptly terminated before the end of the contract period. The Stanford Boys Town grant was so terminated.
4) Such a connection would make us dependent on a company that supplied a significant fraction of our budget. We would become vulnerable to demands to attach new strings or to make other terms of this agreement less favorable. The threat of loss of large dollars would be difficult to combat. We are dependent on federal agencies, but we are buffered from unreasonable demands by the multiplicity of our grants and by the peer review system.
5) Such a contract will threaten our Industrial Affiliates Program. Although the IAP requires work on our part, it has few strings attached and leaves our initiative and reputation intact.[16]

Kaiser's assessment of the situation was unanimously endorsed by the other faculty, although, as Kornberg pointed out, the Industrial Affiliates Program would not be a long term fix for the department's financial problem. In general Kornberg saw a new pattern emerging where industrial support for university research would play a much larger role than at any time previously.

Kornberg's views on the new role for connections between the Biochemistry Department and commercial firms were deeply shaped by his own involvement since October of 1980 with colleagues Paul Berg, Charles Yanofsky, and Alex Zaffaroni in the startup of DNAX. Just prior to founding DNAX the three principal scientists had been invited by Channing Robertson of the Stanford Chemical Engineering Department and Alan Michaels to join with them in a new venture called Engenics. That project did not appeal to Kornberg due to its focus on application and turning a profit within three years rather than on pursing more basic science. Berg was the discoverer of recombinant DNA, a leader in the enzymology and molecular biology of protein synthesis, and at the forefront of the genetic engineering of vectors powered by tumor-virus genes. Yanofsky, a professor in the Stanford Biology Department who was equally proficient in biochemistry and genetics, had been one of the earliest to adopt and advance recombinant DNA techniques to clarify still further the mechanisms of gene regulation and expression. To this pool of talent Kornberg contributed his work in discovering and characterizing many of the enzymes involved in DNA replication that later became the essential reagents in gene splicing and other DNA manipulations. Kornberg, Berg, and Yanofsky envisioned an academic research company that was focused on longer term research, and on honing, refining, and advancing the research coming out of university labs, particularly Stanford's. According to Kornberg, DNAX would not compete with other ventures already started in the cloning of a number of known factors, such as erythropoietin or interferons. Rather the company would focus on immunology, going after antibodies that could be obtained with monoclonal-antibody techniques developed in their own Stanford labs. The monoclonal-antibodies would be honed and redesigned at DNAX in order to solve medical problems and possibly used for industrial purposes. Advice from medical colleagues and their own experience in molecular biology and protein chemistry would enable DNAX scientists to select suitable medical targets for antibodies and direct the engineering to make them.[17]

DNAX and similar spinoff companies such as IntelliGenetics, launched by biochemistry faculty member Doug Brutlag, computer science professor Ed Feigenbaum, and computer science grad student Peter Friedland in 1980, the same year DNAX was founded,[18] were conceived in many ways as extensions of the research mission of the department. In part, the stimulus for these developments was to generate revenue streams to supplement the dwindling NIH and NSF support for graduate student training. There was also an interest in generating research positions and postdoctoral employment for students who might later go on to an academic job or other positions in industry.

But an equally powerful and perhaps the most important motive—a motive that will be explored in greater depth as we move forward with this project—was the goal of technology transfer. As Fred Terman pointed out in his many presentations on building mutually stimulating university-industry relations during the 1960s, relatively small startup companies like DNAX are the ideal institutions for developing university-based intellectual property. Large companies with established research programs have too much built-in inertia and lack incentive to exploit new innovations rapidly. Small companies, on the other hand, cannot afford their own research staff and benefit from close ties to a university research lab for consulting services. The ideas, techniques and innovations being generated in the university lab and transferred through technology licensing and transfer of personnel can become focused and refined into potentially important inventions by the more concentrated effort of the small startup company needing to make its mark. A company like DNAX, then, which was bought up as a separate research institute by Schering-Plough, serves as a kind of intermediary between a large—in this case pharmaceutical—company and the academic research environment. The result is a win-win situation for the university as well as for industry.

One of the best examples of how this relationship works is in the development at DNAX of work on immunology that exploited techniques and discoveries coming out of the Stanford Biochemistry Department. In its early days DNAX focused on T-cell research using recombinant DNA technology to figure out how the T-cell signal elicits the release of highly specific antibodies into the blood and body fluids. Until this work done at DNAX matured, understanding how T-cell signals are tuned and balanced to evoke either a humoral or a tissue-type response had been a major mystery in immunology. The solution discovered at DNAX was a fundamental contribution to basic science, setting the stage for the discovery at DNAX of the cytokine IL-10, which is one of the most important cytokines for stimulating the production of antibodies by the immune system and of potentially enormous therapeutic value.

This work was based on the expression-cloning techniques developed by Hiroto Okayama, a postodoctoral fellow with Paul Berg at Stanford. The Okayama-Berg procedure produced full complementary DNA (cDNA) copies of messenger RNA (mRNA), even in crude cell extracts containing thousands of different mRNAs. When these stretches of cDNA were recombined into DNA circles called plasmids and introduced into an appropriate host cell, they functioned as genes to generate the proteins encoded by the mRNAs. The immunologists at DNAX applied these techniques to the immune system. Coffman, Mosmann, and Rennick at DNAX worked at exploiting these techniques for increasing the range and facility of cell-culture assays for factors made by T-cells that promoted the production various types of cell products involved in regulating or suppressing immune reactions. The molecular biologists at DNAX—Arais, Lee, and Zurwski—sharpened the cloning and isolation procedures for new factors. With other young scientists who joined them, and with ancillary support for the preparation and chemical analysis of monoclonal antibodies, the DNAX team, within three years, filed patent claims for the discovery of numerous interleukins (IL-3, IL-4, IL-5, and IL-6), culminating in the work on IL-10, a regulator of immune responses with clinical uses in treating a variety of disorders of the immune system. According to Kornberg, "The discovery of IL-10, at the time it was made (late 1980s) could have come only from DNAX. The prompt coalescence of all the scientific resources of the Institute to exploit the discovery would have been possible nowhere else….Nor did any pharmaceutical company have the concentration of talents or the organization to make the IL-10 discovery and then to expand it rapidly and effectively."[19]

The new companies were focused on research and created environments for the scientists that worked there similar to those in an academic setting. In many ways the organization of DNAX and the style of work done there was quite reminiscent of the early days at Varian Associates when Felix Bloch's seminar met one week at the company and the next week on the Stanford campus. At DNAX, for example, scientists were recruited with the promise that they could devote a substantial fraction of their time to their own research interests. It was hoped that the work and ideas of those people would eventually shape a coherent program. Moreover, the academic character of DNAX was validated by the US State Department's granting of J-1 visas for foreign scientists working in the Exchange Visitor Program. These were research facilities that became authorized as sites for training postdocs, and scientists were encouraged to publish their work. Kornberg especially wanted to create an environment at DNAX reminiscent of the environment he had experienced at the NIH early in his career between 1947-1952 before he moved to Washington University.[20]

> The ambience at DNAX can be described as an opportunity to work at a particular forefront of science, with excellent resources, in a free and open atmosphere, and with the support of, rather than the intrusion by, administrative staff. An important constraint is that the focus of the research be in productive areas of immunology and molecular biology. Another is that the scientist not be reclusive and have concern for the success of the communal enterprise. The group size of six to ten people for a senior scientist may appear small compared with larger units in other settings, but his limitation is largely offset by the wide range of resources made available for biological, analytical, and preparative studies.
>
> In my view, DNAX is an academy, a company of scholars researching for new knowledge with minimal constraints. …
>
> DNAX also provides generous fellowships from two to three years for some sixty outstanding young people to work under the direction of twenty-five scientists. The responsibility for their guidance is rewarded by the stimulation and enthusiastic effort of the fellows, who bring a fresh variety of skills and attitudes and the drive to do research notable enough to earn staff positions elsewhere. Job placements have been about equally divided between university departments and industry.[21]

Addressing the Biotech Conundrum: The Shifting Sands of Pajaro Dunes

The problems posed by the reductions in federal funding and the emergence of new biotech ventures between academics and commercial firms were mainstream news in 1981 as rumors began to circulate of an impending $6Mil gift from DuPont to Harvard for financing the new genetics department headed by Phillip Leder. The gift and arrangements for the new lab were concluded and made public in July of 1981. DuPont gave Harvard $2Mil initially to get the lab going and $1Mil each year until 1985. The gift was free of strings and did not support any specific lines of inquiry. Rather it provided general research support and start-up costs for the department. Harvard Medical School collected its standard federally-based overhead charges in addition. The arrangement provided for DuPont scientists to consult with Leder and his associates. DuPont was also to receive preferential treatment with regard to patents and received an exclusive right to licensing arrangements that resulted from research in the department of genetics. DuPont approached the arrangement with a long-term interest in improving the company's base of knowledge in molecular genetics rather than acquiring specific products.[22] A similar, even more lucrative arrangement ($50 Mil over 10 years) had been made in May 1981 between Massachusetts General Hospital and Hoechst Pharmaceutical. Among the advantages of the corporate sponsorship were the greater flexibility in the use of the funds than allowed by federal grants and the extensive reporting requirements required by federal funding.

These and related events prompted a public discussion of the matter sponsored by the Committee for Corporate Support of Private Universities in New York City on May 20, 1981, involving Harvard President Derek Bok and Stanford President Donald Kennedy. In his remarks Kennedy stated that 20 members of the Stanford biomedical research faculty had recently concluded or were in the process of concluding arrangements with outside companies in support of their research. What was new about these relationships, Kennedy observed, was that they were not the fee-for-consulting arrangements that had been the normal means of contracting academic time for industry since World War II, but involved equity participation in some form. A second radically new feature potentially disrupting the health of the research organizations in American universities was venture finance and the importance of corporate proprietorship of research with potential future value:

> The financing of venture companies in the field of biomedical genetics is a caricature even of the bold style of corporate organization that we have seen in microelectronics. There are dozens of small firms, many of them organized and managed by venture capital partnerships, that sprang up after recent changes in the tax laws. The value of these "Gencos" or "Clotechs" or whatever can increase suddenly in a way that does not depend upon the proven ability to manufacture a product, but rather upon the perception of second- or third-generation investors that there is ultimate promise of such a product. Enormous changes in value can be realized through successive generations of investment.
>
> The impact of this new style upon the division of research roles between university and corporation is significant. It pushes the line between basic and applied research well over toward the corporate sector. An important determinant of the value of the new corporations is the public sense that they have an important idea ready for application. The essential element in this perception is that the good ideas are corporate property, and that the growth potential associated with them will therefore be yielded to early investors. Thus, the new mode of capital formation is an incentive for corporate proprietorship of basic research ideas and talent.[23]

Kennedy argued that we were entering a new era of university-industry relations and rather than attempting to return to the previous status quo, we should seek means to increase the relatively small portion, typically around 3-4 percent, of university research funded by industry. Kennedy urged that incentives, such as tax credits, be offered for industrial investment in university research programs. This strategy—or others to be considered—Kennedy argued, would have the goal of keeping the basic research organizations of universities intact, yet through specific forms of affiliation and licensing agreements, would allow industry to realize longer-range benefits from investments in university research.

Following up on these ideas a few months later, Kennedy organized a meeting to take place in March 1982 of the presidents of MIT, Harvard, UC Berkeley, Cal Tech, and Stanford at Pajaro Dunes in order to discuss measures for dealing with the new realities of commercialization of university research. Also in attendance at the meeting were representatives of 11 companies involved in biotech, including Eli Lily, Genentech, and DuPont. In preparation for this meeting Kennedy wrote a prospectus for the conference, entitled "Commercialization and Basic Research," which set out proposals for specific areas of policy to be discussed. The prospectus reaffirmed Kennedy's view that the nexus of relations emerging among venture capital, biotechnology startup companies, and university researchers signaled a new era in which industry would play a greater role in the financing and conduct of university research. Biotech, Kennedy cautioned, was just the beginning of a movement that would spread to other areas of research, and with the advent of new media technologies, such as cable television seeking richer cultural content, the commercialization of research would possibly spread even to the humanities.

Referring to biotechnology Kennedy attributed the shift to three major factors:

- The ripening of the field of molecular biology to the point where an entire range of applications become possible.

- New economic incentives, especially a pattern of capitalization in which large changes in value are associated with successive generations of investment. In the case of biotechnology this pattern places a premium on the early possession of valuable intellectual property, and pushes the zone of corporate interest into increasingly "basic" research areas.

- The prospect of massive losses in government support for basic research, and the resulting incentive for scientists and universities alike to seek new sponsorship.[24]

In our earlier discussion of Frederick Terman's ideas about the future direction of high technology we pointed to Terman's insistence that deeper levels of basic research would become essential to the life of technology companies. Terman argued that this development would draw industry to establish closer ties with university research, including participation in the research ventures on campus. Terman's strategy for anticipating these developments was to create an entrepreneurial professoriate in numerous areas poised to encourage and take advantage of those developments should they arise. While Terman had microelectronics mainly in mind when he made these prognostications, Don Kennedy was now giving witness to the fact that the new age had come, and that it had started with biotechnology. Like Terman before him, Kennedy's main interest was in seeking to preserve the strengths of academic research in the university environment, while at the same time recognizing the importance of establishing a framework within which technology transfer would be efficient and financially rewarding for the university.

At the March 1982 Pajaro Dunes conference (sometimes called Asilomar II in reference to the 1975 meeting organized by Paul Berg, which first drew attention to the need to establish guidelines for recombinant DNA research), the discussion centered on the potential conflicts of interest raised by the new relationships with industry. The participants agreed on three principles for moving forward in this new area:

1. Universities should establish explicit conflict of interest codes to guide the conduct of their professors.
2. Universities generally should not own or have substantial equity in companies staffed by their professors.
3. Association between businesses and universities should not impair "openness and communication" among researchers, and if that openness is limited for commercial reasons, the period of secrecy should be brief.

4. The direction of research in universities should not be governed by commercial interests but by the intellectual demands of the research itself.[25]

In his summary of the meeting, Vice President for Public Affairs Robert Rosenzweig elaborated on the conclusions arrived at by the group regarding the licensing of patents developed in the course of university research and on investment by the university in companies based on intellectual property developed by its own faculty. A key principle adopted in the discussion was that universities should not influence the nature of the research proposed by professors, postdocs or graduate students by pressing them to do work of potential commercial importance or to become involved in other commercial activities. The general consensus was that the university should not be improperly influenced in choosing a licensee for intellectual property developed in the course of university research by the fact that a faculty member, or the university itself, is a substantial stockholder or has other significant ties with at particular company.

Another principle emphasized in the meeting was that licensing agreements between a university and a company are intended to accomplish the transfer of technology in an effective way. In those rare instances where a faculty member of the university has a major financial interest in a company seeking such an agreement, and where the technology to be licensed has been in whole or in part developed by the faculty member, licensing should ordinarily be on a non-exclusive basis. Exceptions might arise if the transfer of technology is best accomplished through an exclusive arrangement for a limited period, as, for example, in the case of companies possessing unique skills necessary to such transfer on a timely basis.

Another issue the group addressed was that of the university holding equity in a company developed by its faculty. Rosenzweig summarized the position developed at Pajaro Dunes regarding conflicts of interest arising through combinations of public funding, private consulting, and equity holding in a faculty member's area of research as follows:

> At times, the research of entrepreneurial efforts of a faculty member may have the potential materially to affect the economic condition of a company. (In such cases the faculty member is often a substantial stockholder in the firm.) Under these conditions, investment by the professor's own university in the firm gives the institution a financial stake in the activities of its faculty member. This situation may cause others to believe that the university encourages entrepreneurial activities by its faculty. However, it may cause, or appear to cause, the university to extend preferential treatment to the professor, for example, in such matters as promotion, space, or teaching loads and thus undermine the morale and academic integrity of the institution. Hence, it is not advisable for universities to make such investments unless they are convinced that there are sufficient safeguards to avoid adverse effects on the morale of the institution or on the academic relationships between the university, its faculty, and its students.[26]

The conference members agreed that the area of equity was difficult to address and that each university should work out its own policy according to its own internal code of ethics. "Although we see no single 'right policy'," Rosenzweig concluded, "we do believe that each university should address the problem vigorously and make effort to publicize widely and effectively the rules and procedures it adopts to avoid compromising the quality of its teaching and research."[27]

Venture Capital and the Dilemma over Equity Investments

Indeed, Stanford had already been addressing the issue of equity ownership in companies spun off from research in Stanford labs and patents generated in the course of university research for several years. Stanford-generated technology was fueling a substantial part of the development of Silicon Valley, and now in the area of biotechnology, Stanford- and UCSF-generated technology was in large part the source of the biotechnology revolution. Why should the University's benefit from its role in this economic bonanza be limited solely to fees and royalties from technology licensing? In some cases such fees were substantial, as would soon be evident in the revenues generated by the Cohen-Boyer patent. But in many areas patents were not the crucial means of transferring intellectual property, and some areas of technology development did not aggressively pursue patenting as the principal instrument of technology transfer. In an era of declining government and foundation support for basic research, more aggressive measures needed to be taken to profit from the knowledge being produced by the University.

One of the most innovative solutions was developed in 1978 during Richard Lyman's tenure as President of Stanford. A decision on equity investment had been taken by the Board of Trustees on 9 November 1976. The policy at that time, as stated in paragraphs b) and c) of the decision, was:

> b) As a general rule, Stanford will not consider investing in any start-up or seed-money situations.
> c) Rather, Stanford will be receptive to outstanding opportunities where there is a professional lead investor who has already made an investment commitment.

This 1976 policy statement had been the subject of debate in the Finance Committee of the Board of Trustees since 1970. In explaining the background to the policy of being "receptive to outstanding opportunities" adopted in paragraph b), the document explained that in May 1970, the Board of Trustees implemented a formal policy and procedures relating to investments in venture capital opportunities and "special situations." At that time it was recognized that responsible asset management of the University's resources dictated that the Trustees and their investment advisors should not limit their view to that of being an investor in bonds and seasoned stocks. Historically, Stanford had not done this, as evidenced by investments in some small companies and the undertaking of capital commitments to such pioneering ventures as a regional shopping center and an industrial park. In explaining the rationale for the new policy the document went on to note that during this same period of time, however, there were missed opportunities in investing and participating in the growth of nearby successful high technology ventures. "The 1970 policy formulation was needed to better position Stanford to avail itself of such opportunities, especially regarding participation in new, or young, companies that had spun off from the University or were capitalizing on technology transferred out from our academic research."[28] In 1973 a further review was undertaken, again reiterating the stand that Stanford should not directly undertake actively to pursue venture investments. But at the same time the financial officers of the University were encouraged to pay attention to superior opportunities, keeping the door open to those who for one reason or another are prompted to show us a prospective investment.

Thus, by comparison to previous policy, the 1976 policy on investments was an aggressive step forward. But already by 1978 President Lyman, acting on an initiative generated by the Director of Finance Rodney Adams and Vice Provost for Research William Massy, was interested in modifying this stand in order to participate more actively in venture capital funding. Rod Adams and John K. Poitras co-authored a 48-page paper on venture capital in October 1978 in which they recommended changing Stanford's policy on investments while maintaining the general intent behind the dictum of not investing directly in faculty-generated start-ups. By investing in venture capital funds that were focused on developing Stanford intellectual property, the University could benefit from the technology being generated in its own labs. Moreover, by being one of numerous investors in a venture capital fund the problem of direct investment in the company of a faculty member could be circumvented. And at the same time, the management of the investment would be supervised by responsible and knowledgeable financial managers.

With this basic rationale, Adams and Poitras suggested the following changes in paragraphs b) and c) of the policy on equity investment:

> b) Stanford will consider investing in pooled funds managed by venture capital firms and partnerships.
>
> c) In addition, Stanford will be receptive to direct investment in outstanding opportunities where there is a professional lead investor who is making or has already made an investment commitment.

Adams and Poitras did not think Stanford should develop a large staff of its own venture capital investors. More critical for Stanford's financial officers was to be privy to a stream of opportunities. Adams' plan was that Stanford staff would make a concerted effort to be invited to participate in the highest quality offerings. Adams, Poitras and a small staff would develop close working relationships with key venture capital investors with a known and ongoing interest in Stanford, bringing a select number together for a continuing dialogue with both staff and trustees. A further key resource would be the participation by individual trustees. The investment staff would seek close working relationships with several Bay Area venture firms interested in technology emanating from the University's research activities. As Adams saw it, the role of Stanford as a continuing source of emerging technologies represented an effective quid pro quo for the established firms to provide Stanford the opportunity to review other proposals. Such associations would leverage Stanford's efforts by providing it with pre-screened opportunities:

> Stanford's office of Technology Licensing frequently obtains patent rights in technologies of interest to venture firms. For example, Collagen Corporation is a biomedical start-up situation of Institutional Venture Associates in which Stanford received equity in exchange for a patent license.
>
> It is anticipated that a further source of quality opportunities will be the University's faculty, staff, and friends. Several eminent local venture capital professionals have informally expressed interest in being a resource for the University.[29]

Proposals received from Stanford faculty and staff were to be referred to an outside venture firm for review and evaluation to provide a third-party perspective, and to reinforce the policy of not investing unless there are other identifiable, professional lead investors involved. The University would be a resource to the faculty and staff in introducing proposals to venture firms. Should the outside firm decide to fund the proposal, Stanford would review its interest in investing at that time or wait for a subsequent round of financing. If there was no interest by an outside investor, the University would likely decline to invest unless it was decided to make an exception to stated policy. Potential conflict-of-interest situations would be discussed with Staff Counsel and the Vice Provost for Research.

Apart from returns on investment Adams argued that an active venture capital investment program by the University would be a substantial asset in generating gifts, particularly restricted securities of small companies. Donors such as entrepreneurs and venture capital investors would be encouraged by Stanford's commitment to venture capital investing, which in turn might prompt gifts of small companies' stock at a much earlier point in time. Whether or not gifts come sooner rather than later, the Stanford Development Office would be able to better initiate and establish relationships with venture investors and entrepreneurs as potential donors.

Adams and Poitras recommended that Stanford’s investment in venture funds should be focused on companies in Stage I, II, and III development. Stage I companies are companies that have already gone through seed funding and start-up phases but still has a product that is only partly developed, and profitable operations are still some years away. Stage II companies are firms that are breaking even or are projecting profits within a year. Stage III companies are still private but have an operating profit history. This stage is generally the last stage before shares are sold to the public. Alternatively a Stage III company may be an operating division of a larger company available for sale or an independent business available for sale to a larger company. Stage IV companies are publicly traded companies, but with large blocks of shares privately held that may be purchased at substantial discounts from market. Also, leveraged buy-outs are included in the Stage IV. While they would invest preferentially in StageI-III companies, Adams and Poitras did not rule out funding start-ups. “Most of our investments are expected to be in Stage I, II, and III types of opportunities. While we should not rule out other types, we will not seek or solicit such investments. Our pooled investment participation might well cover these other areas, especially seed capital and start-up opportunities.”[30]

Adams and Poitras proposed to start off small. The annual investment in venture funds would be 1% of the endowment, which initially would be around $3.8Mil. The size of the initial investments proposed were between $250,000 and $750,000 depending on the investment stage of the company and the attractiveness of the opportunity. With these constraints at most one to three new investments would be placed per year. Assuming an average investment size of $300,000, it was estimated that the total new investments at the end of the first two years would be between $2Mil-$3Mil.[31]

These were modest beginnings in venture capital investment aimed at leveraging the products of research coming out of the university. I am still exploring the history of investments in venture funds and intend to report on that more fully in my next quarterly report. By the 1990s, however, Stanford had large commitments to venture fund investments. The table below lists the recorded and market values for venture funds listed in the Annual Financial Report of Stanford University for the years 1990-93.

Unitized Funds	1991	1992	1993
Recorded Values	$136,849,860	$173,037,779	$244,175,358
Market Value	$151,481,399	$197,501,250	$287,634,416

Source: Stanford Annual Reports, Merged Pool B.

Final Reflections

I have argued that Fred Terman was instrumental in establishing an entrepreneurial culture at Stanford. Having first demonstrated the power of his strategies for program building in the Engineering School, Terman continued to populate other parts of the University with similarly styled academic entrepreneurs in his role as Provost. The impact these policies had on the Medical School can be clearly seen through the lens of the Biochemistry and Genetics Departments. In the 1950s it was common at Stanford to refer to the plan to move the Medical School to the main campus as “Wally’s Folly,” due to the large fundraising requirements and total reorientation of purpose needed to see it through. Having committed itself to building a new style of medical school oriented primarily around biomedical research, it was paramount to appoint imminent research faculty determined to be aggressive in building programs and funding their operations through obtaining federal and foundation funding. Kornberg and his colleagues in Biochemistry and Lederberg and his colleagues in Genetics could not have better fit Terman’s recipe for creating steeples of excellence through entrepreneurship.

But the picture I have painted of Terman’s idea of an entrepreneurial culture had another crucial dimension. The hallmark of Terman’s strategies was to be aggressive in getting federal funding, but an additional key component was to establish liaisons with industry. His purpose in this was twofold: to transfer technology and ideas developing in Stanford labs into industry, and to move industry ever more in the direction of dependence on basic research. Terman could not have foreseen the biotech revolution coming, but the dependence of biotech firms on university research and new partnership between industry and university it entailed could not have been better scripted by Terman himself.

Don Kennedy was chosen to lead Stanford in 1980 because of his abilities as an academic statesman. In an era when government funding for research was key to the expansion of the University Kennedy came to Stanford with outstanding credentials in government, having just served as director of the FDA. But Kennedy was no sooner in office than he began to see that the model that had guided Stanford throughout the 1960s and 1970s would no longer be viable at a time of retracting government resources. The issues first surfaced in biotechnology. I have suggested that in his thinking about how to adapt the University to the new circumstances, departments like Biochemistry with its Industrial Affiliates Program and links to startups like DNAX and IntelliGenetics provided useful examples of how to proceed. Kornberg, Berg, and others were keen on preserving the best and most productive features of traditional academic research while at the same time adapting to the new environment where technology transfer would become a key ingredient in focusing and accelerating academic research.

It is possible to see some of the effects of these changes and the ways that entrepreneurial departments managed to meet the new challenges by considering the increased importance of unrestricted gift funds in supporting the academic mission from the early 1980s to the present. I chart data for the decade 1974-1993 in Figure 3. What is notable in the chart is the use of gift funds to support the instructional budget of departments. Electrical Engineering set the pattern. As federal grants and contracts fell during the 1970s, Electrical Engineering shifted funds from gift accounts to support the activities previously funded from government grants and from unrestricted university funds, chiefly tuition and income on endowment. At the highpoint of this sort of activity in the mid-1980s more than 50% of the instructional operating budget in Electrical Engineering was being funded from its gift accounts. As we have seen above, Biochemistry faced a similar crisis in the late 1970s as a result of reduction in NIH funding for graduate and postdoctoral programs. Like the Electrical Engineering Department, Biochemistry used its gift funds from the Industrial Affiliates Program and other departmental income to offset the loss of government funding, in some years by as much as 30% of its instructional budget. Genetics responded similarly. To reinforce the point here it is instructive to compare the responses of departments less able to attract federal funding for research, such as History or Philosophy. What one finds is that such humanities departments' instructional budgets, and indeed nearly their entire operational budgets are covered by unrestricted funds from endowment and tuition (99%). Figures such as these drive home the importance of the vision of an entrepreneurial culture that Terman and others have had here.

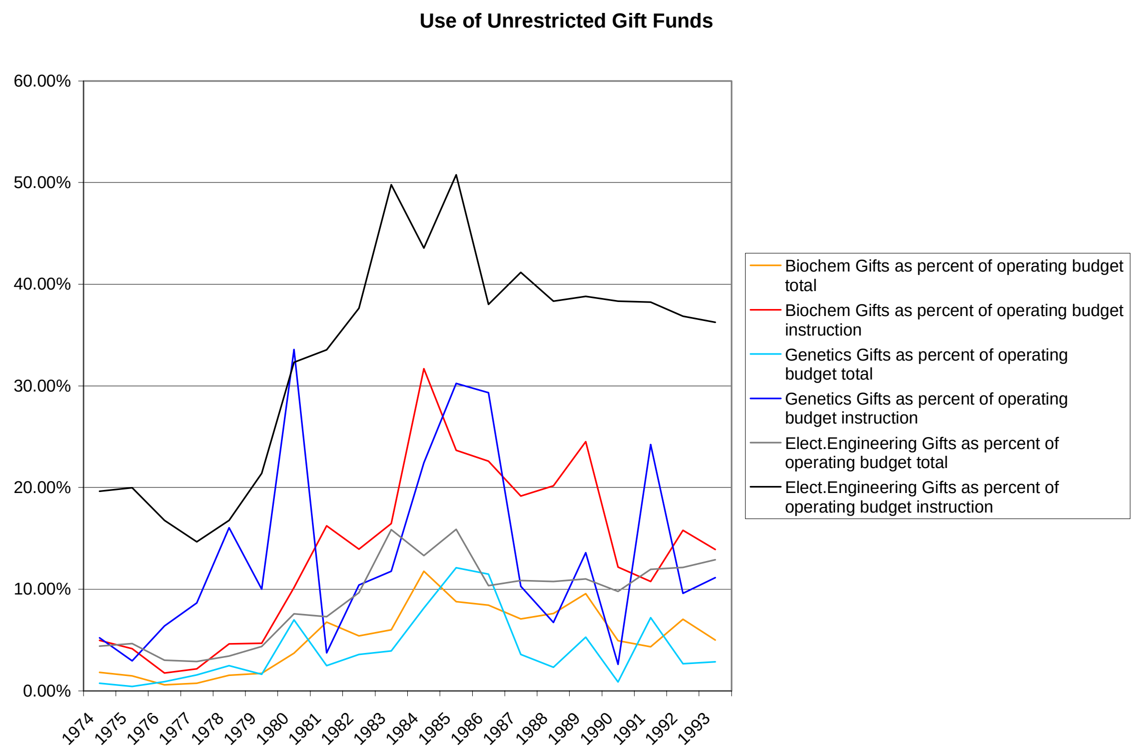

Figure 3 Use of Unrestricted Gift Funds by Three Departments
Source: Stanford Annual Reports

Endnotes

[1] *Medical Care, the University, and Society*. Speeches Delivered at the Dedication of the Stanford Medical Center, September 17 and 18, 1959. Stanford; Stanford University Press, 1959, p. 3.

[2] Spyros Andreopoulos. "Stanford University Medical Center. 25 Years of Discovery." *Stanford Medicine*, Fall 1984, pp. 3-4. Also see *The Alway Years*, 1957-1964, published by Stanford University School of Medicine, 1964.

[3] Terman-William Walter Greulich 1 August 1956, SC216, Box 62, Fol 8, Medical School 1956-57.

[4] Ibid.

[5] See for instance Terman's memo to Dean Robert Alway, 19 January 1962, Terman Papers SC160, Series III, Box 43, fol 1:

> I understand that you and your staff have recently developed a consensus in favor of charging faculty salaries to research grants, to the extent consistent with the time devoted to such grant-supported research and with the overall funding of research, instruction, and service. I heartily approve of this policy and of its long-run contribution to the financial well-being of the school.
>
> I would, therefore, suggest that full consideration be given to the use this year of an appropriate portion of the NIH general research support grant for faculty salaries which otherwise would be charged to university general funds.
>
> I understand that it is NIH policy that any institutional funds which may be released by the use of the general research support grant will continue to be used for the direct costs of research or research training. I am sure that there must be substantial research and research-training related expenses in the medical school on which any recovered salary dollars could be spent within the spirit of the policy.

[6] Kaplan threatened to leave Stanford if Alway and Teman did not succeed in getting Kornberg or someone comparable to join the effort to restructure the medical school.

[7] See Lederberg to Kornberg, 27 January 1958, Kornberg Papers SC359, Box 31, Fol. 1958.

[8] On limiting faculty size to 10 and maintaining the size of research groups at 9 graduate students and postdocs per faculty investigator, see "Long Term Plans for Biochemistry discussed in the faculty meeting of 8 September 1981. http://www.stanford.edu/dept/HPS/TimLenoir/Startup/KornbergSC359/Box5/Fol1981/FacMinutes8Sept81.pdf

[9] Joshua Lederberg to Susan Wright, 30 October 1982. The letter was written in the context of Wright's research for her book, *Molecular Politics: Developing American and British Regulatory Policy for Genetic Engineering*, 1972-1982 (Chicago: University of Chicago Press, 1994). Personal communication from Joshua Lederberg.

[10] Described in detail in Arthur Kornberg, *For the Love of Enzymes: The Odyssey of a Biochemist* (Cambridge, Mass.: Harvard University Press, 1989).

[11] Arthur Kornberg, *The Golden Helix: Inside Biotech Ventures* (Sausalito, California: University Science Books, 1995), pp. 2-3.

[12] Clayton Rich, Revised Financial Forecast for the School of Medicine, 30 December 1974, in Kornberg Papers, SC 359, Box 5, Fol. 1974-75. See especially the graphs on pp. 11-12 of the document. http://www.stanford.edu/dept/HPS/TimLenoir/Startup/KornbergSC359/Box5/Fol1974-5/RichFinancialForecast30Dec74.pdf

[13] Dale Kaiser to Department of Biochemistry Faculty, "Effects of Budget Cut-backs of Training Grant," 17 April 1981," Kornberg Papers SC 359, Box 5, Fol 1981. http://www.stanford.edu/dept/HPS/TimLenoir/Startup/KornbergSC359/Box5/Fol1981/BudgetCuts17Apr81.pdf

[14] Arthur Kornberg to Dale Kaiser, 10 September 1979. Kornberg Papers SC359, Box 5, Fol. 1979. http://www.stanford.edu/dept/HPS/TimLenoir/Startup/KornbergSC359/Box5/Fol1979/Kornberg-Kaiser10Sept79.pdf

[15] Ibid., p. 2.

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[16] Dale Kaiser to Biochemistry Faculty, "Creation of a substantial financial relation with a company," 4 December 1981. The memo is bound with notes by Arthur Kornberg, "Existing Problems." Kornberg Papers SC359, Box5, fol. 1981. Arthur Kornberg's notes for the discussion of this matter add an additional dimension:

Existing Problems

1. Chronic under funding
   a) lack of equipment renewal
   b) lack of equipment innovation
   c) Remodeling
2. Pattern of postdocs support
   a) Competition has grant-supported fellowships
   b) Aging faculty—spotlight keeps shifting
3. General decline of federal support
   a) Shift to industrial sources
   b) Increasing competition
   c) Shift to smaller grants and increased nuisance
   d) IAP will decline and become increasing burden

Historical Patterns

1. Cori's resistance to federal support
2. Hard vs. soft money
3. Times keep changing: pre-war to post-war; 80s to 90s
4. Attitudes change rapidly, but rigor in doing science remains the key thing
5. UCB, UCSF, MIT

http://www.stanford.edu/dept/HPS/TimLenoir/Startup/KornbergSC359/Box5/Fol1981/KornbergProblems4Dec81.pdf

[17] Arthur Kornberg, *Golden Helix*, p. 30.

[18] More on the startup of IntelliGenetics can be found in my paper, "Shaping Biomedicine as an Information Science," online as a resource for our project. http://www.stanford.edu/dept/HPS/TimLenoir/shapingbiomedicine.html
I will return to discuss this and related enterprises in the next quarterly report.

[19] Kornberg, *Golden Helix*, p. 151.

[20] See Ibid., p. 152.

[21] Ibid., p. 153.

[22] *Harvard Gazette*, 2 July 1981, I-B. Also reported in the *Wall Street Journal* on June 30, 1981, page 1C.

[23] http://www.stanford.edu/dept/HPS/TimLenoir/Startup/KornbergSC359/Box5/Fol1981/IndustSupportSept81.pdf

[24] Donald Kennedy, "Commercialization and Basic Research: Prosepectus for a Conference," 27 July 1981, Pajaro Dunes Papers, Stanford Special Collections, pp. 1-2.
http://www.stanford.edu/dept/HPS/TimLenoir/Startup/PajaroDunes/ConfProspectusDraft.pdf

[25] Phillip J. Hilts, "`Rules' Drawn for Marketing Gene Research, *Washington Post*, 28 March 1982, p. A1, A6.

[26] Robert Rosenzweig, Press Announcement, 27 March 1982, Pajaro Dunes Papers, Stanford Special Collections, pp. 10-11.
http://www.stanford.edu/dept/HPS/TimLenoir/Startup/PajaroDunes/PressAnnouncement.pdf

[27] Ibid., p. 11.

[28] Section excerpted in Rodney Adams and John Poitras, "Venture Capital: A Policy Paper for Stanford University," 28 October 1978. Lyman Papers SC 315, Box 33, fol Ad12.2.
http://www.stanford.edu/dept/HPS/TimLenoir/Startup/LymanPapersSC315/Box33/folAD12.2/AdamsVentureCapital20Oct1978.pdf

[29] Ibid. pp. 14-15.

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[30] Ibid., pp. 17-18.

> The following investment types, by stage of development, are considered as candidates for investment by Stanford:
>
> 1. Seed Capital
>
> "Seed Capital" (pre-start-up) investments will normally not be considered. However, Stanford will continue to participate in such situations through its technology licensing program where equity will be received in exchange for a patent license. Any proposal to invest will be recognized as an unusual exception to our policies.
>
> 2. Start-Ups
>
> Start-up situations will be considered under special circumstances: the management team and lead investor(s) should have prior experience in a start-up success, and the product development time should be short (1-2) years.

[31] Ibid., pp. 20-21.