CHEMICAL HERITAGE FOUNDATION

DAVID W. GOLDE

Transcript of an Interview
Conducted by

Audra J. Wolfe

at

New York City, New York

on

15 December 1999

(With Subsequent Corrections and Additions)

CHEMICAL HERITAGE FOUNDATION
Oral History Program
FINAL RELEASE FORM

This document contains my understanding and agreement with Chemical Heritage Foundation with respect to my participation in a tape-recorded interview conducted by Audra Wolfe on 15 December 1999.
I have read the transcript supplied by Chemical Heritage Foundation.

1. The tapes, corrected transcript, photographs, and memorabilia (collectively called the "Work") will be maintained by Chemical Heritage Foundation and made available in accordance with general policies for research and other scholarly purposes.

2. I hereby grant, assign, and transfer to Chemical Heritage Foundation all right, title, and interest in the Work, including the literary rights and the copyright, except that I shall retain the right to copy, use, and publish the Work in part or in full until my death.

3. The manuscript may be read and the tape(s) heard by scholars approved by Chemical Heritage Foundation subject to the restrictions listed below. The scholar pledges not to quote from, cite, or reproduce by any means this material except with the written permission of Chemical Heritage Foundation.

4. I wish to place the conditions that I have checked below upon the use of this interview. I understand that Chemical Heritage Foundation will enforce my wishes until the time of my death, when any restrictions will be removed.

Please check one:

a. _____ **No restrictions for access.**
NOTE: Users citing this interview for purposes of publication are obliged under the terms of the Chemical Heritage Foundation Oral History Program to obtain permission from Chemical Heritage Foundation, Philadelphia, PA.

b. ✓ **Semi-restricted access.** (May view the Work. My permission required to quote, cite, or reproduce.)

c. _____ **Restricted access.** (My permission required to view the Work, quote, cite, or reproduce.)

This constitutes my entire and complete understanding.

(Signature) David W Golde
David W. Golde

(Date) 7/19/00

Revised 7/8/99

Chemical Heritage Foundation
Oral History Program
315 Chestnut Street
Philadelphia, Pennsylvania 19106

DAVID W. GOLDE

1940 Born in New York City, New York on 23 October

Education

1962 B.S., chemistry, Fairleigh Dickinson University
1966 M.D., McGill University

Professional Experience

University of California School of Medicine, San Francisco
1972-1973 Instructor in Medicine
1973-1974 Assistant Professor in Medicine

University of California, Los Angeles [UCLA] School of Medicine
1974-1975 Assistant Professor of Medicine
1975-1979 Associate Professor of Medicine
1979-1991 Professor of Medicine
1991-present Professor of Medicine Emeritus

Cornell University
1991-present Professor of Medicine, Medical College
1992-present Professor of Molecular Pharmacology and Therapeutics, Graduate School of Medical Sciences

Memorial Sloan-Kettering Cancer Center
1991-present Member
1991-1996 Head, Division of Hematologic Oncology
1996-present Physician-in-Chief, Memorial Hospital

Honors

1965 Alpha Omega Alpha Honor Society, McGill University
1962-1966 University Scholar, McGill University
1966 J. Francis Williams Prize in Medicine, McGill University
1986 Outstanding Faculty Research Lecturer, UCLA
1986 MERIT Award, National Institutes of Health
1991 Enid A. Haupt Professor of Hematologic Oncology, Memorial Sloan-Kettering Cancer Center

ABSTRACT

David Golde begins the interview with a discussion of his early years and education in Bayonne, New Jersey. In high school, Golde developed an interest in medicine, which was stimulated by his biology teacher. He received his B. S. in chemistry from Fairleigh Dickinson University in 1962. He then attended medical school at McGill University, graduating in 1966. After graduation, Golde completed his internship under the supervision of Dr. Holly [Lloyd] Smith at the University of California, San Francisco [UCSF]. Golde joined the faculty at UCSF after completing his residency at the National Institutes of Health. His experience in clinical pathology at NIH steered him into hematologic research at UCSF in Martin J. Cline's laboratory. While at UCSF, Golde met several influential scientists who first sparked his interest in hormones. In 1974, Golde left UCSF for the University of California, Los Angeles [UCLA], where he continues his affiliation today as Professor of Medicine, Emeritus. Throughout most of the 1970s, Golde's major field of research was in colony-stimulating factors. Golde observed cell lines to determine which tissues make colony-stimulating factors. In his laboratory at UCLA, Golde developed a major cell line called KG-1 with H. Phillip Koeffler. The KG-1 cell line was later used to clone alpha interferon. Golde began studying hairy-cell leukemia, researching the cell origins for the disease. Studying cultures of the Mo cell line (named after John Moore, a hairy-cell leukemia patient), Golde's laboratory was the first to purify human GM-CSF [granulocyte-macrophage colony-stimulating factor]. With Robert Gallo he discovered a specific strain of retrovirus named HTLV-II, and with his postdoc, Irvin Chen, was the first to clone the HTLV-II virus. Golde concludes the interview with a discussion of the relationship between the biotechnology and the pharmaceutical industry, issues regarding federal transfer of information, and thoughts on his contributions to medicine.

INTERVIEWER

Audra J. Wolfe is a doctoral candidate in History and Sociology of Science at the University of Pennsylvania. She received an M.A. from that program in 1999 and a B.S. in chemistry and biochemistry from Purdue University in 1997. She has been the recipient of a National Science Foundation Graduate Fellowship and was named an Honorary Mellon Graduate Fellow in the Humanistic Studies for 1997-1998. In addition, she was the 2000 summer Othmer Student at the Chemical Heritage Foundation. She is currently researching and writing a dissertation on the public role of American biologists in the postwar years.

TABLE OF CONTENTS

1 Early Years

Born in New York City. Growing up in Bayonne, New Jersey. Working as coffee chemist for Maxwell House. Attending medical school at McGill University. Residency at NIH. Important influences for choosing medical field. Holly [Lloyd] Smith. Internship at UCSF.

3 Early Career

Joining faculty at UCSF. Interest in hematology. John Beck. Working in Martin J. Cline's laboratory. Gordon Tompkins. C. H. Li. Leaving UCSF for UCLA. Importance of role models. Research interests in the 1970s. Setting up first normal bone marrow donation program. Theodore Finley.

7 Research

Growing interest in colony-stimulating factors. Uses of colony-stimulating factors. Obtaining patient materials for research. Establishing cell lines. Ethical issues in medical research. Development of KG-1 cell line. H. Phillip Koeffler. Studying hairy-cell leukemia.

11 Discovery

John Moore. Purifying GM-CSF. Judith C. Gasson. Robert C. Gallo. HTLV-I. Irvin S. Y. Chen. Studying retrovirology. Discovery of HTLV-II. Cloning HTLV-II. Molecular biology as an influence on biomedical research.

15 Conclusion

Biotechnology business and the pharmaceutical industry. Consulting for Genetics Institute. Intellectual property rights. Contributions to medical science. Recent research on Vitamin C.

18 Notes

19 Index

INTERVIEWEE: David W. Golde

INTERVIEWER: Audra Wolfe

LOCATION: New York City, New York

DATE: 15 December 1999

WOLFE: Let's start by discussing your education and training. Can we start by describing your educational background?

GOLDE: Sure. I was born in New York City and I went to public schools, graduated from high school in Bayonne, New Jersey. It was Bayonne High School. I then went to Fairleigh Dickinson University in New Jersey and got a bachelor's degree in chemistry. I graduated almost a year early, and so I worked as a coffee chemist at Maxwell House in Hoboken, New Jersey. Good memories of that. I used to eat lunch in a little park called Elysian Field where *On the Waterfront* was filmed.

WOLFE: That's wonderful.

GOLDE: Then I went to medical school at McGill University. I had gotten a scholarship, and graduated from McGill in 1966. During the summers I did research in cardiology in Costa Rica. And then I did my internship in medicine at the University of California in San Francisco [UCSF], 1966 to 1967. That was during the Vietnam era and I was in the Berry Plan, assigned to the Navy. They were preparing to send me to Vietnam when I got a job offer from the National Institutes of Health [NIH] in the Division of Regional Medical Programs, which was headed by Robert Q. Marston, who later went on to become the Director of NIH. So I came to NIH and I did one year with the Division of Regional Medical Programs. Then I began a residency in clinical pathology at the NIH Clinical Center, and I completed two years, which is the full residency period. I returned to the University of California in San Francisco as a resident in medicine and then a fellow in oncology. The hematology training was largely at NIH. Of the two years in clinical pathology, I spent about a year-and-a-half in hematologically related work. Then I joined the faculty of UCSF as an instructor in medicine. That ended my formal education, but not my education.

WOLFE: Of course. What factors influenced your choice to go to medical school? How did you become interested in medicine?

GOLDE: Well, I had some good motives and perhaps some motives that weren't as high-minded. The good motives were: an interest in biology that was engendered by a biology teacher in high school. And the memories I have of that were looking through the microscope at a drop of water from the aquarium and seeing all these life forms. I liked science and I liked biological science, and I wanted to combine biological science with some service to mankind. I didn't want to just do science in isolation, but wanted to do it in a way that I could apply it directly, in one way or another, to patient care. I suppose I had another motivation, too, as I recall. I came from a poor family and there's a strong desire to—for lack of a better term—"make it." I don't know what exactly constituted "making it," but I think in my mind at that time, becoming a doctor was equivalent to whatever "making it" was supposed to mean. And in retrospect, particularly in that era, in the 1960s, a physician was held in respect. Once you became a physician, you had a title of respect that was different than, for example, simply becoming a lawyer. If you became a lawyer, you then had to become a successful lawyer. So I think there was some attraction to a very clear level of accomplishment, and maybe that wasn't the most high-minded goal, but it was there. It influenced me. Primarily I was influenced by the good things: by an interest in biology and a desire to be of service.

WOLFE: You mentioned the cultural limits of the 1960s. Did any of that change how you felt about medicine, since this was the time that you were completing your education?

GOLDE: No. It was—particularly at McGill—a very classical school and I considered that I was privileged to have an unusual quality of medical education. Frankly, a quality that I'm not sure is easily available today. Not only the depth of medical and biomedical scientific learning, but a deep sense of heritage, respect for patients, and the privileged position of the physician with respect to the responsibilities that the physician takes on by accepting that role. And I can recall that I was shocked when I made rounds at other hospitals when I was looking for an internship—particularly in New York—at the extreme informality of the house officers. We pretty much stood at attention by the bedside, one foot away, and it was something that stuck with me. One professor, a Professor [Francis A.] McNaughton who was a famous neurologist, used to demonstrate various signs and symptoms of neurological disease to students—this was before the CAT scan era, and a time when clinical skills in localizing lesions were highly prized. He would point these out in patients who had deficits and would do so in such a way that patients were never embarrassed, and never made to feel that they weren't being treated with the greatest respect. And that's something that stands out in my mind—the exquisite attention he paid to the patients and to the patients' feelings regarding their participation in the teaching exercise. So it was a great school, not only for content, but also for philosophy and tradition.

WOLFE: All right. So then what drew you to hematology and oncology?

GOLDE: Ah, that's interesting. When an individual from a poor background goes to medical school, I think they have a different image than, perhaps, someone from a more privileged origin. I considered medicine to be surgery. This was before I got to medical school, because that basically was how you fixed people. [laughter] And so I believed I was a surgeon without giving much thought to it. I simply didn't question it. Also, I was very focused on day-to-day efforts in medical school. At that time, in McGill, the examinations were given at the end of the year, and if you failed one or two examinations, I think you were allowed to make it up in the summer. If you failed again, you would be asked to leave the school, and a large number of students were, so there was a survival element. We really wanted to succeed. And that's where all my attention was. But I just assumed I'd be a surgeon. Then when I got to do the surgical rotations, I did notice that I was a little bored just holding the retractors. [laughter] I was so confused that I actually applied for surgical internships as well as medical. The head of medicine, then, at the Royal Victoria Hospital in Montreal, was Dr. John Beck, who subsequently went to UCLA [University of California, Los Angeles] and I got to be reacquainted with him there. He was a very accomplished endocrinologist and certainly the senior physician at Royal Victoria Hospital.

So he called me into his office and said, "Golde, what is this I hear about you going into surgery?" I remained fairly mute, or I stammered, probably. [laughter] And he then said, "Do you like to sew?" And I said, "No, not particularly." He said, "Then why go into surgery?" [laughter] Well, I didn't reply coherently, I'm sure, and then he said, "Well, you know, where you should go is the University of California in San Francisco, and you should go into Dr. [Lloyd] Holly Smith's program." So I went to Dr. Holly Smith's program at UCSF. There was an intern-matching program and I ranked UCSF at the top, but I am sure Dr. Beck must have called to seal the deal. When I got there—internship was pretty much like leaving your life. Not that medical school wasn't intense, but internship was a total immersion, and that year—it's hard to remember any details. But at the end of the year, one had a somewhat "superman-like" feeling. I doubt it was justified, but it's like the most extended boot camp that you can imagine. This was at a time when lifestyle—that phrase didn't exist.

WOLFE: Right. [laughter] Yes. Let's move on to your early career after your formal education was completed. How did you end up at UCLA?

GOLDE: Well, when I first joined the faculty at University of California, San Francisco, I got into hematology because when I was at the NIH, I was in the clinical pathology program. One had to choose among hematology, chemistry, or microbiology. I chose hematology and even though at medical school I felt I was a surgeon, it turns out I was quite capable—in fact, fascinated—to sit for hours on end and look through the microscope. So I repeat this to my junior colleagues that sometimes we think we know what our nature is and it turns out that the perception is a prejudice. It's a view that one gets of oneself that's not a studied view. So I saw myself as being very active, physical, and hence surgery, or at least cardiology. Not a passive kind of specialty like hematology, which involves morphology and looking through microscopes. But you find out a lot about yourself and what types of things you have great

patience for. And so I always tell youngsters, "Don't say you're no good at this, or you can't do that, because you have to try these things and find out where your inclinations are."

So I joined the faculty and began my laboratory work. I worked in the laboratory of Martin J. Cline, who later would become famous for the first attempts at gene therapy, which had an unhappy end. I was a junior faculty member and only partially independent. I still depended on Dr. Cline for support in my research. But I got a great start in hematologic research because while I was at the NIH I had extensive experience in reading bone marrows and dealing with the enormous pathologic material that was available. We also had a ritual in which I would sit at the microscope and the clinicians would bring me the bone marrows of their patients and I would, like the Oracle at Delphi, declare remission or relapse, and I really became involved in the whole process. And I got to be a fairly accomplished hematological morphologist.

So when I began to do my studies in the laboratory, I directed my work at where blood cells were formed, which was in the bone marrow. What I wanted to do was to understand what regulated the production of blood cells because I had the, then, somewhat naive dream that once we knew what regulated the production of blood cells, that we could actually control the production of blood cells, which was really a novel thought for that era. Even many of the leaders in hematopoiesis never believed that we would find information about the humoral factors regulating blood cell production and how we could find a way to use them. That's been the greatest scientific joy of my career—going from a period where it was almost unthinkable, to actually seeing it and participating in the development of some of the first hormones that would regulate blood cell production.

While at the University of California in San Francisco, I got to know Gordon Tompkins, a leading biochemist whose life was cut short by an acoustic neuroma, and C. H. Li, who was the first man to purify growth hormone—these were two senior scientists at UCSF. Gordon Tompkins was famous for dissecting the biochemical steps of corticosteroid hormone action, and C. H. Li, of course, for polypeptide hormones, particularly growth hormone. That's the wonder of our academic communities.

I met Dr. Tompkins on the bus, the UC bus that used to go to Marin County. On Fridays we would stop and buy beer and have pretzels and we had a nice bus ride. I was worried about the people who got off at Santa Rosa, which was the end of this long bus ride—because the longer the bus ride, the more beer you drank. [laughter] So, when I explained what I was working on, Gordon Tompkins said, "Well, you don't have purified cells and you don't have a purified hormone, so it's hopeless. You either start with purified cells and look for a hormone, or you start with a purified hormone and figure out the cells." So he advised me to begin working with corticosteroids. C. H. Li told me the same thing, only he advised me to work on growth hormone. And it was through my connection with these great scientists that I got the vision of hormone action and hormones working through receptors, and I could actually picture hormones in the body interacting with blood cell precursors, regulating their production. That's at the stage where I was searching for human colony-stimulating factors, which had been

identified about 1966, or at least it had been surmised that they existed based on the *in vitro* culture techniques that had been developed in Israel and Australia.

There were many contacts at UC-San Francisco that also stimulated my interest. There was a pulmonary physician [Theodore N. Finley] who developed pulmonary lavage. It was through him that I began working on pulmonary macrophages and came to understand the macrophage system as an extension of cell production in the bone marrow.

I left UC-San Francisco on the first day of January 1974 to go to UCLA because Dr. Cline had been recruited to UCLA the previous year. I was still very junior in my development and under-funded, and I felt that I needed additional support before I could build up the kind of laboratory I felt that I wanted to have. So I went to UCLA. That was the hardest move I ever made, because the difference between San Francisco and Los Angeles was a lot greater than many people might imagine. But I survived it and I stayed at UCLA for eighteen years.

WOLFE: So while you were building up the laboratory there, did you think of yourself primarily as a clinician or as a researcher and how did you envision the balance between doing laboratory work and working with patients?

GOLDE: Well, in those days there were very good role models for physician-scientists. There was a clear path for the physician-scientist. I don't think they were called that then. I think we just used the term "academic medicine" to cover this. Certainly, at UC-San Francisco there were an enormous number of role models including the Chairman of Medicine, Dr. Holly Smith, whom we could emulate. And they used the phrase "the triple-threat man," and it was "man" because at least prior to that time, most physicians were men. The "triple threat" referred to research, teaching, and clinical care. And so you should be a clinician like Sir William Osler, a teacher of mythological proportions, and of course a fabulous investigator. There's a lot of talk now about whether such a person did exist, or could exist. But I believe a person something like that did exist. It was a simpler time. The amount of medical information was much more limited. In fact, there were very clear role models for this, and the goal of the academic pathway, of course, was to become an Associate Professor with tenure. That usually happened at the time you gained acceptance to the American Society of Clinical Investigation, otherwise known as the "Young Turks." [laughter] So the pathway for the physician-investigator in those days was rather clearly delineated.

WOLFE: Do you feel such role models are now lacking?

GOLDE: Yes. It's a lot harder now. The truth is, it takes so much to become a superb clinician that it would be hard to have the time to do other things and still achieve at the highest clinical level. What I find myself doing over the years to try and maintain my clinical prowess, such as it is, is to constrain my clinical activities to a narrower and narrower range. When I finished my

fellowship, I took the boards in oncology the first year they were given—I'm not sure I know what that year was, but it was the early 1970s—and I thought it was a fairly easy examination. Now it's much more comprehensive. But my clinic was made up of patients with brain tumors, breast cancer, hematologic cancers, gynecologic cancers, cancers of all kinds, because the surgical specialists didn't want to deal with advanced cancer, with metastatic disease. That was a medical-oncologic problem. Also I'd have to say that oncology was not held in high esteem in that era. It was not one of the classical medical specialties such as metabolism or endocrinology, or cardiology. And I would see at clinic sometimes fifteen or twenty patients with a potpourri of tumors, which today would be unimaginable, particularly at the institution where I am now where the whole basis of our care is super-sub-specialized. We also used to mix up our own chemotherapy, which would be unheard of today.

WOLFE: If you could put yourself back in the 1970s, where did you see your research going at the time? Where did you see your career going at the time?

GOLDE: Well, in the early 1970s, I was pretty well set on the quest to understand what regulates the production of blood cells. I was in a very good environment to pursue that because there was ample scientific collaboration and collegiality, in an informal environment, which in some ways is lacking today. It was a culture of scientific collegiality—a very strong culture. I mentioned the bus to Marin story and I'm sure there are many stories very much like mine of the direction of people's research being governed by interaction with people on the bus, so to speak. Also there was a culture of studying human disease—studying it in humans and taking blood and studying that blood. And of course the hematologists would be particularly focused on that. I set up the first normal bone marrow donor program. Bone marrow donations were considered very painful in those days. I think they were painful because they weren't done very well. Frequently they were done in the sternum. And when I put up the signs saying that we would pay fifty dollars for a bone marrow donation, my colleagues laughed at me and said, "No way!" So I became the first volunteer, and Dr. Cline did a bone marrow on me. Unfortunately, he did a sternal bone marrow and they are painful. Subsequently, I've had many bone marrows done in the posterior ilium, which is the preferred location. A bone marrow aspirate can be done without much pain, and not much discomfort at all, and fifty dollars was a lot of money in the early 1970s. Ultimately I had a lot of donors. I remember my secretary was a conscientious donor. And so we obtained the human material to work on human bone marrow. I was working on these bone marrow cultures where I could use both my morphologic and biological skills. As I mentioned, we also looked at macrophages and got an understanding of how macrophages evolved from bone marrow progenitors as well. And in addition, we subsequently found out that macrophages can proliferate *in situ*. One of the exciting works at that early time resulted in a *Nature* publication showing that the human alveolar macrophage was capable of replication (1). And that was done in collaboration with a pulmonary colleague. Unbelievably, he used a Foley catheter. Foley catheters are normally used to drain the bladder, but they're made of soft rubber and we found them ideal for doing pulmonary alveolar lavages. I even did an alveolar lavage on him. His name was Theodore Finley, originally from the University of Washington in Seattle.

A lot of the early work was what we might call descriptive now, but I was searching for cells that produced colony-stimulating factors. One of the early works showed that the monocyte in the peripheral blood produced it, and subsequently we showed that the activated lymphocyte, which we later came to understand was the T-lymphocyte, produced colony-stimulating factors. So the early work was focused on ascertaining the cellular origin of these colony-stimulating factors and determining some of the modulators of their production. For example, endotoxin is known to stimulate colony-stimulating factor production in mice. I ultimately went on to do this in humans, and there's a well-known story of an auto-experimentation where I almost died at UC-San Francisco. We'd shown that if you inject endotoxin in humans (often myself), you could increase the serum concentration of colony-stimulating factor. I had the notion that one could produce colony-stimulating factor by injecting endotoxin, take off the plasma, and then use that plasma therapeutically. And here again, the advantage I had was that, due to my background and contact with endocrinologists, I had a vision of how these colony-stimulating factors worked as hormones. When I say "vision," I mean it quite literally. I had an actual picture, just another hormone that interacted with a receptor on a cell. Now, others in hematology, even though they themselves discovered many important components of the hematopoietic system, somehow never believed—they were very skeptical that these factors were actual physiologic factors that we could use to actually control blood cell production.

So these early experiments with endotoxin came to an end when I injected myself with perhaps too much endotoxin and went on a cell separator so we could obtain an adequate amount of plasma. I guess the combination of the endotoxin and the fact that I was having a reasonable amount of my plasma volume removed caused me to lose consciousness. But I had an agreement with the woman who was running the machinery that should I pass out, just give me back some of that plasma, and she did that, but in the interim she also called a "Code Blue." Called the cardiac team. Luckily, my consciousness returned before this team may have dispatched me to my eternal rest, and that's a famous story. Ultimately, we showed that this plasma, when given to a single patient, a child with neutropenia, actually stimulated the production of neutrophils in that child. Of course, that experience left me absolutely and totally convinced that we could isolate these colony-stimulating factors and they would prove therapeutically useful.

WOLFE: So can you just reiterate what colony-stimulating factors are useful for?

GOLDE: Well now, of course, they're actual drugs and they're not called "colony-stimulating factors." But the hormones that regulate hematopoiesis are a broad family. Erythropoietin is the best known and erythropoietin stimulates red cell production. It's used in renal dialysis and kidney disease, and it's used very widely in cancer therapy. Now it seems commonplace to think of stimulating red cell production, but it was hard to conceive of this at one time. The white cell colony-stimulating factors that are known as CSFs have been developed as drugs, used to stimulate white cell production, mainly in cancer-related conditions.

WOLFE: Could we return to this question of materials for a bit? You talked about self-experimentation and also obtaining materials from other lab workers and from donors. Do any of these come from patients, and how are materials obtained for research purposes from patients? Or how were they obtained in the 1970s?

GOLDE: Yes. It was very commonplace in the 1970s, even the late 1960s, to study patient material. Before the biotechnology revolution, I would say that it was only medical scientists who did that. That's what defined the medical academician—someone who studied human disease in humans. It was uncommon for a Ph.D. scientist, I think, to actually directly study human material. Cell lines were derived much earlier, in the 1960s, and these cell lines became important reagents for biologic study. But directly studying human material was in the province pretty much of the academic physicians. By the time I began my career, we had IRBs [Institutional Review Boards], we had human subject protection committees and review committees, and one got informed consent. I think the hematologists probably were most used to this because drawing blood was so common. Bone marrow was a little bit of a step, and I'm sort of bemused now that it's so commonplace. As you know, people donate large volumes of bone marrow for actual transplantation with no compensation.

WOLFE: Who would have access to these kinds of materials, and would researchers share those, or would they remain with them?

GOLDE: The primary tissue was shared within laboratories and among related laboratories. I don't really recall sending them anywhere. They were perishable anyway. Cell lines were more available, but many of them weren't useful, particularly some of the hematopoietic cell lines, a large number of them were EB [Epstein-Barr] virus transformed B-cells and didn't always represent the underlying disease process.

WOLFE: Did you have much interaction with the ATCC [American Type Culture Collection], at that point? Did people who worked with cell cultures do much with them?

GOLDE: Well, I don't remember when I learned of them. I didn't have a lot of contact with them, but yes, I think they've been in existence quite a while. I dealt almost exclusively with primary tissue, and frankly, I didn't have a clear notion regarding the utility of cell lines in what I was doing, initially. Subsequently, I of course did.

WOLFE: As cell lines started to become more useful to you, what kind of things would you look for to determine whether it would be worth the effort to do a cell line? I know in the 1970s, it took a lot more—it was more complicated to establish a cell line than it might be now.

GOLDE: I frankly did not know much about cell lines. I knew of their existence. I didn't use them because there weren't great hematopoietic cell lines. I was working with myeloid tissue. There was not a myeloid cell line that you could use. The lymphoid cell lines were frequently transformed normal B-cells, which weren't the things I was interested in. And I would have to say that I was sort of determined that primary normal tissue was the important thing for me to work on. I would say my early work was entirely focused on that. I think I ignored established cell lines until later.

Later, getting back to my conversation with Gordon Tompkins, who said, "You either have purified cells or purified hormone, if you have neither, forget it," I came to understand that I did need pure cell populations to work with, particularly when we were looking for a source of colony-stimulating factor to purify. We looked at a number of established cell lines. I didn't have a sense that nonhematopoietic cells would make the colony-stimulating factors. Others found nonhematopoietic cell lines that produced useful substances, for example, a bladder cell line, from which G-CSF was purified. My initial work showed that monocytes and macrophages made the colony-stimulating factor that I was studying, as well as activated T-lymphocytes. So that's where I focused my efforts. There weren't good macrophage cell lines, and most of the T-cell lines that were available weren't mature T-cells so they tended not to make it. Our techniques then were crude, too. So I think with finer techniques, we would have found that there are many cells lines and many tissues that make these colony-stimulating factors, but we didn't know it then.

WOLFE: All right. You mentioned at one point that your hospital up there did have IRBs and a human subjects committee. What impact would you say that the bioethics movement has had on biomedical research?

GOLDE: Well, I don't know what the bioethics movement is. There have been many swings in the ethics of biomedical research. All the way from the "guinea pig" notion of scientists taking advantage of the patients, certainly an extreme example being the Tuskegee experiments. There are other examples, such as medical scientists using prisoners.

[END OF TAPE, SIDE 1]

GOLDE: More recently, it was deemed unethical to use prisoners because it was a population under compulsion. Things have turned many times because from the "guinea pig" notion, the abuse notion, it came to be believed that certain types of medical research represented access to

modern medicines. Therefore if you are not eligible for these types of investigations, you are "denied access." I think that came to the fore at about the beginning of the AIDS [Acquired Immune Deficiency Syndrome] epidemic. So it's gone through a lot of transformations. In fact, I can remember when there was a movement whereby it was said that prisoners shouldn't be "denied access" to clinical trials in the context of the AIDS epidemic. It was felt that "access" represented the ability to be treated by what were, perhaps, better drugs. So it's been somewhat of a moving sociologic phenomenon. I think our current methodology for regulating human experimentation is reasonably thorough. And there are always the risk/reward issues and the changing sociologic notions of what the clinical trial or clinical research represents, all the way from perhaps unnecessary intervention to access to important new innovations in care.

WOLFE: All right. I'll ask a related and more specific question. In 1978, the California legislature passed a Protection of Human Subjects in Medical Experimentation Act. It basically stated that explicit, informed consent had to be given to use materials for research. Did that have any effect? Was there any discussion of that among people in your field?

GOLDE: Yes, well the law still requires interpretation, because even if informed consent is obtained for tissue, let's say, in surgery—pathologic tissue, the question is: what can be done with that tissue? If the informed consent is general and says, for example, that it's for scientific research, then some might argue that it's not sufficiently informed on the basis of lack of specificity. If it is specific, then the research is solely delimited to that specificity. There are many arguments surrounding this, and there are competing rights. Privacy issues are very important. But also there's the imperative to advance medical science. To me, the question of appropriate consent hinges on a properly informed subject.

WOLFE: On the topic of advancing medical science, can you say a bit about the discovery of HTLV-II [human T-cell leukemia virus, type II] and how you saw that fitting into your work and what that meant for you?

GOLDE: Well, that was an accident. There were two important cell lines developed in my laboratory at UCLA. One was the KG-1 cell line, which was a myeloid leukemia cell line that proved to be important because the cells responded to colony-stimulating factors and underwent differentiation with appropriate stimuli. So here was a cell line that was a pure cell population that could respond to a colony-stimulating factor. The cell line turned out to be important—it is the cell line from which at least one of the alpha interferons was cloned, and it was developed by a fellow working in my lab, Phil [H. Phillip] Koeffler, hence the name KG-1—Koeffler-Golde 1. That cell line has been useful in biomedical research. It was the second myeloid leukemia cell line. The one previous to that was known as HL-60, and that also has been an extremely useful cell line.

The other thing that came from the KG-1 cell line that turned out to be very important in hematology was CD-34—well, CD-33 and CD-34—which defined a stem cell and a progenitor population and CD-34 cell selection is a common means of enriching stem cells. There were many other myeloid cell lines that were developed subsequently and they've proved to be useful, and all for different reasons. Some had chromosomal abnormalities and were useful in cloning the breakpoints. Others are useful for studying signaling.

In my laboratory at UCLA we developed a number of cell lines. In those days, it was very much like cooking. The development of cell lines was not a rigorous scientific undertaking. We thought we were pretty experienced cell culturists and that some of our techniques were particularly useful, but this was not the kind of thing that was studied formally.

I was studying hairy-cell leukemia, which is a disease I became interested in because as soon as I arrived at UCLA I was formally presented at a conference with a patient with hairy-cell leukemia. I'd gotten to know that condition from my time at the NIH. It was not a well-known entity, and when I told them I thought the patient had hairy-cell leukemia, some of the senior hematologists were somewhat taken aback, and this particular patient was not treated optimally, in retrospect. He became very sick and I got to know him, and I suggested that he have his spleen taken out. Once the spleen was taken out, he had a long remission that lasted more than twenty years. Splenectomy was very counter-intuitive treatment. The thought was, why take the spleen out if the disease is in the blood and the bone marrow? Still today, we don't understand completely the role of a splenectomy in hairy-cell leukemia. But it was an effective therapy and some of the other more-traditional treatments at the time should have been avoided.

Because of my familiarity with the disease, other patients were referred to me. How does one become an expert in a disease? I guess the first thing is, you get thought of as an expert, and then it becomes a reality because you see so many patients with it. Everyone was concerned with what the cell origin of hairy-cell leukemia was. What kind of cell was it? And there were great debates in the literature at the time. So with some colleagues, I undertook a study of this, and we came to the conclusion that they were B-cells based on the fact that they could synthesize immunoglobulin in culture. We were trying to develop cell lines so we could study them in more detail. And then a patient [John Moore], subsequently to become famous, was referred to me, again because I was known as an expert in that area. He was a younger patient than you would normally see, and he had absolutely massive splenomegaly, perhaps the biggest spleen I had encountered in that disease. Otherwise, he appeared to have typical hairy-cell leukemia. So we recommended a splenectomy, which was performed, and as usual, we went to the pathologists to get a piece of tissue and try to make a cell line. What was unique about this cell line was that it was composed of T-cells. Mature T-cell lines were not common. They were very rare at the time. This would sort of contradict what we thought we had determined with some precision, and that is that the cell of origin with the hairy-cell was the B-cell. There is a hard-to-interpret literature of variant hairy-cell leukemias composed of supposed T-cell origin. We concluded that he had a T-cell variant of hairy-cell leukemia, which I now doubt.

In any case, knowing that activated T-cells made colony-stimulating factor, we tested the cell line for the production of colony-stimulating factor and we found in fact that it was a good producer. So, ultimately, I decided that we'd try and purify this hormone—again, I had this notion of hormones—from the cell line, and that turned out to be a difficult path. We worked on it for many years. We did purify it. With Judy [Judith C.] Gasson in my lab, we finally purified a very tiny amount in about 1984, I think. So I'd been working on the colony-stimulating factors since 1972. That was a long, long trip.

We found other things in there that we could have found elsewhere, but we were so fixated on T-cell factors. We found an activity we called erythroid-potentiating activity, EPA, which stimulates erythropoiesis. We purified that, and working with the Genetics Institute in Boston, ultimately cloned it. That turned out to be what is now known as TIMP-II—tissue inhibitor of metalloproteinases II. And so it was a very exciting time because of the impact of molecular biology on the more classic biomedical research. There was the ability to clone genes, to express proteins, and to do that which previously was undoable. And also a lot of surprises. Many people would purify proteins, thought they were all working with different proteins, and found out they were all working with the same one. People who thought they were working with the same one, when ultimately they were cloned, found out that they were different. Erythroid-potentiating activity would tend to be somewhat of a diversion, but the techniques we used for purifying what we called EPA, were used to purify GM-CSF [granulocyte-macrophage colony-stimulating factor].

So we were busy purifying GM-CSF, and I'll finish that story. We finally purified it. Judy Gasson was in my laboratory at the time, and she was the first author of the *Science* article (2). She is now the director of the Jonsson Comprehensive Cancer Center at UCLA. It's always rewarding when your young colleagues and students turn out to be so successful. Phil Koeffler is a professor at UCLA, he's very successful as well. So in the midst of all this exciting activity, a human leukemia virus—retrovirus—was isolated in Bob [Robert C.] Gallo's laboratory from a T-cell line that came from a patient who was believed to have a type of T-cell leukemia that affects the skin. This was called HTLV-I. I was presenting some material, I believe, at a meeting in Europe that described the Mo cells and what they were producing, and Dr. Gallo felt that this was very reminiscent of the cells where he'd found HTLV-I. Ultimately, we sent him material to look for a virus, and he found a retrovirus that had properties that were somewhat different from HTLV-I, and justified it being given a different designation, a different strain, so we found HTLV-II.

Then at that time, I had a post-doc, a very skillful young man, Irvin [S. Y.] Chen, who'd just finished his Ph.D. with Howard [M.] Temin at McArdle [Cancer Research Laboratory] in Wisconsin. He came to my lab because he wanted to work on GM-CSF. His background was in retrovirology and his mentor was at [University of] Wisconsin. He felt that retrovirology wasn't going places because there was no human retrovirus at the time. He was an extremely bright and hard-working young man, and here HTLV-II pops out of one of our cultures! So he turned to me one time and he said, "What do you think if we try and clone HTLV-II?" Well, cloning a virus in those days wasn't a trivial matter at all. You know, there were no kits then.

You had to get or make reagents. It was quite an undertaking—particularly since my laboratory was not a virology laboratory.

So we frankly discussed what that would entail and the competitive nature of it, given that Dr. Gallo had a huge effort in human retrovirology at the National Cancer Institute [NCI] . The brashness of youth has its advantage and he said, "Well, if you're committed to it," then he would be willing to do it. Of course, I said, "Well, if you're committed to it!" [laughter] And so we made a mutual commitment, and with a very small band of people, and reagents that he got from his mentors at McArdle, we successfully did this. Now, what Irvin did was to do a partial sau 3A digest. The issue here was that in cloning the virus, you have to pick restriction enzymes to use to clone into phage, and you don't exactly know which restriction enzyme to use. Well, we luckily came up with the whole viral genome. I don't remember the year, but it was a meeting in Keystone where we used to put on exciting hematopoiesis meetings, and we were sitting in the audience. Irvin was going to present the cloning of HTLV-II. Bob Gallo was there, and Bob got up first and showed a half of the genome of HTLV-II because he had used the *Eco* RI. HTLV-I had no *Eco* RI site but HTLV-II did in the middle of the genome. So the Gallo lab cut it in half, and we were the first to clone HTLV-II.

WOLFE: Right!

GOLDE: And I was sitting there with Judy Gasson; she was sitting next to me. Well, you know, there's a competitive nature to this business, and she let out a gasp of delight, looking at half the genome. [laughter] And of course we published that as a full article in the front of *Nature* (3). Irvin went on to great success. He's the head of the AIDS Center at UCLA.

WOLFE: So was this the first cloned human retrovirus?

GOLDE: No. HTLV-I had been cloned. But the cloning of HTLV-II turned out to be important because it's somewhat of a complex genome; not as complex as HIV [Human Immunodeficiency Virus], but an appreciation for what was then known as the X-region, the tax region, started to become clear by looking at the homologies between HTLV-I and II. Then a group at UCLA went on to actually study what were then called the X-proteins, including Dennis Slamon, who's now the head of hematology and oncology at UCLA. I remember we had a paper in *Science* that dealt with a transcriptional detail that had not been seen before (4). It was an unusual skip in transcription within the viral genome, but it was so exciting in those days that even a detail raised all sorts of interest. The clinical issue was another matter, because this virus pops out of a culture and the question is: does the patient have the virus or is this just something that appeared in the culture? Ultimately, the NCI group came to UCLA to meet the patient and the family and we did some studies of our own, too. It turned out that he, in fact, was infected with HTLV-II. But no one else in his family was. Well, HTLV-II is now a

common virus. Blood banks screen for it, and it's widespread across the world. We don't know what, if any, disease it's associated with.

We subsequently found another patient with hairy-cell leukemia who was infected with HTLV-II, and that patient ultimately died. We were able to do a pretty definitive study that showed that his hairy-cell leukemia was a B-cell clone, and that he had a clone of T-cells infected with HTLV-II. So in retrospect, I now believe that the original patient, Mr. Moore, may have had a B-cell hairy-cell leukemia and a T-cell clone infected with HTLV-II and that the cell line we obtained was this HTLV-II infected T-cell that had nothing to do with the hairy-cell leukemia. Or maybe there's a relationship, but the relationship is not directly causative.

WOLFE: Related to this in a different way, some historians of science have talked about the 1970s and the early 1980s as a time when oncology researchers were jumping on a "molecular biology bandwagon"—that's a term they've used. Do you think this was an appropriate term, or how do you think oncology has reacted to this?

GOLDE: Well, I think the advent of molecular biology was one of the major turning points in biomedical research, and certainly oncology. Molecular biology involved an understanding that individual genes could be isolated and studied, and that proteins could be made, usually from cDNA. The leverage of this technology was enormous. In fact, so enormous that to this day I don't believe we fully appreciate what a huge step it was. And, you know, rightfully, the double helix, the early discoveries, are seen as seminal events in science. It's equivalent to relativity and radioactivity. Huge. Things happen in science at certain intervals that are unpredictable that simply change the whole paradigm of what's possible. There are something like fifty thousand genes, and soon we'll know every gene in the human body. We're almost there. We'll know every gene in every microorganism, and that kind of knowledge will transform medicine. I should mention that I did a sabbatical at the very end of the 1970s with Tom [Thomas] Maniatis at Cal Tech [California Institute of Technology] and that sort of changed my life. Tom had constructed the first human genomic library—and the fears at that time! He had to do it from fetal liver because if you used some adult tissue, you could be cloning an andromeda strain. There was great trepidation regarding molecular biology and the dangers of cloning. My time with Tom—who's now at Harvard University—was seminal in my thinking about what could be done medically. Tom went on to found Genetics Institute, and the other founder was Mark Ptashne, who happens to be here at Sloan-Kettering Institute. That was the connection to a biotechnology company. But I think by actually working in Tom's lab I was able to visualize genes and to see the leverage of molecular technology. Yes, I think it's underestimated to this day.

WOLFE: All right. Let's switch gears a little bit to biotechnology in business and medicine. How did you begin consulting with a pharmaceutical company, and how do you think consulting has changed and how do you think the perception of consulting has changed in the past twenty years?

GOLDE: That's an interesting question. I'd have to say I knew very little about pharmaceutical companies except they used to give us cheap pens and little lights and things, before it was considered immoral to accept such gifts. I'd say I had almost no contact with the pharmaceutical industry until the advent of biotechnology, and then through my friendship and contact with Tom Maniatis. I knew that many of the things that we needed to do, particularly in cancer, but in biomedical research in general, required industry, and I found the biotechnology industry very appealing because it was composed mainly of young people who were wildly enthusiastic, Genentech with their "Clone or Die" t-shirts. [laughter] It was a special era, something to appreciate. So that was my first contact. The reality is that people like myself don't make drugs, nor is that our role. We're not capable of doing it. It's something that requires industry. It's hard to make heroes out of pharmaceutical companies, but the truth be told, they are the ones that make a lot of the things that are useful to mankind, medically. It's done on a substrate of basic academic science, without question. I think we've now come to appreciate that that appropriate interplay between the academic enterprise and the for-profit biomedical industry is in the interest of society. Of course, conducting that relationship properly is a challenge at times.

I was a consultant for Genetics Institute for seven years, and it was in collaboration with them that we cloned GM-CSF and this erythroid-potentiating activity, and we did a number of other things. With the GM-CSF cDNA we produced GM-CSF in the lab. Judy Gasson did this work, a very tedious process. So we got to do some of the early biologic studies with GM-CSF. Shortly, Genetics Institute would produce huge quantities of it. Then many scientists had this available for their studies. There's always room for improvements in relationships, but I see a lot of the advances in medicine coming from this interaction of the private and public sector in biomedical research.

Finally, I performed the first clinical studies of GM-CSF with another great postdoc in my lab, Jerry [Jerome E.] Groopman (5). We showed that GM-CSF stimulated the production of neutrophils and monocytes in humans. I believe that was the first demonstration that a CSF would work in man. A long trip!

WOLFE: How did the changes in federal technology transfer that were associated with the biotechnology industry change your work? Or did they have any effect? Were you aware of them?

GOLDE: Well, everyone, I think, came across the issues of universities protecting intellectual property and things like inappropriate transfers. With molecular biology, information is the important issue, because the sequences are a blueprint. You can transfer a gene without transferring any physical substance. Simply a sequence. And so there were a lot of things that had to be worked through. We had one of the early agreements with a biotechnology company. But it's like any other era where the pendulum swings to both sides. Now it seems to have

gotten somewhere near the middle where the rights of all parties have to be recognized and accounted for. Universities now are addressing and protecting their intellectual property, and the pharmaceutical industry has always been interested in that area. I think even with all of the contentiousness regarding patents in the biomedical area, the alternative to patents are trade secrets, and that's anathema to academic science, and it's not generally in the public interest. Balancing private enterprise with public interest will always be challenging.

WOLFE: All right. How did your experience with the Moore case change your attitudes toward medical research, or toward these kinds of technology-transfer issues?

GOLDE: Well, a lawsuit, even one that you win, is unpleasant, and that was unpleasant. It highlighted the fact that there are unexpected pitfalls out there that one has to be aware of, and it's made biomedical research more complex. I said that the pendulum has swung to different extremes and that may have been one of the extremes. I was gun shy for quite a while thereafter. It's not easy for an academic physician or for anyone to have constant dealings with lawyers and the extensive publicity associated with legal conflicts. Who knows? Maybe to this day I still am a little gun shy. I don't think that's a good thing. I was hesitant to continue to use patient material. But, for example, the use of the HTLV-II virus to establish cell lines has proved very productive because in looking at genetic disorders, the T-cells are usually more reactive cells and therefore sometimes better to work with. So with the virus we could construct permanent cell lines, cell lines that recapitulate the genetic nature of the individual from whom they were obtained. We developed some useful cell lines with this technique. Interestingly, now most of my work is with normal blood, cell lines, or primary human tissues obtained from laboratory supply companies.

WOLFE: If we could just turn to the big picture, we haven't spoken much about your more recent work, but looking back over everything that you've done, what would you consider to be your most important contribution to medicine?

GOLDE: Well, it's hard to know because it's hard to know what, in retrospect, will be the most important many years from now. The use of colony-stimulating factors in human therapy is so commonplace now that it's hardly considered unusual. Some of our discoveries were just shortly ahead of those of others, so the field would not have been hurt by my absence. Maybe in the end, the most important discovery was a more recent one involving vitamin C. We discovered that there is a fundamental mechanism, even, probably a universal mechanism by which vitamin C is taken up in cells. It had been known for many years that there was a relationship between vitamin C uptake and glucose uptake. But the nature of that relationship was unknown, and when I came here to Memorial Sloan-Kettering, I met Juan Carlos Vera, who began working in my laboratory on the oncologic and hematologic issues that I was interested in. He started talking to me about his interest in cellular transport—much like my conversation with Irving Chen many years previously. I guess I'm easily sold. [laughter] It caught my

interest, and we worked on this together, and we ended up proving that in fact vitamin C enters cells in the form of dehydroascorbic acid [DHA] through the glucose transporters. There is another family of transporters that requires energy and is less widely expressed, but every cell has glucose transporters. And I got very excited about it. We published that in *Nature* (6). We basically showed that dehydroascorbic acid goes right through the glucose transporter, whereas ascorbic acid does not, and this has all sorts of implications. It says many things, among them that extra-cellular oxidative events lead to the generation of the transportable form of vitamin C, so that the body has a set-up whereby oxidation itself facilitates the acquisition by cells of vitamin C. I was very attracted to that notion and we've done many detailed studies. For those not interested in transporters, I'm sure it is exceedingly boring. But we did an exciting study *in vivo* where we ascertained the form of vitamin C that crossed the blood/brain barrier in rodents. We injected labeled ascorbic acid and dehydroascorbic acid, and the dehydroascorbic acid crossed right into the brain. The ascorbic acid did not. So that led us to the notion that dehydroascorbic acid might be used as a therapeutic. We thought that, with regard to the brain, its utility might lie in degenerative central nervous system disease. We ultimately licensed the technology to a biotechnology company. We're not neurologists. But if, in fact, oxidation is a fundamental mechanism for generating mutation, and indeed underlies aging and perhaps other degenerative diseases, then DHA being such a potent antioxidant, might have a real role in reversing some of these diseases. We would be most interested in, obviously, prevention of cancer. So I'm enthusiastic about the development of dehydroascorbic acid as a potent pharmaceutical to regulate the cellular content of vitamin C and thereby regulate the cellular content of antioxidant. Now, of course, everything has to be connected to hematopoiesis, so the reason I became enthused with the glucose transporters is because GM-CSF signals will increase glucose and vitamin C transport. I saw the connection to GM-CSF, hormone action, and host defense. But history will determine what was important. [laughter]

You know, sometimes it's something you discover that you, yourself, don't put that much import upon, and it turns out to be the most important thing.

WOLFE: Great. I think that's a good place to stop. Thank you.

[END OF TAPE, SIDE 2]

[END OF INTERVIEW]

NOTES

1. David W. Golde, L. A. Byers, and T. N. Finley. “Proliferative capacity of human alveolar macrophage.” *Nature* 247, no. 440 (Feb 8 1974): 373-375.

2. Judith C. Gasson, R. H. Weisbart, S. E. Kaufman, S. C. Clark, R. M. Hewick, G. G. Wong, and D. W. Golde. “Purified human granulocyte macrophage colony-stimulating factor: direct action on neutrophils.” *Science* 226 (1984): 1339-1342.

3. Irvin S. L. Chen, J. McLaughlin, J. C. Gasson, S. C. Clark, and D. W. Golde. “Molecular characterization of genome of a novel human T-cell leukemia virus.” *Nature* 305 (1983): 502-505.

4. W. Wachsman, D. W. Golde, P. A. Temple, E. C. Orr, S. C. Clark, and I. S. Y. Chen. “HTLV x gene product: requirement for the env methionine initiation codon.” *Science* 228 (1985): 1534-1537.

5. J. E. Groopman, R. T. Mitsuyasu, M. J. DeLeo, D. H. Oette, and D. W. Golde. “Effect of recombinant human granulocyte-macrophage colony-stimulating factor on myelopoiesis in the acquired immunodeficiency syndrome. *New England Journal of Medicine* 317 (1987): 593-598.

6. J. C. Vera, C. I. Rivas, J. Fischbarg, and D. W. Golde. “Mammalian facilitative hexose transporters mediate the transport of dehydroascorbic acid.” *Nature* 364 (1993): 79-82.

INDEX

A
Acquired Immune Deficiency Syndrome [AIDS], 10
Alpha interferon, 10
American Society of Clinical Investigation, 5
American Type Culture Collection [ATCC], 8
Ascorbic acid, 17

B
Bayonne, New Jersey, 1
  Bayonne High School, 1
B-cells, 8-9, 11, 14
Beck, John, 3
Bone marrow, 4-6, 8, 11
Boston, Massachusetts, 12

C
California Institute of Technology [Cal Tech], 14
California, University of, Los Angeles [UCLA], 3, 5, 10-13
  AIDS Center, 13
  Jonsson Comprehensive Cancer Center, 12
California, University of, San Francisco [UCSF], 1, 3-5, 7
cDNA, 14-15
Cell lines, 8-11, 16
  bladder, 9
  CD-33, 11
  CD-34, 11
  hematopoietic, 7-9
  HL-60, 10
  Koeffler-Golde 1 [KG-1], 10-11
  lymphoid, 9
  T-cell, 11
Chen, Irvin S. Y., 12-13, 16
Cline, Martin J., 4-6
Colony-stimulating factor [CSF], 4, 7, 9-10, 12, 16
Corticosteroids, 4

D
Dehydroascorbic acid [DHA], 17

E
Endotoxin, 7
Epstein-Barr virus [EB], 8
Erythropoiesis, 12
Erythropoietin, 7

F
Fairleigh Dickinson University, 1
Finley, Theodore N., 5-6
Foley catheter, 6

G
Gallo, Robert C., 12-13
Gasson, Judith C., 12-13, 15
Genentech, 15
Genetics Institute, 12, 14-15
Glucose transporters, 17
Granulocyte colony-stimulating factor [G-CSF], 9
Granulocyte macrophage colony-stimulating factor [GM-CSF], 12, 15, 17
Groopman, Jerome E., 15

H
Harvard University, 14
Hematology, 1-3, 7, 11
Hematopoiesis, 4, 7, 13, 17
Hoboken, New Jersey, 1
Hormones, 4, 7, 12
Human Immunodeficiency Virus [HIV], 13

I
Immunoglobulin, 11
Institutional Review Board [IRB], 8-9

K
Koeffler, H. Phillip, 10, 12

L
Leukemia, 10, 12
  Hairy-cell leukemia, 11, 14
    B-cell hairy cell leukemia, 14
    T-cell variant, 11
  Human T-cell leukemia virus, type I [HTLV-I], 12-13
  Human T-cell leukemia virus, type II [HTLV-II], 10, 12-14, 16
    Eco RI, 13
  T-cell leukemia, 12

Li, C. H., 4
Los Angeles, California, 3, 5

M
Maniatis, Thomas, 14, 15
Marston, Robert Q., 1
Maxwell House, 1
McArdle Cancer Research Laboratory, 12-13
McGill University, 1-3
McNaughton, Francis A., 2
Memorial Sloan-Kettering Institute, 14, 16
Monocytes, 9, 15
Montreal, Quebec, Canada, 3
Moore, John, 11, 14, 16
  Mo cells, 12
Myeloid tissue, 9

N
National Cancer Institute [NCI], 13
National Institutes of Health [NIH], 1, 3-4, 11
  Clinical Center, 1
  Division of Regional Medical Programs, 1
Nature, 6, 13, 17
Neutrophils, 15
Neutropenia, 7
New York City, New York, 1-2

O
Osler, William Sir, 5

P
Protection of Human Subjects in Medical Experimentation Act, 10
Ptashne, Mark, 14

R
Retrovirology, 12-13
Retrovirus, 12-13
Royal Victoria Hospital, 3

S
San Francisco, California, 5
Science, 12-13
Slamon, Dennis, 13
Smith, Lloyd “Holly”, 3, 5

T
T-cells, 9, 11-12, 14, 16
  T-cell factors, 12
    erythroid-potentiating activity [EPA], 12
Temin, Howard M., 12
Tissue inhibitor of metalloproteinases II [TIMP-II], 12
T-lymphocyte, 7, 9
Tompkins, Gordon, 4, 9

U
U.S. Navy, 1
  Berry Plan, 1

V
Vera, Juan Carlos, 16
Vietnam War, 1
Vitamin C, 16-17

W
Washington, University of, Seattle, 6
Wisconsin, University of, 12

X
X-proteins, 13