

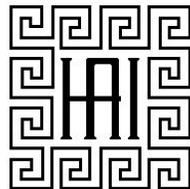
DIVISION OF CANCER PREVENTION

ORAL HISTORY PROJECT

INTERVIEW WITH

Dr. Vernon E. Steele

December 5, 2008



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Dr. Vernon E. Steele

Biographical Statement

Dr. Vernon E. Steele currently serves as the Acting Branch Chief of the Chemopreventive Agent Development Research Group, Division of Cancer Prevention, National Institutes of Health. Dr. Steele received his Bachelor of Science degree in 1968 from Bucknell University, and later earned both his Masters degree and PhD in Radiation Biology from the University of Rochester. He first began work with the National Cancer Institute (NCI) between 1975 and 1977 when he served as a Postdoctoral Trainee with the Carcinogenesis Research Program at Oak Ridge National Laboratory. Dr. Steele later served as a manager in the Cellular and Molecular Toxicology Program at ManTech Environmental, Inc. in North Carolina. In 1989 he joined the Division of Cancer Prevention as Program Director to the Chemopreventive Agent Development Research Group. In 2008 Steele became the Acting Branch Chief of the Chemopreventive group. Dr. Steele has received numerous awards while at the Division of Cancer Prevention, including the Outstanding Performance Award from the NCI, as well as the Division of Cancer Prevention Award for Outstanding Scientific Contribution to Cancer Chemoprevention in 2001.

Dr. Steele discusses contributions to the Division of Cancer Prevention and his role in the development of the Chemopreventive Agent Development Research Group. He highlights the difficulties that arise from public misconceptions or aversions to chemopreventive drugs and the role of the Division in addressing these issues. Dr. Steele also covers the process of prioritizing which chemopreventive agents should be researched and collaborating with private companies, institutions, and the scientific community.

April 2009

**National Cancer Institute
Division of Cancer Prevention Oral History Project
Interview with Vernon Steele
Conducted on December 5, 2008, by Philip L. Cantelon**

PC: I'm speaking with Vernon Steele, S-T-E-E-L-E, on the 5th of December, 2008, and may I have your permission to record the call?

VS: Yes, you may.

PC: Thank you. What I'd like to start out this morning, a little background. From a biology major to radiation biology in graduate school in Rochester. How did you make that transition?

VS: I had an interest in radiation biology as an undergraduate, and the Atomic Energy Commission kindly agreed to pay for my graduate education with a fellowship, and I accepted that, and I spent five years in Rochester, New York, getting my Master's and Ph.D. in radiation biology.

PC: And Rochester was well known in the AEC circles.

VS: Oh, it was a mecca of training for health effects of radiation.

PC: I guess since they found the fallout from the '52 weapons testing in the Kodak film?

VS: I'm not sure of that, about that story, but they had a large staff in the Department of Radiation Biology and Biophysics there, and I was impressed by their staff and the training they offered, so that's one reason I went there. And I had a training assistanceship and a research assistanceship to complete training, so that was –

PC: And had Bucknell provided the interest in radiation biology?

VS: Yes. Yes, I actually took a course there long ago.

PC: And Rochester had a number of people who did work for the AEC then, so you did work for them in part on AEC projects or research projects?

VS: No. I was supported by a fellowship from the Atomic Energy Commission, and my project was effects of radiation on cell differentiation.

PC: Uh-huh.

VS: So that's how I got into it. The Atomic Energy Commission, supported some of the people at that institute. But they had a large training fellowship program – I was one of several that took part in that.

PC: And from Rochester, you moved south?

VS: Right. I moved to Oak Ridge, Tennessee. And I took part in a National Cancer Institute post-doctoral Fellowship Program they had at Oak Ridge. And I kind of switched gears a little bit. I got into chemical carcinogenesis as a post doc. The reasons are varied [laughter] why I made that change, but fortunately, it was a fork in the road kind of – I was still interested in, health effects of chemicals and radiation, but I steered more into the chemical carcinogenesis area, I guess because I felt there was more employment in that area.

PC: In the sense of cancer-causing agents.

VS: Right. I was into cancer-causing agents.

PC: Okay. And that's what NIEHS was studying as well?

VS: Yes. NIEHS was studying that. I went to NIEHS after that as part of Staff Fellow Program and looked at pulmonary toxicology and carcinogenesis using environmentally-related agents.

PC: Now had you looked in this – for example, things of interest about that time were the health effects on uranium miners.

VS: I didn't actually do any of that research. I did research on tobacco-related carcinogens.

PC: Uh-huh.

VS: And I was trying to develop a cell culture model to study lung carcinogenesis process, how lung cells go through the process of going from normal to cancer. That was my primary focus because there wasn't a model available to study that process in detail, and I was focused on developing a cell culture model where we could dissect the process and study it more thoroughly.

PC: Popular topic in North Carolina in the 70s?

VS: [Laughter]. Yes. I guess so.

PC: From all sides, it was popular, huh?

VS: Well, I don't know. They didn't tar and feather me and run me out of town, if that's what you mean.

PC: [Laughter]. Well, I think Research Triangle Park was a little different.

VS: We were a haven for research. We were a mecca and a haven, and actually, I was approached by the tobacco industry several times to do some research for them, but had made the decision that I wouldn't accept money from that industry to do any research. But NIH has supported me quite well, and so did the National Cancer Institute.

PC: In 1982, I noticed that you went over to ManTech.

VS: Right.

PC: And what did you do for them?

VS: That's a contract, research company, and I did work under contract with the Environmental Protection Agency, with NIEHS, with NTP, for the Air Force. I did a lot of carcinogenesis and toxicology work and was concentrating on respiratory tract epithelial cells, primarily looking at toxicity. We had a wide range of projects. I did everything on teratology to testing rocket dust. [Laughter]. It was an interesting time in my life. I had a large staff of technicians and scientists, and we had multiple things going on at once. It was quite exciting. And then it was during that time that I met people at the Division of Cancer Prevention here through a friend, and introduced me to preventing cancer, which I hadn't given too much thought to before because I was trying to promote cancer to study it.

PC: In the best NIH tradition.

VS: Yeah [laughter]. So I had switched, I decided I would get into preventing cancer, after spending twenty years trying to initiate and promote it. And so I did that for a couple years toward the end of that tenure with ManTech, which changed names a couple times.

It started out as Northrop, the company that made airplanes, and switched to NSI Environmental, and then it switched to ManTech during those seven years I was there.

PC: And who recruited you for DCP?

VS: Dr. Gary Kelloff .

PC: And what was the approach?

VS: Dr. Kelloff is an M.D., and had very few people there that had any experience in animal or cell culture work, and Dr. Kelloff wanted to develop a program for screening new drugs to prevent cancer, because there were multiple, multiple drugs that were promising, but we had no animal data, or cell culture data to justify their use in the clinic. So I was recruited to develop a program in pre-clinical drug development.

PC: Explain to a layman what that, exactly, entails.

VS: That entails everything from discovery through cell culture studies, animal studies to human studies.

PC: I mean, discovery of the chemical, preventive chemical compounds?

VS: Right. And we had a contractor at that time which would scan all the literature, all the published literature, look at drugs from drug companies, look at all different kinds of agents and produce a list of potential agents that, maybe 200 a year, and then the job that I had and the other staff here was to go through that and pick maybe twenty or so that we could put in our cell culture screens to get some indication that they might prevent the cancer process. And so then we'd narrow it down to a couple, maybe five or six, that would go into the animal testing, because that's much more expensive, and then from there we would select one or two to go into toxicology and then perhaps a clinical trial. So it was kind of like a drug development pipeline, not uncommon to what you see in pharmaceutical companies.

PC: Were they doing the same thing?

VS: Well, the pharmaceutical companies weren't interested in prevention drugs back then, but this is similar to what they use to develop treatment drugs or other types of drugs as a similar-type process. We call it a linear array process. This process goes from in vitro cell culture to animals to the clinic.

PC: Uh-huh. Okay. And were – and you would do these, you say pick a couple. Is this a year? And this was all for intramural, or do you do extramural granting on this as well?

VS: Well, we had a contract mechanism in place when I arrived. And so we would contract out everything, all the work, because it's fairly routine testing work. We'd never get past

a study section for a grant. And it's directed, we told them exactly what assays to use, what end points in those assays to use, and we actually told them how to statistically analyze the data. It was a very applied science program. And then we would collect the data, and then decide if the chemical qualified for the next step or not.

PC: And these were with – contracting with universities, or laboratories or –

VS: Yes. We contracted, I guess, primarily universities, but we had contract research companies like Battelle or Midwest Research or other – Illinois Institute of Technology. We had a number of research institutes and universities that worked with us. Mostly, at that time, mostly national. They were all within the U.S. Since then, we've spanned out. We now have some in other countries.

PC: And in doing this, now the branch itself had been set up in 1982, so when you got there –

PC: I'm sorry. No. I'm sorry, I said branch, but the chemical preventive branch.

VS: ChemoPrevention Branch. That's what it was called when I got here. Gary had come, I guess, in the mid-80s. They had done some work with animal testing, but not extensive.

PC: So when you came – in '89, right?

VS: Right.

PC: Then you came as a program director and then moved up.

VS: Right.

PC: And did you change things as you – the way it worked, or have you kept the format pretty much the same throughout?

VS: Things have changed a little bit. Not significantly. We had always done things by contract, and we'd always written either work statements or work assignments. The name change, not the actual process. So that's how we'd get our work done. We've developed a lot of new animal models, a lot of new cell culture models. We also studied surrogate intermediate biomarkers, and that field has drastically changed with all the genomics and proteomics and epigenomics and all the new research that's going on now, we're heavily into all those new fields.

PC: Does that mean that you collaborate with other institutes –

VS: Yes.

PC: — to do them?

VS: Yes, we gather – ideas, we don't claim to be the sole brain power of this whole chemoprevention field. We depend on the outside people to bring us ideas. And they do. We get ideas from published literature, we get ideas from collaborating with scientists. They send them to us – when they have a good idea for a compound or they have a good idea for a new assay. We collect a lot of ideas from the outside. I get letters with ideas almost every week here [laughter].

PC: So you've become a clearing house for chemo preventive –

VS: Drug development ideas.

PC: — drug development?

VS: Exactly.

PC: And is that part of the reason that, not only you, but others are so active, others in the division are so active in professional journal editorial work and the like? It seems that's, to me, professionally, it's a good way to keep your hand on the pulse of what's going on.

VS: Oh, exactly, because, we get to see a lot of manuscripts before they're published. And, attend a lot of meetings. You have to stay two or three years ahead of the published data to stay current, and so that's why, you know, we attend a lot of professional meetings and we're on editorial boards and review panels and things like this. I review a lot of papers

for journals. I'm on a couple editorial boards, but it really pays off as far as keeping up with – the technology is changing so fast, and there's – you got to stay current in this field.

PC: Well, like other institutes, do you set a research agenda, or do they come to you on this? I mean, you say you collect ideas, but –

VS: Well, we have a research agenda. We have a mission, and it's published on our web site, actually. So anybody can read our mission. And, we get good ideas and off-the-wall ideas, and we'll sit down as a group and discuss these at our weekly meetings.

PC: Now this is a group within your branch.

VS: Our branch.

PC: Yeah.

VS: Our branch will sit down and will discuss new ideas that come in. And we can either decide that we're going to issue a contract to do the work, or we'll decide not to – we don't have money to do that, or we might just table it, put it on the back burner. We may determine, “this is a good idea; we just can't fund it right now.” Because our budget, not gone anywhere the last eight years, and research costs have skyrocketed, so we do less and less work each year.

PC: You say you haven't – your research funding hasn't gone up, but NIH's has.

VS: Right.

PC: How do you explain that within, like, NCI?

VS: I can't. I don't have control of the purse strings. It's, other people have control of the purse strings. Ours hasn't kept up with inflation.

PC: Well, is this a function of something we, I guess – I never quite joke about it, but it's the idea of NIH is set up to be disease oriented, not prevention oriented. That is, if you want to – you find the cures, not preventions.

VS: Yes, the Division of Cancer Treatment is about ten times our size, and they get about ten times the money and manpower that we get. That's a rough estimate. Yes, I hope that with each new director we get, I hope they put more emphasis on prevention, because I go around and preach it. It's the medicine of the 21st Century. And so far – I would like to see our division grow. It just hasn't.

PC: Well, what was the impact of the *Journal* article from last – was it last week it came out, about the decline in cancer rates?

VS: That's encouraging news. That's really – and, I hope it's due to prevention.

PC: Well, I think certainly part of it, you know, when you have good news, you take credit for it anyway, right?

VS: Well, there has been a decline in smoking rates –

PC: Right.

VS: — in the last twenty years. That's partly the reason. And people are changing their diets, not profoundly, but enough to make some difference in these rates. And people are getting, their mammographies, and their colonoscopies and they're getting their screening done, and they're more aware of that disease – I think people are realizing that disease could be prevented, and even some of the health insurance companies are now paying for some of these – I mean, they pay for my PSA and my colonoscopy, and they pay for a lot of disease prevention tests. I think they could do more, but all of these things, I think, are bringing the rates down, and that's encouraging news. And, hopefully, we can continue that decrease.

PC: And let me just go back again. We talked about the editorship, and I had a series of questions here.

VS: Oh.

PC: What – was that encouraged, generally, within all the – within the whole division? Did Peter want to set a tone, certain tone for that, for example?

VS: I don't recall him saying anything about that.

PC: Okay. But you're not the only branch chief who works and does these editorial things.

VS: I imagine I'm not, but I don't know exactly which other branch chiefs are on what journals. I have no idea. I think it should be encouraged. I mean, I think it's a good thing to have people on boards, on editorial boards.

PC: Well, it strikes me somewhere – in some regard that you help – it's not only monitoring the field, but you also have some control over publications, and it put you – I don't know, this is probably too harsh a term, but at a professional choke point, where a lot of things funnel through that and how they come out on the other side. So, for example, if you have the odd idea and write – you know, someone has the odd idea, the different idea, you have that choice of promoting it or not. I mean, not that you make the – you're the sole decision maker, but there's a certain power to that position.

VS: That's correct. There is a little bit. And that's what you have to deal with. You have to make some decisions. If you're in an editor's job, you have a decision to make, go or no go with publication, and it's based on your reviewer's comments.

PC: And these publications are independent of the Division of Cancer Prevention. They're not publications of the division.

VS: No, I wouldn't – no, that's a conflict of interest. We can't do that.

PC: Right. But at one point, they were inside, and they moved them out, I think one person told me.

VS: Yes. I don't review or make judgment on anything that comes out of our division. No, that's a conflict of interest.

PC: Right. But only within – you said you decided which ones to pursue in terms of the research, that is whether you go from cultures to animal studies and the like, but those are the decisions you make intramurally.

VS: Right. We make decisions. We have an agent development committee that meets on a regular basis, and we make decisions. Prioritization is one of our main activities here. We have far too many chemicals to pursue, so every day, we must prioritize those which can be pursued within our resources, and those that we can't. It's tough to decide, so we try and gather as much information as we can about a compound to make a decision whether to pursue or not to pursue. You know, we just don't have the resources to pursue a lot of promising things.

PC: Now since you were at NIEHS, and I know that they also pursue chemical compounds and toxicology of chemical compounds and working in this field for some time, do you collaborate with them or parse things out to them that you aren't doing or don't have the time to do?

VS: They're mainly interested in toxicology, and we're mainly interested in non-toxic drugs. I had sat on an NTP panel for a while to pick drugs for the carcinogen testing program. They're mainly interested in drugs that cause cancer, and identifying them.

PC: That's right, yeah.

VS: So we don't collaborate with NIH or NTP that much.

PC: So you've made a complete break now from that end of the world.

VS: Right.

PC: On the opposite end. And I know that they had done a lot of work with chemical companies and drug companies. And do you do the same, or keep separate from that?

VS: We collaborate extensively with the pharmaceutical industry because we'll have a lot of legal agreements with chemical companies and mostly pharmaceutical companies to

jointly develop drugs because the pharmaceutical companies feel it's too risky to develop drugs to prevent cancer on their own, and they would – plus, they don't have the expertise that we have here, so we collaborate with them, we generally do the – pay for the clinical trials, or the agent development, and they generally provide the chemicals to us.

PC: Okay.

VS: So we do this under various types of legal arrangements.

PC: Now can you explain to me how the field of chemo prevention has changed over – well, you've been there twenty years, right?

VS: Right.

PC: Over the past two decades.

VS: Right. How has it changed? That's a broad question. I think it's become more and more mechanistically oriented. We started out testing agents that were suggested without much regard to its mechanism, and over the years, we've looked at, more and more, how agents prevent cancer, what mechanisms are working here, and it differs for each target organ. Each target organ that you look at is a little different in the types and classes of compounds it'll respond to. So we'll become more and more, looking agents and their mechanisms first, and then deciding what target organ should we go after? Is it going to

be colon? Is it going to be lung? Is it going to be breast? These respond to different types of agents, very different types of agents. So we've become more and more mechanistic and that, I think, has helped us become more efficient.

PC: Now define mechanistic for me.

VS: Okay. One extremely valuable mechanism for, especially, breast cancer has been the Selective Estrogen Response Modifying agents. They're called SERMS. And these antagonize the estrogen receptor, and they block the progression of a lot of mammary cancer. So that led to our first, one of our first successful trials, a Tamoxifen trial, that prevented breast cancer in a large proportion of women. That's one mechanism, blocking that estrogen receptor, that's worked quite well. And we're also finding inhibiting aromatase activity also works quite well for blocking breast cancer, so there's a clinical trial that was very successful for that. The use of anti-inflammatories, we call them NSAIDs, Non-Steroidal Anti-Inflammatory Drugs. That class and that mechanism of drugs look very potent in preventing colon cancer and bladder cancer and skin cancer. Those three organs respond extremely well to NSAIDs. And that –

VS: They're Non-Steroidal Anti-Inflammatory Drugs.

PC: Okay.

VS: Recently, Frank Meyskens published a paper using Sulindac, which is an NSAID, and he used it in combination with the DFMO, dimethylfluroornithine (sic), which is an inhibitor of polyimmune synthesis, that's another mechanism, which required for cell proliferation. That combination prevented majority of colon polyp reoccurrence in his latest publish trial, an extremely important result for our division anyway, and for the whole field. We need positive trials in the whole field. Those are two or three examples of mechanisms that show promise in preventing different kinds of cancers.

PC: And these were done in animals trials, mice?

VS: Right. These came through the animal trials.

PC: And then what's the protocol for moving into human trials? I mean, Tamoxifen, I know, is – I think was in human trials, as I recall.

VS: Tamoxifen was an agent for adjuvant therapy, for women that had a primary cancer to prevent their second cancer.

PC: Correct.

VS: That was an approved drug. But we did the prevention trial that actually showed, demonstrated that in real numbers.

PC: In human trial?

VS: Yeah. We did the Tamoxifen human trial.

PC: And there was also – wasn't there also a –

VS: Several publications on that.

PC: A – what's the word I want? I'm sorry, but a substitute –

VS: Raloxifene came along and –

PC: But other than just Tamoxifen with the same kinds of –

VS: Right. Raloxifene is the same class of drug, same mechanism, but it had fewer side effects than Tamoxifen, so that drug, Raloxifene is also, an anti-osteoporosis-type drug. And probably better accepted than Tamoxifen, so those have been successes. You ask about how we get drugs into the clinic. After we do our animal testing and show promise there, then we do extensive toxicology work, which is required by the Food and Drug Administration. The FDA requires certain kinds of toxicology work be done before you can move it into the clinic. And then we would file an IND, investigational new drug application, which also has to be approved by the FDA, and then you can begin clinical trials. It's a formalized process. You have to get all these approvals from the FDA before

you can give a drug to a human. We give drugs to healthy people, so the FDA has very different guidelines for us than, say, for a treatment drug. They allow very few adverse effects before you give a drug – then we go into phase one trials to establish safe dose. So it's a very formal process.

PC: And then when – let's say a drug is approved, then do you – that has been developed in your work, does that then go to – does that automatically become generic right away because of the federal monies involved?

VS: No. Depends on the agreement we have with the drug company. We jointly own the data, and the drug company is hoping to make a profit on some of these drugs, so it's written in there who owns what. The big problem we have is it takes so long to get a phase three trial done that, usually, drugs are out of patent by the time –

PC: By the time – yeah, the seven years are gone, right?

VS: Before we get an NDA, a new drug approval, from the FDA, you know, your patent life is done. So that's why pharmaceutical companies are reluctant to help us jointly develop drugs. So we need to make some new laws to encourage the pharmaceutical companies to develop these types of drugs. That's beyond my expertise.

PC: Well, does that mean the public attitude changes more slowly than the scientific advances?

VS: Oh, yes. Exactly. Science is moving at light speed. It's incredible. And we have to get, the patent laws changed. There's been a lot of suggestions batted around of how we can encourage drug companies to get more interested in this field. Limited liability because you don't want to get sued to give a drug to a healthy person, and they get sick. You've heard the Vioxx and Celecoxib story.

PC: Uh-huh. Uh-huh.

VS: All you need is a couple lawsuits from people that had heart attacks after taking those drugs on a trial, and that discourages drug companies from getting re-interested in helping us.

PC: Is cancer prevention a harder sell – that is, chemo prevention a harder sell than chemotherapy?

VS: Oh, yes. Harder sell to who?

PC: To the public, I guess.

VS: Well, in some ways. I mean, if you have cancer, you want treated, you want cured.

PC: Yes.

VS: Everybody knows somebody with cancer. So the public accepts that easily. Preventing cancer is a new concept that came about in the last twenty years, and I think the public's finally grasping it, but they're not beating down the walls of Congress demanding more action being taken. Only Lance Armstrong is [laughter].

PC: Right. Well, I just recall how long it took for the smoking thing.

VS: Oh, yes.

PC: From the first surgeon general – well, was it the guy in –

VS: C. Everett Koop?

PC: Well, before Koop. I think Luther Terry in the Kennedy administration was the first to talk about it. Koop made it a bully pulpit, and we haven't had a surgeon general that's been quite the, I suppose, the Teddy Roosevelt of health, public health, as Koop has.

VS: Oh, yes.

PC: At least at that time.

VS: He made a difference, and he should be remembered for that because, you know, he cut the smoking rates in half in the 70s and 80s. It hasn't gone down too much since the 90s, but –

PC: One of the other things that I notice that you've been involved with is nutrition and the whole idea of – well, I was looking at a paper you were doing on garlic, soy and licorice as cancer preventives.

VS: We've done –

PC: I'm sure there are more than that, but –

VS: That's mostly John Milner's area. He's nutrition. We have tested a few garlic compounds. I don't think we've put any in the clinic, as far as from our program. The soy compounds, BBIC, Bowman-Burke Inhibitor, that's part of our development and is in the clinic. And we have a soy extract that we developed in our program here. It's a defined soy extract, and it has a number that we're jointly developing with a company.

PC: As long as it doesn't taste like Vegemite, I'm okay.

VS: We have a few nutritional gents, like green tea concentrate we developed, and Resveratrol, which is an agent or chemical found in grapes. We have that one in our

clinic. So there are selective compounds, but as far as general nutrition, we leave that to the other group, John Milner's group, to develop that whole area.

PC: Has this – the impact on the public's awareness of, I suppose, preventive measures, that is you – whether it's organic food that doesn't have chemical on it –

VS: I believe the public's aware of it. I mean, my friends ask me all the time, "What should I eat?" [Laughter].

PC: Well, you know, blueberries and pomegranate juice, and all the stuff that has all the health claims anyway.

VS: Yes. We stay away from mixtures especially undefined mixtures. They're just simply too hard to develop for us. We've developed a few mixtures. The Polyphenon-E is a green tea polyphenol mixture. We know exactly what's in there. And a soybean mixture, I think, are the two examples of mixtures. A lot of compounds that you find in foods turn up in our list. Nature is a great pharmacy [laughter].

PC: Well, it always has been, I guess.

VS: Yeah. So we tend to stay away from, like, raspberries and blueberries and undefined things like that. Although people are getting the message that they need to eat lots of fruits and vegetables.

PC: Well, that's right. And roughage and, you know, that –

VS: Fiber.

PC: Fiber, yeah.

VS: They got that message. I'm not sure the data supports it, but they got the message.

PC: Yeah. And over the time you've been doing this, how has the research agenda changed for the past two decades?

VS: As far as we're involved, not that much. Our job, our agenda is to develop agents and get them into the clinic. That's our agenda. We mark our progress by how many INDs we file. That's one of our measurements on how many agents we can get into the Phase 1 trials and Phase 2 trials. Our agenda has been pretty constant the last twenty years. We've varied our approaches and techniques, sure, but our basic agenda as far as getting things done has not changed.

PC: And this is both in intramural and extramural programs?

VS: We're an extramural division, so I don't know what your question is.

PC: Oh, there are no intramural programs in the division at all?

VS: No

PC: Well, there are none in your branch then.

VS: No, there's nothing intramural in our branch at all. I'm not sure if biometry is intramural or extramural. I don't know that answer. I think most of our intramural things were removed by Dick Klausner a long time ago. He took a lot of our intramural programs out of our division.

PC: And moved them?

VS: Moved them to the intramural, CCR mostly. No, all of our work is extramural. We are also program officials on some grants in our area. Some of our staff does a lot of grants-management type work, and that keeps us in the field knowing what's going on in the grant world. We get a lot of grants referred to our branch here.

PC: And this is from the general group at NIH that distributes –

VS: Right. They are triaged a couple times.

PC: Yeah, yeah.

VS: And the ones that deal with prevention as far as chemical development come down our way. And there are people involved in triaging these to various people. So we get a number of ones that are interesting to us. We can either accept them or not, but we have quite a grant portfolio here.

PC: Has the division itself changed? I'm not sure how I want to phrase this.

VS: Yes.

PC: But changed, and its position changed within NCI, over the twenty years you've been with it?

VS: It's gotten smaller.

PC: Uh-huh. Well, that's one change.

VS: When I came, it was called the Division of Cancer Prevention and Control, DCPC. And we had a large number of staff. And over the years cancer control was made a separate division, called Division of Cancer Control and Population Science, DCCPS. I think it is. That was set up as a separate division. So a lot of people went with that. And then some of our intramural programs were removed from our division, and so we lost more people,

so it's gotten smaller over the years. But as far as our mission, as far as – we're still in the cancer prevention mode here.

PC: Well, has cancer prevention become more accepted within NCI than it was twenty years ago?

VS: I hope so. I don't have any measure of that. I wish they would give us more slots, more employees, and I wish they would give us more money. But the directors always talk about prevention and treatment in one sentence. That's one change I've seen.

PC: That's an interesting one.

VS: Yes. Actually, Klausner did mention prevention once or twice but von Eschenbach routinely did it, and Niederhuber does it all the time, prevention and treatment of cancer, all in one sentence. He always says prevention and treatment. He doesn't say treatment and prevention.

PC: Well, prevention should come first.

VS: I think so. I'm biased.

PC: Well, just in the natural order of things.

VS: Right.

PC: Have you noticed changes in the kinds of cancer that have become, I suppose that we have, you know, the popular cancers of the, not the month, but perhaps the year where there's a lot of focus.

VS: Yes.

PC: Used to be lots of focus on lung cancer.

VS: Right.

PC: We had lots of focus on breast cancer, prostate cancer.

VS: We tend to focus our efforts on developing drugs to match the top ten concerns in this country. We don't do much work on liver cancer or esophageal cancer. Those aren't in the top ten and we focus on the main ones. We don't have the resources to focus on too much beyond that. I wish we could have programs in leukemia and brain cancer and other types of cancers, but there's simply not the resources and staff to do all that. Plus, a lot of times, we don't have good animal models in these areas, and so we don't have an idea of what kinds of drugs these kinds of cancers might be prevented with. And a lot of times, like pancreatic cancer, we don't know enough about the disease to identify a cohort that's a high risk yet. I think that's going to come in a year or two. I think the field's

moving fast enough. And we don't know who's going to get brain cancer. How do you identify a high-risk population for brain cancer?

PC: What's been the impact of genomic research on that?

VS: Oh, it's been tremendous. Just tremendous. In order to identify how drugs are acting, we're using it to identify who would respond to drugs, how to select populations. We're using it to try and look at surrogate end points we can use in clinical trials instead of cancer. There's a lot of different uses in our field for genomics. And I think we make good use of it. We're working with some of the leaders in the field. We have projects on micro RNA now, which is the latest thing.

PC: Micro – micro RNA?

VS: Micro – right.

PC: Uh-huh.

VS: These are small RNA molecules that do a lot of controlling of gene expression. And we're working with some of the leaders in that field now.

PC: But do you get genomic research to demonstrate a predisposition to cancer? Is there such a thing as predisposition?

VS: Yes. That's one area where it can be very useful to identify high risk people. And pretty soon, I think everybody's going to be carrying their genome on a wristband or necklace or something [laughter]. And the more we learn about the risk factors from genomic research, the more we can tell people what diseases they're at high risk for. Some people don't want to know, but I think it's useful as far as prevention because you don't want to, you know, give people drugs to prevent brain cancer if they have no risk for it.

PC: Uh-huh.

VS: Or you don't want to give people drugs for, you know, prostate cancer if they don't have the risk factors for it. I think it's becoming a very useful tool. It's not quite there yet, but I think – we're working with a researcher in North Carolina who's a leader in genomic research. His name is Charles Perou, and he's identifying a lot of genomic changes that predispose women to breast cancer.

PC: Well, wasn't BRAC –

VS: BRCA 1, BRCA 2.

PC: Yeah. Wasn't that at NIEHS?

VS: Yes, I think the original thing came out of there.

PC: Yeah.

VS: Yes. So each day, we're learning more about – from genomics about risk factors. High risk and low risk for diseases in people.

PC: And does prevention go through the same kind of ethical debates about this as others might in terms of how much should someone know about their genetic makeup?

VS: Yes, yes.

PC: How do you handle that?

VS: I don't know. I'm not in that field. [Laughter]. I don't have to handle it, because all my animals don't care [laughter].

PC: It's just when you get into clinical trials.

VS: When you get into clinical trials, and they want to do a genomic endpoint, you know, how much information do you want to share with the patient? I don't know. I don't do that. There are people now that are trained to do that, genetic counselors, and they're trained to tell women, "You have a BRCA 1 gene mutation. You're at high risk for

mammary cancer." There are people that do that. We don't. Our group doesn't do that [laughter].

PC: Well, but as it becomes more and more a public health issue –

VS: Right. I think we're going to have to deal with it from a standpoint of ethics, and from a legal standpoint of, is this information – can this information be made public, or can insurance companies have access to this information? Health insurance and life insurance companies, they'd love to know your risk factors. It helps them set your rate.

PC: It's better than just – well, what are they using now? Family and age, right? Past health.

VS: Age and, you know, actuarial tables –

PC: Yeah.

VS: Populations in your state even. What's the average age people in your state, locality, die? They use all kinds of semi-information, but if they had access to genetic information they could more accurately determine your risk and that would be very useful for them to set rates.

PC: Well, we've talked about some of the things that moved in the past, but where do you see things going, let's say, the next ten years?

VS: I think the whole field will accelerate in the next ten years. I think we're getting much more efficient and smarter at selecting drugs to prevent cancer. I foresee – I hope we have a large increase in positive results in our prevention trials. We have a large number of trials going on in this field, probably forty or so active trials. I'm not sure of the exact number. But we're getting some successes, and yes, we've had some failures, you know, like the SELECT trial with Vitamin E and Selenium was recently announced as being ineffective, but we've had successes. And I hope that we continue with the support of NCI to produce more successful clinical trials. And I would hope that, if we can get some of the hurdles overcome as far as intellectual property and patent rights, we can get more pharmaceutical companies interested in helping us and working with us to develop drugs. I foresee that. We also, as I didn't mention, have a program called RAPID in which we get chemicals nominated by outside people and we provide some development and work on these agents for them, and that's been a popular program. We've got a few agents, actually, in clinical trials now that came through that program.

PC: And this is provided by researchers at drug companies or at universities?

VS: No, this is not for drug companies. This is more for small, very small businesses, or mostly universities. People at a university, they come up with a chemical entity, and they apply to our program for development, and we have a review panel that looks at all these applications and decides which ones we should support. And so we set aside a portion of our budget to develop agents under this program. And it's been quite profitable so far.

We've gotten a fair number of good agents that, probably, we wouldn't have had otherwise because the data generated under this program belongs to the person that suggested the compound. So they have full I.P. rights on it.

PC: That's the future endowment of universities.

VS: Yes. That's the incentive [laughter].

PC: Yeah.

VS: In most all of our other contract work we do, the data belongs to NCI, or jointly belongs to a drug company in NCI. But under this program, the data belongs to the investigator, and they can patent it and or the university can patent it or something. So that program is also on our website, a lot of information on that if you need some more.

PC: Okay. And are there other things in terms of the twenty years you've been at the division that we haven't talked about that you think are important that we should cover?

VS: It's been a very interesting place to work. I've enjoyed working here. And I think there's a lot to be done. I tell people that one of the frustrations of working here is that there's so many stones left unturned that we don't have the resources to investigate. One area that I've always thought we need to get into is immunomodulation, modulating the immune system to prevent cancer. I think that's one of our most promising ways to prevent cancer

but we don't have the staff or the resources to get into that field, and there's a lot of untouched organs that we need to get into. We're slowly getting into different areas that I think we should get into. But in the government, things occur slowly, and you have to accept that things aren't going to change overnight here.

PC: Well, in the prevention area, if it weren't for the government, would anybody else be changing it more quickly?

VS: I doubt it. I don't think the field would be where it is today if it wasn't for the program here in our division. I seriously don't think the drug companies would've picked it up. There might've been a few hit-and-miss operations at universities, but without an organized field that has some resources to drive it, I'm not sure this would've gone as far as it has. So that gives me some self-satisfaction.

PC: Well, let me – one last question. What encouraged you to go back to Hopkins for an MPH?

VS: Couple things. Actually, I was a bench scientist all my life, mostly cell culture person. And I wanted to get a better understanding of public health. And also, I noticed that all the other group leaders had MPH's – a lot of other group leaders had MPH's behind their name, because I had no clinical experience. And so I used this as an opportunity to learn about clinical trials, how they're done, their limitations, advantages, and I learned a lot about various aspects of public health that I had no education in, basically, because I just

was, as I said, a bench scientist. And this has really broadened my perspective because cancer prevention is a public health thing. It is. We're trying to improve public health. It was valuable. I went to night school for four years to get that degree, and I did it at the age of fifty, which is kind of scary.

PC: Was that down here at the Rockville Gaithersburg campus?

VS: It was the Shady Grove campus.

PC: Shady Grove. Yeah.

VS: Of Hopkins. So I just had to drive up the road and take an evening course once or twice or three times a week. But I got through it, and I learned an awful lot about public health and public health problems and how to try and make an impact on public health. And I learned a lot about clinical trials, which I didn't know before [laughter]. That was the main reason.

PC: Okay. Well, I want to thank you very much for taking the time this morning.

VS: Okay. I hope –

PC: And I appreciate the interview.

VS: Hope this has been useful.

PC: It has. Very. If I never learn anything in a day, it's a bad day, and I've learned a lot today.

VS: Oh, good. Me too.

PC: [Laughter].

VS: If you have any other questions –

PC: Okay. I would like –

VS: — you know, feel free to call me back.

PC: Terrific. I will do that. And thanks very, very much.

VS: And what will this come out as? What's the product here?

PC: They're collecting material on the office from a number of division – or branch chiefs, and also interviews with Peter.

VS: Okay.

PC: And what happens to that afterwards, I don't – I do know they'll all go into the history office at NIH.

VS: Oh, great.

PC: So –

VS: Okay. All right.

PC: All right. Terrific. And I'll probably get a transcript to you so you can correct – sometimes the transcribers don't pick up a lot of the – some of the terminology or the spelling might be funny, especially in medical terms.

VS: That's fine. I'll be happy to do that.

PC: Wonderful. Thanks very much.

VS: Thank you.

PC: Bye-bye.

VS: Bye-bye.

[End of Interview]