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CLARA M. SZEGO, PhD

Interview conducted by
Adolph Friedman, MD
February 16, 2001

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MEETING DR. SYDNEY ROBERTS

Dr. Friedman: Dr. Szego, am I doing this with your permission?
Dr. Szego: Yes, of course.

Dr. Friedman: In reviewing the book that you referred me to yesterday, I got about as far as where you were--your husband was going away for the summer, and you had also met Dr. Roberts. That's where I stopped. Would you please go into that part for me?
Dr. Szego: That's not particularly contributory to my career except that my then husband and I parted company very soon thereafter, and I was able to devote myself totally to my career.

Dr. Friedman: How did you meet Dr. Roberts, and what did Dr. Roberts do?
Dr. Szego: He was a graduate student in the same laboratory as mine--both directed by Dr. Leo T. Samuels, who was a past president of the Endocrine Society--eventually, some years later, a very vigorous laboratory where we all had lots of interaction. Sydney Roberts had just arrived from his first-year graduate studies at Harvard where he felt he was not making appropriate progress in terms of independence. So he and I met there after I had been at the University of Minnesota for a year or so.

Dr. Friedman: Do you have children?
Dr. Szego: Well, we have godchildren and "grandchildren." Which would you like for me to talk about?

ON HER DECISION NOT TO HAVE CHILDREN

Dr. Friedman: But you have no biological children?
Dr. Szego: No biological children by design, which I think was a dumb decision. But it was necessary at the time because each of our families after we were married depended on us for financial help. The other reason was that in my time, which was in the early 1940s, it was out of the question to have a family and be a woman scientist, and I had total dedication to science. It was like mother's milk to me, so there was unlikely an opportunity for children until a great deal later. We contented ourselves with each other

and with our godchildren, which we have two--a goddaughter, Pamela, who's an engineer architect at Berkeley and the daughter of M.C. Chang, member of the National Academy and someone well known to the Endocrine Society--no longer living. That is, Dr. Chang is no longer living, and his daughter is a very warm goddaughter to us.

Dr. Friedman: What does she do?
Dr. Szego: She's an engineer-architect and is both Berkeley-trained and a very "green" architect--if [you] know what the term "green" means these days. She's very conscious of energy conservation and the environment. The "grandchildren"--we have many and these are our former graduate students and postdoctoral fellows. We are staying in close touch with them.

LEO SAMUELS'S LABORATORY CULTURE

Dr. Friedman: Was your relationship with Dr. Samuels very close? Was he active in the laboratory, or was he one of those people who told you to "work on this," and you'd never see him again?

Friendly divergence with Dr. Samuels over the mechanism of steroid relationships to protein

Dr. Szego: Well, we had sparks flying all of the time. He was very much in the laboratory, and he had a lot to talk about with us on a regular basis daily. We went about our work in a very independent way, but saw him frequently in terms of data review and evaluation. It was much later when our paths so diverged that we went along different tracks. Dr. Samuels believed in one mechanism of steroid relationships to protein, and we ourselves, who had opened the field, had a different opinion. So a path did diverge, but we were always very warm friends.

Dr. Friedman: What was the nature of your two different philosophies?
Dr. Szego: Well, I would like to get into that after I get into the brief steroid-protein binding concept, if you don't mind.

COLLABORATIONS WITH SYDNEY ROBERTS

Dr. Friedman: I noticed that your productivity in conjunction with your husband was intermittent. I mean, you could go along for a year or two, three, and write several papers, work on several projects; then suddenly a couple years would go by before you wrote some more.
Dr. Szego: That--I wrote some more with him--but in the interval I was writing.

Dr. Friedman: Oh, yes? Continuously?
Dr. Szego: Yes.

Dr. Friedman: What was the reason your personal interest diverged in these different times?
Dr. Szego: Well, I think it was in part a question of focus. I was determined to follow the hormone. You know, like "following the money" these days. I was looking for where it went and how soon I could identify and detect it in the cell that was responsive to it. He, on the other hand--although we collaborated in this stage rather early as I will demonstrate; in fact, I can because I brought with me something of which I made, a slide; i.e., our first paper identifying the protein binding concept for steroid hormone, which has often been misunderstood. Anyway, he went on into a more neurobiological direction in the regulatory biology. So we then could converge once again and pick up where we had been, each offering something to the joint effort. That soon stopped. You will notice that he is no longer on our publication list after a given number of years.

Dr. Friedman: In between there were times there was an interval of two or three years; then you worked again. For example, here's a paper in 1953, and the last one prior to that was 1949. Nineteen forty-nine was the influence of ovariectomy on chemical composition of regenerating liver. The next one was 1953 in which you discussed the influence of steroids on urine restoration in glycolysis. Then you went on again for another couple papers you worked on in 1953.
Dr. Szego: That may not necessarily imply that we were in the same laboratory doing work side by side. It may mean that we picked up data from a former period, which we

could now interpret more clearly then [when] it was possible to do a joint paper on it. Do you visualize that?

Dr. Friedman: Yes. So he was working on the neurobiology in between your doing the hormone work.
Dr. Szego: Yes.

Dr. Friedman: Who was H. A. Reame?
Dr. Szego: He was a graduate student of mine.

Dr. Friedman: And where did he go when he left?
Dr. Szego: Well, I hate to tell you that he was probably the oldest associate professor in the United States. He just "petered out". He was an extremely active and vital fellow, and I just don't know what happened to him. He went to State University of New York in Brooklyn. There, I think, he sputtered a little--then there was silence.

Dr. Friedman: They call it burn out.
Dr. Szego: Burn out? I guess, but he did not burn out in the laboratory. I think he burned out in bars and saloons. That was not intended as a slur; it was a silly little joke because I don't know that for sure.

Dr. Friedman: That's perfectly all right. Then there was a paper in 1955 where you and your husband worked on a paper lecture on protein-bound estrogen in vitro. Again, that was about two years after you went down another road.
Dr. Szego: Well, I think for technical reasons. I don't believe that it was significant that we had intervals and did not live together. Most of the work that has to do with my later career was really quite independent.

Dr. Friedman: It was more the estrogen work.
Dr. Szego: Yes. Actually, other hormones as well, but the estrogen lead the way.

Dr. Friedman: Who was Spaziani?

Dr. Szego: Another graduate student. Now, *he* has continued to be very active. When he left my laboratory, he went to England on a Porter Fellowship. He went to work with Hugh Davson at the University College, London, the home of the Starling Valets Team of many years before that. He then went to the University of Iowa and is presently a professor there.

DR. PINCUS AND THE WORCESTER FOUNDATION

First demonstration of steroid protein binding; Roberts's pituitary-hypothalamic work leads to the birth control pill; her work on transplantation of ovarian tissue

Dr. Friedman: Would you like to discuss with me your work during this period of time?

Dr. Szego: Well, I want to go back a little, if you would permit it, to the first demonstration of steroid-protein binding. This has been written up in a memoir of the Pincus Memorial Lecture--and I think this was about 1974--was the place where I put all this [in] context. To do that I must go back to when I was working at the Worcester Foundation. Dr. Pincus put Sydney and me on two separate programs. Sidney was working on the pituitary relationship--hypothalamic relationship to ovulation--and that was to eventually lead to the so-called contraceptive pill. I, on the other hand, was involved in the potential of transplantation of ovarian tissues from one animal to another. This had to do with the donor of the grant on which I was working, Mr. Tom Slick, who is the owner of a cattle ranch, a Texan, and very well to-do, and from whom Dr. Pincus had obtained a grant for the struggling Worcester Foundation on inception. My job was to try to have the future. The weans in the eye of both Dr. Pincus and Mr. Slick--that ovaries from pure-bred cattle that had non-properties for milk production and so forth--our wedge could be transplantable into scrub cattle as incubators for the offspring with potential for the good genetic background. Ovarian tissues, let's say. Later, it would have been the eggs themselves, but here it was just simply the ovarian tissue--the grafting of ovaries from one animal to another. And, in this case, we began with rabbits. I was going ahead doing this, but at the same time I had so much curiosity about nature and about the mechanisms of action of regulatory substances that I just couldn't let the urine

and the blood of these animals--of which I, doing the surgery--be wasted. Therefore, I decided to look for the steroid hormones in these products, the blood and the urine.

Studying ovarian steroid biosynthesis with a perfusion apparatus

Dr. Friedman: Before and after.

Dr. Szego: Before, after, during, and everything--I collected a great deal of material, and we were also perfusing ovaries; and I was collecting the fluid from that. I had a loose collaboration with Dr. Nicholas Werthessen at the Foundation. He did the tinkering of the apparatus of the perfusion system, and I did the chemistry. So the first thing to do in looking for steroid hormones in body fluids, of course, was to precipitate the protein, then work with the supernatant. Most of that was done with organic solvent, and I did that. But Nick Riverson [Werthessen??] said, "Don't bother with the residue because all of the estrogen is going to be in the supernatant." Then I said, "Oh, no, no, no." I believe in thoroughness, and so I set up a Soxhlet apparatus. It's simply an extraction of material that puts the solids in a perpetrated vessel in the anterior annuleprosol drip through--and keep that going with heating and cooling condensation for a long time. Finally, you end up with a concentrate--extracting the solid--the solids and the blood with the proteins, of course. Nick said, "Just throw those away". I said, "Oh, no, no, no." So I went ahead and did that and--to nobody's surprise except the doubters--there were two-thirds of the steroids present in the protein. Now, you would say, "Well, maybe they were tracked there because they coagulated so fast."

Dr. Friedman: How did you find them?

Dr. Szego: No, it coagulated so fast that it trapped the "free steroid." I said, "No, no. We'll do this with non-denaturing conditions." And sure enough, there were; two-thirds of the estrogen were protein bound. That's where my husband's interest was aroused.

"The Nature of Circulating Estrogen" and early work on cellular membrane recognition of steroid hormones

Dr. Friedman: Came back.

Dr. Szego: Yes, he went right through this with me. And we did the chemistry, and it was a revelation. It turned into this paper called "The Nature of Circulating Estrogen," which appeared in the *Proceedings of the Society of Experimental Biology and Medicine* in 1946. I go back quite a ways. It demonstrated that a large and constant proportion of the total steroid was present and in close association with the protein, and it was dialyzed past the collodion membrane and has followed the laws of mass action, and it was at the equilibrium with the free. So we were really excited. Consequently--since we were close to Boston, we knew that in Boston there was a laboratory devoted to huge pools of human blood being prepared for various purposes. This was wartime, and some of this was for coagulatory purposes in surgeries in the fields, and some were for intravenous administration, and so forth. All these blood fractions were being prepared in the laboratory of physical-chemical biology headed by Professor Edwin P. Cohn. So we went to Harvard and discussed with him the possibility of getting samples of the pool from which the bloods was being fractionated.

Dr. Friedman: Knowing you might have both male and female.

Dr. Szego: Quite so. But we also followed androgen in this--as you pointed out--we were looking for both estrogen and androgen. It happened that the estrogens turned out to be concentrated almost exclusively--the entire pool of estrogen could be accounted for in one fraction, the so-called III-0. Where, actually, the male hormones were in fractions IV-1. We were elated, astounded, and excited. You can imagine the young investigators who had stumbled upon this phenomenon and could pursue it. So this was the beginning of my concern about how the steroid hormones are recognized at the cell surface. Because--if you can visualize--the circulation is not in direct contact with the target cells or with cells, instead there is an intervening layer, an unstirred layer--if necessary to visualize--around the cell. And it is the blood exudates and transudates that wash the cell. These contain protein, and it's in this proteinase form that the steroid approaches the target cell. When I began concentrating on this matter, I realized that since we had found an equilibrium in the dialyl and the dialysis experiment between the internal and external fluid which cross the membrane, we could also visualize that there would be an association from the down stage. We could capture the hormone--if there were--at the

target cell surface, proteins that had a higher affinity, selectivity and specificity, than the circulating proteins. That is what has turned out to be the case. That the association at the cell surface is such--from the protein bound state of the circulation is such--that the higher affinity of the proteins that are present in the surface of the target cell can extract from that in a progressive fashion the active H. That led to another paper in *Endocrinology* demonstrating that the fractions of the blood could account for the steroids. But to get back now to further developments, this paper "The Nature of Circulating Estrogen" was very well received.

Dr. Friedman: May I have that later?

Dr. Szego: Yes, I have a slide made of it; that's why it's enlarged. However, I do want to point out that it was in 1955 at a Woods Hole Symposium that I first indicated that the steroid and the peptide hormones shared the property of being recognized by proteins at the cell surface.

STEROID HORMONE RECEPTORS COUPLED TO INTRACELLULAR SIGNALING PATHWAYS

It was a dozen years after that that we demonstrated the first cyclic AMP (cAMP) elevation in the target cell. By then at my own laboratory--we had come to the University of California and each had independent positions--although that's another story. My laboratory showed that estrogen would double the amount of cyclic AMP, a very powerful agonist, in an intracellular direction towards cascade of one agent leading to another. So that which would be entirely a function of peptide hormone was shown in 1967 in our laboratory to be a function of the steroid hormone. I'm in the midst of doing the proof on this latest review. Although I am technically retired from my teaching duty, I have the deepest commitment to continue to think about these things with two of my former associates, who are now professors on their own. We have a review about to be published in the journal *Endocrine*--probably in March or April--entitled "Steroid Hormone Receptors in Target Cell Membranes."

STEROID HORMONES: CHALLENGING CONVENTIONAL WISDOM CIRCA 1967

This is the crux of my controversial history in the endocrine field, because at this time--in 1967--the current conventional wisdom was that all steroid hormones--being fat soluble--enter the cell of all cells, and they are restrained from exit only by receptors, which are present in the cytoplasm at that time, which keep the hormone from being eliminated only in those cells where it's going to do something and where the so-called target cell has receptors. These receptors are protein--although our early work demonstrating the interactions with protein steroid hormones were not broadly recognized--therefore, why worry about how estrogen's recognized. It's there in the cytoplasm. The cytoplasm--as we showed some years later--is an artifact. It is an extract of membranes and other cell structure, and it's done with hypotonic solvent with bashing the cell as hard as you can with homogenization. We showed that the more you homogenized and the less nearly your appropriately tonic homogenizing medium is, the more likely you're going to find that the steroid is removed from its native state in association with protein. I will go on to say, at any rate, that the concept of cytoplasmic recognition of the steroid was rapidly exploited and then forgotten totally, the field as a whole--with the exception of Dr. Zagon, one of the few people who want to believe me, the true evidence. [laughs] I'm laughing, and I want that to show in the record. Because it's all good natured, really, with some exceptions; the controversy that surrounded it, that the field simply wheeled as one, turned 180 degrees, and said, No, no, no. The receptor is not in the cytoplasm; it's in the nucleus already. So there you have the receptor in the nucleus--a big no-hands side of plasma and a self-service with its plasma membrane and the hormone that's supposed to recognize at the outer cell surface--that there's a receptor waiting for it in the nucleus. That's a little difficult to swallow.

ENDOCYTOTIC VESICLES TRANSFER INFORMATION TO THE NUCLEUS FOLLOWING HORMONAL IMPACT TO TARGET CELL

Dr. Friedman: The question is does the hormone recognize it, or does the receptor and nucleus recognize it? In other words, does one come to the other?

Dr. Szego: No, I don't think the nuclear receptor is swimming out to meet and escort the hormone in. I think it's much more likely--as we have said over and over again--that the entire pattern is one of coordinate function. The portion of the receptor may be in the nucleus, may be on the cytoplasm--not all of it. Some of it is on the cell surface, not all of it. But the hormone can get the initial impact to the target cell. At the surface there's an immediate explosion of secondary reaction; psychogam-P is one of them, phosphorytase, tarnayes et cetera, that are affected by the nucleotide cyclase system and by the product of cyclonucleotide linked to the G-crediums. And this is the route by which the information is transferred towards the nucleus. The entry is vesicular--the membrane becomes invaginated on moving itself--self-invaginated into little vesicles. We have shown that in ultra-structural studies--you will find them in my bibliography--and these vesicles tend to fuse with other organelles and to travel in straight lines, which are reminiscent of microtubule towards and around the nucleus. Some of the pictures of uptake of this steroid in the vesicular are quite dramatic. At one point, when I was giving a talk in the first of these series in Hamburg, Germany--it was an abstract at an International Congress--and I first showed this colored photomicrograph of life at soma perinuclear array after staining. There was a real audible gasp in the audience because it was such a revelation to find. Most people believe that the nuclear preparation, which this represents--and I'm looking at a figure in a review of ours on recent progress in hormone research in 1974 in which the control nuclear preparation shows intact organelles--when exposed to estrogen, just within minutes or seconds, is surrounded by organelles that correspond to life.

Dr. Friedman: What year did you say this was?

Dr. Szego: In 1974. That was really quite exciting. Here in this new review, we have put down in sequential form the evidence for surface recognition of steroid hormone in parallel with the means by which peptide hormones are recognized at the target cell.

Dr. Friedman: Please, send a review copy to me.

Dr. Szego: Oh, I don't have that any more.

Resulting turmoil in the field and disputes with Robison

Dr. Friedman: Not that, of this one.
Dr. Szego: Oh, this one. Yes, I will. I have a list of people waiting for it. So don't worry, I will remember that. I think this will summarize it best because it does not reflect the terrible turmoil that these ideas introduced into the body scientific. There were, of course, confirming papers, but these were inconvenient. Sometimes those who tried to detract from our observations were essentially regretful about it. They wrote, We regret that we did not give this enough thought. This was the laboratory of Robison, who had been a colleague of Sutherland, who had worked on the psychogam-P production and the regulatory events there. He was very embarrassed about having unequivocal findings, which have recently been confirmed by Benita Katzenellenbogen.

Dr. Friedman: I know Benita Katzenellenbogen.
Dr. Szego: Can I coax you into interviewing her?

Dr. Friedman: No, she's too young.
Dr. Szego: [laughs]

Dr. Friedman: It's interesting how I first got to know about her. Her daughter and my nephew were graduating from Hopkins Medical School.

Support for Szego's work

Dr. Szego: Oh, my goodness! I knew her as a little creature. I knew Benita's children when I gave a lecture there. They were little children, then. Medical school, my goodness. I just want to add that there was a lot of controversy, but there were also many supporters.

Richard Pietras: evidence of estrogen interaction with receptors on cell membrane

Richard Pietras has done dramatic work in our laboratory [and] is now an associate professor in the Department of Medicine, here at UCLA. His work has continued in the

direction of breast cancer and the recognition of hormone at the cell surface of those cells. In addition, he turned up in our laboratory as a young graduate student before he became postdoc. He was very intrigued with trying to do something that would demonstrate binding of the isolated cells to the hormone. So we proceeded and worked together, closely. He was able to demonstrate that when you bind estrogen in co-balance form to a nylon fiber through a series of chemical reactions--he washed it exhaustedly free of the steroid that was unbalanced and then suspended these fibers in a medium [in] which the cells from the uterus were suspended, then you would find, rinse them off, take photographs of them, and find the fibers loaded with cell capacity to bind. But if you take intestinal cells, for example, they don't bind. You can liberate the balanced cells from these fibers by appropriate amounts of pre-steroid in the medium. They come off. So that was a very exciting time, and that came in 1977. I think I have a photograph of that. I didn't know we were going into so much detail.

Dr. Friedman: This is nothing compared to your two volumes.
Dr. Szego: Here's an example of how the fibers that release the cells with the bound estrogen, which happen to be liver cells that also have some binding sites. I have an even better demonstration. That was so exciting and that really captured people's attention.

On the courage to follow the data; coordinate events of intracellular signaling

We received a letter immediately thereafter from a colleague in Germany, whom I did not know otherwise, [who] said, "We, too, have observed this phenomenon by slowing down entry into the cell of free hormone that was balanced receptor by cooling the whole preparation and by doing very short observation times. We, too, have seen surface binding of steroid hormone at the cell surface. We did not dare to tell it loud." I was intrigued, and my response was that when you have unequivocal data in which you have real confidence, well-controlled data, which told you something, you have to follow the data wherever they land with "real civilian courage" and suggested by the term used for it by Bismarck. I respect that idea, regardless of what I thought of Bismarck in other contexts. There was great commitment in supporting these ideas from our laboratory. First of all, the fund granting agencies were very skeptical. The committees were headed

by people who had their own ax to grind and didn't want the waters roiled by having any new stuff coming in to their well-developed ideas. We pointed out many times in one review after another how much respect and admiration we had for the people who went ahead and did the unraveling of the events from the nucleus, which came many hours after the first impact of the hormone at the cell surface. There was no reason to decide that these were alternate theories. Contrary, we visualized, but the information from the cell surface was relayed in a cascade of chemical events leaning towards and into a nucleus, would support such activity. The two were coordinate events, well separated, but which we were trying to identify the links between. So there you have it.

Pietras work on breast cancer and HER2 recognition

Dr. Friedman: That's been fascinating. Tell me more about Dr. Richard Pietras.
Dr. Szego: He is a very active, thoughtful person with a very powerful intellect. Whatever he gets into, he does some clean unequivocal work. He did a lot with us. You will find his name associated with mine throughout. He's in the Department of Medicine. He works on breast cancer and is involved with the HER2 recognition [of the] breast cancer cell with the gene corresponding to the substance and the impact to the hormones around it. He's working from the point of view of an antibody towards the gene product, which is in the testing phase and has a secretive influence upon the progression of the cancer.
Dr. Friedman: That's great.
Dr. Szego: It's very exciting and comes from his interest in the cell surface.

Dr. Friedman: What is his rank now?
Dr. Szego: His rank is associate professor in residence.

Dr. Friedman: Does he have his own laboratory?
Dr. Szego: Oh, yes, he does. And he has his own grant, but he's not line appointment because funds for his position come from an external source. It's not a university division yet, but he has been promoted to this fairly recently.

FELLOWS AND ASSOCIATES

Dr. Friedman: Who was Seeler?
Dr. Szego: Barbara Seeler was my very trusted, very capable technician. I should call it a technologist--for nineteen years. We did a lot of good things together. She was totally dedicated--as I was--to the work. She came day and night if necessary, worked in the cold room for many hours, and did excellent technical work and taught me as much as I taught her.

Dr. Friedman: Who among your fellows and associates have become famous in their own right and has established their own departments or laboratories, and so forth?
Dr. Szego: You scared me when you said departments, but they had to be chairman. Well, I can mention a few.

Dr. Friedman: Please do.
Dr. Szego: Well, we mentioned Richard Pietras, Spaziani at Iowa, and Nemere who has her own laboratory but is seeking to advance elsewhere. She's at State University of Utah. Richard Pietras, we've spoken of. There's James Allen Roberts--no relation--who was an undergraduate and is coauthor on one of our early papers in the *Biochemical Journal* in 1969 to 1971. He is a very research-oriented gynecologist interested in ovarian cancer who has headed the laboratory as a department head--actually at the University of California, San Francisco and Stanford. He is head physician at Stanford, and there is a joint venture between Stanford and UC, San Francisco on OBGYN. Norbert Swislocki was a chairman of the Department of Biochemistry at State University of Newark School of Medicine and Dentistry. Dr. Barbara Lippe was the chair of the Division of Pediatric Endocrinology, here at UCLA. She had been an undergraduate researcher at my laboratory, and with whom I published a couple of papers. She is vice president, or at least director of research, on peptide hormone at Pharmacia. I have a set of bound reprints at home and one at the university, of which you have seen.

Two others are Judith Hopkins and John Creange; [both] are in industrial research. Alexander Lopata is professor of obstetrics and gynecology at the University of Melbourne, and he is one of the leading protagonists of fertility clinics. He has done the appropriate fertility and procedures in very early times, which he was one of the leaders of opening this field. Robert Ezzell has his own firm and Web site related to structural biology. Carol Rambo, who now uses her maiden name, Otoatey, is likewise in industry. Michael Horton is in Pittsburgh at a community college as a teacher of biology. These are all the people that come to mind at this moment.

SZEGO'S SERVICE TO THE ENDOCRINE SOCIETY

Public Affairs Committee and the diethylstilbestrol (DES) controversy

Dr. Friedman: I'm sure that some of the highlights of your career were the 1980 and 1990 invitations back to Budapest. I'm sure you were thrilled about that. I would appreciate it if you would tell me about your functions in the Endocrine Society and your relationship with the Society. Who did you work with that you enjoyed the most, what did you do for the Endocrine Society that you received a certain amount of satisfaction?
Dr. Szego: I functioned on two committees. I was appointed to the first one by Ernie Knobil--the late Knobil, unfortunately. This was the Public Affairs Committee. On that, I think I really contributed because I spearheaded the movement to eliminate diet-filled stilbestrol from cattle feed and from animal feed altogether. That took a great deal of effort, and we received some support from Congress. There is correspondence on that in my oral history at UCLA. I could give you a reference number, but it appears in the marginal notes as an addendum. I felt great satisfaction from this because it made a real difference in public health. Then years later, I served on the Awards Committee and became chairman at the end of the five-year stint. I think there was some useful input from me on that committee, but the public affairs one was the most exciting.

Dr. Friedman: You didn't do any other work for them.
Dr. Szego: I don't recall any. My husband became vice president of the Endocrine Society and chairman of the program in 1969, something of that order. He's listed in your roster, I'm sure.

SIDNEY ROBERTS'S CURRENT WORK: ORAL HISTORY AND EVALUATING PEW FOUNDATION GRANT RECIPIENTS AT UCLA

Dr. Friedman: What does your husband do now, is he retired?

Dr. Szego: Semi-retired. He's been recalled to serve in the Division of Oral History. Very much up your alley here. There's a grant from the Pew Foundation, which he wrote, essentially, a committee of which he serves now at UCLA. He evaluates the work of the recipients of the Pew Foundation grants in chemical biology. It's called the Pew Foundation Biomedical Scholars Program. This is a nation-wide, very competitive effort to bring up the most promising young assistant professors. They have to have a university position to begin with--support for a five-year period of uninterrupted funds for any purpose. They can use this for advancing their laboratory program. One candidate from each university alone is--totally a candidate--one from every university that is interested in competing is nominated annually. I believe they select twenty or twenty-five candidates. At the end of the five-year period, they are interviewed by an experienced interviewer--like yourself--and they evaluate their own programs and how well they have advanced, and what they think about their competition, and so forth. It's this committee at UCLA on which my husband sits that evaluates the interviews, which are then transcribed and analyzed in a meeting of the committee, and that is transmitted to the Pew Foundation. They are now in their seventh or so year of following this program and its result. They are very interested in the evaluations that come from UCLA.

Dr. Friedman: Well, I knew of Pew because I come from Philadelphia. He made his money in oil and gasoline in Pennsylvania. He had a chain of gas stations among other things--J. Allen Pew.

Dr. Szego: It's remarkable what they have invested in this program. It's quite amazing.

GENDER ISSUES IN SCIENCE: WOMEN IN ENDOCRINOLOGY

Dr. Friedman: Let me deviate, now. This is more of my personal interest than for the Society although it's going to be used for the Society. I'm interested in your thoughts on

women in endocrinology. You can say whatever you want; I don't care how you criticize--

Dr. Szego: I was anticipating it from our correspondence--and that is I took a very dim view of segregation of any kind.

Dr. Friedman: I don't mean it as a form of segregation; I mean more in form of a recognition.

Dr. Szego: Well, I don't care for that either. I care for it as a scientist.

Dr. Friedman: You're just like Roz Yalow.

Dr. Szego: I know; I see that, but I want to say why. Very recently in the newsletter at the American Society for Cell Biology, there appeared what I thought was the most sickening column. It was called "For the Love of Science," sponsored by Women in Cell Biology. They did something on role modeling, and it had to do with how much she is "victim" in the laboratory, and how her chairman upgrades her for not doing this and that, and how terrible it is to compete with others outside. She gets home, and her little children hug her, and she's all happy, and then she goes back to the laboratory and down again. I was just sickened by it. So I wrote the following letter:

[reads letter]

Letter to the American Society for Cell Biology

Women in Cell Biology Committee
The American Society for Cell Biology
Rockville Pike
Bethesda, Maryland

Dear Colleagues:

I'm compelled to take the time to comment on the statement “For the Love of Science,” which appeared in the June 2000 issue of the *AFCB Newsletter*, presumably with the approval of your committee. To say that I was appalled by this pitiful example of what passes for poetry is an understatement. But it is the sentiment more than innocuous expression that gave me the determination to give "vent" to my outrage. If the signal that

the writer is sending is that of "victim," she and you are undercutting the significant progress made by scientists of both sexes in our joint efforts to advance knowledge and our discipline without referral to the chromosomal make-up of the individual colleague responsible for the work. Role playing, indeed. True, I did it the hard way, but do not discount that factor in my urging [you] to abandon the masochistic tone in dealing with the usual choladial snipping. Such a negative image of a woman scientist is counterproductive and certain to promote further denigration of the species. I have long counseled my graduate students and postdocs of either sex to ignore the "bark" and do good science. There was much satisfaction in that approach, and I continue to encourage it. I need hardly remind you of the classic Harry Trumanism, "If you find it too hot, get out of the kitchen." I should be so pleased to see your committee's name changed to something less divisive and one that would express a more constructive attitude towards the young aspirants of both sexes who are at the early stage of their career, for example, "The Young Scientists in Cell Biology." Remember that solidarity overturned an entire system of government in Eastern Europe. These politically incorrect comments are not intended for publication without my expressed approval.
Yours Sincerely"--and my signature.

I thought you ought to hear that because whether it's pastry cooks, or artists, painters, poets, et cetera, I see no reason to call them women poets, or women artists, or women chefs. There is just no relevance to it.

Dr. Friedman: You're going to be annoyed with me, but part of my work entails having an exhibit at the annual Endocrine Society Meeting, called the History Project. I sort of been running out of topics, and I selected *Women in the Endocrine Society* for this coming June in Denver. I don't know whether you plan to go or not.
Dr. Szego: No, I don't plan to go, but I'd like to tell you that the _____is nothing like the list that I gave you, of Jane Russell, and Anderson.

Dr. Friedman: Well, I interviewed Janet McArthur.

Dr. Szego: You did. Well, I'm not talking about Janet McArthur. I don't think she's necessarily in that first echelon. I'm talking about _____, which you couldn't have interviewed, Jane Russell, and Evelyn Anderson who worked on pituitary. These were really first-line major.

Dr. Friedman: How about Anne Carter of the United Press?
Dr. Szego: Well, I'm not going to put this down for the all-time record. I'm impressed, but not to that extent.

Dr. Friedman: I didn't get to talk to her, but I did get to interview Roz, and I was hoping to devote my attention to the women who became presidents of the Endocrine Society, which I think is quite an achievement and an accomplishment--Neena Schwartz, Kate Horwitz--from a year or two ago.
Dr. Szego: I'm blank.

Dr. Friedman: Definitely it's not to denigrate those two.
Dr. Szego: Of course, but to segregate them, I think is not appropriate. I wouldn't feel proud of that.

Dr. Friedman: Since you've met me, won't you forgive me?
Dr. Szego: [big laugh] Of course, I would forgive everyone who cares enough about this to see justice done. I don't care about the fact that I've been in this. It was an uphill struggle because of the fact. But at the same time, there were always people who were supportive, always someone at NIH and NSF who would listen; and I never had an interruption of my research funds from those agencies and others because the work kept pouring out. I say, “Go where the data are.” And that's what I think made my career successful to the extent that it was.

Dr. Friedman: You did get shafted in terms of one of your fellowships. I read that in the volume.
Dr. Szego: When was that?

Dr. Friedman: You were given fellowship for four years--for twelve hundred dollars, or something like that, which was a big thing at that time. Then they took one of the appointments away from you. I dictated that for myself from volume--
Dr. Szego: You mean, when I got married at Minnesota and lost my instructorship.

Dr. Friedman: Correct.
Dr. Szego: Yes, that was the anti-nepotism law. When we got here to UCLA thinking we had two positions, we had only one. We had to battle, but it was successful. I don't want to conclude this session, which I gather is near the end of.

OBSERVATIONS ON SCIENTIFIC CONFLICTS: HONORING YOUR ADVERSARIES; RESPECTING THE INITIAL WORK

Dr. Friedman: Is there anything else you think I should know about you? I have plenty of tapes in my bag.
Dr. Szego: Well, I'm not interested in extending this any longer. I just wanted to add a word--the primacy in science--and that is the necessity, as the president of--our late Sidney Ingbar said in one of his presidential addresses that "Our ideas are the mark of our identity, representing our imprint in the field of endeavor". And our good name is what Shakespeare felt was more important than our purse. It's [in] this framework that the honorable intention of somebody who disagrees with your interpretation of data is important. I kept them very honorable adversaries whose criticism has been helpful and whom I deeply respect. But I've also had the experience of having people not cite our data even when they're first--after they have made a minor change to the source of the cells or the type of extraction. The little technical change that in no way altered the outcome. And I think that where the lack of citation in some cases was very aggravating--and I nailed it whenever I could in subsequent papers to point out the initial effort of the pioneering work must be respected.

Dr. Friedman: Well, they made a big to do about this in the ethics department of the Endocrine Society.

Dr. Szego: Did what?

Dr. Friedman: The ethics.
Dr. Szego: Ethics Department, let me hear more about that.

Dr. Friedman: They're very careful in the editorial permission to publish and editorial critique of the paper that's submitted.
Dr. Szego: Yes, I have known instances--not necessarily in my case by any means--of work that was reviewed by a reviewer, turned down, and then published by the reviewer. That's one of the ugly sides. But that's not been one of my concerns.

Whole-animal hormone processes

I've been called a lot of names, and you have to have pretty thick skin if you're being politically incorrect sometimes, which is ultimately now shown to be correct. One of my favorite names was "anti-reductionist," because I believed in seeing the whole picture: the entire continuum of hormone recognition to gene--on agreed--out--and beyond. It was a perfectly honorable adversary--and I understood that--someone who's focusing entirely on the nuclear sphere. But you don't see the whole picture that way. Although we don't detect it one piece after the other in a very logical way, it comes together like a jigsaw. It is very rewarding to have had so much of our work turn out to be correct.

Dr. Friedman: It's also worthy of much compliment/recognition. You got the recognition.
Dr. Szego: It's nice to be alive while this is going on because there's a real ferment now in this area, and I'm thrilled to think that I helped open this field.

Dr. Friedman: Thank you very, very much for your time, and your frankness.
Dr. Szego: I appreciate yours.

Dr. Friedman: I'm very happy to be here.
Dr. Szego: I've never been anything but frank.

End of Interview

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