Oral History: Elaine S. Jaffe, M.D.
National Cancer Institute
Interviewed by Kate Nagy for ONHM on March 17, 2023

Kate Nagy: Dr. Jaffe, tell me a little bit about yourself. Where did you grow up?

Elaine Jaffe: I grew up in White Plains, New York. I was actually born in Brooklyn and moved to White Plains to start first grade when I was six years old.

KN: What did your parents do? What were they like?

EJ: My parents were both born in Ukraine and came to the U.S right after World War One. They both were born and lived in *shtetls*, or villages, in Ukraine; a lot of [Ukrainian] Jews in that era emigrated to New York after World War One.

KN: Do you still have ties to Ukraine?

EJ: Not really. I had one cousin on my father's side. I had one [Ukrainian] cousin who was living and working as an engineer in Moscow, but he ultimately left Russia and moved to Israel, so I have no remaining ties there.

KN: Did you have siblings?

EJ: I had one sister who was six and a half years older than I was. Unfortunately, she's deceased. She developed a fairly rare form of intestinal cancer when she was relatively young and died of her disease some years ago.

KN: I'm sorry about that. When you went to school, what was that like?

EJ: I went to public high school in White Plains, New York. I was kind of shy in high school and not very social, and I was fairly serious about my studies but not involved in a lot of other activities, I confess.

KN: Were you drawn to science at that time?

EJ: I was always interested in the sciences. When I was growing up, I was a Girl Scout, and I was interested in geology and rocks and astronomy and biology, so I was always drawn to the sciences in one way or another.

KN: Did your family support that?

EJ: My parents were very supportive. In our family education was very important. My sister went to Cornell – she was a very good student. She was interested in history and government. I wanted to follow in her footsteps, so I applied to Cornell and was accepted early. I was excited about following her path to Cornell.

KN: So how did you go from history and government to the sciences in college?

EJ: Well, no. *Her* interest was in history and government. I was always interested in biology, so I registered in pre-med, actually, as a freshman. I was a zoology major in the College of Arts and Sciences.

KN: Do you recall any mentors or professors who made a big impact on you at that level?

EJ: You know, the Pre-Med program at Cornell, there were a lot of students in it, and I'd say there was not a lot of opportunity to get to know professors. And I think one actually great advantage of a liberal arts education is that you get to do a lot of things outside your major area of interest. And so I took a lot of history; I took English classes; I took history of art. I think those experiences probably had more long-term impact on me as a person than my science classes.

One of my favorite professors was Walter LaFeber. He was a really exciting history professor – died in 2021– and that was, I'd say, a very memorable class and got me interested in public affairs, not professionally, but just as a citizen of the world. I really liked art history, and as I think back to it, I'm a pathologist. Pathology is very visual, you know, you look through a microscope and you see images, and you have to remember those images and make a diagnosis. Art history is very similar: you have to look at a painting and know who the artist is even though you never saw that painting before, because you're recognizing the artist by his or her style or approach to the field.

KN: That's a theme I'm starting to see through some of these interviews: people who are scientists but had this broader liberal arts education and really appreciated and valued that. So it's something that I'm encouraging my kids to look into as well.

And so you completed medical school, it looks like, in the 1960s and you were one of only a few women in your graduating class. Can you share some experiences about that?

EJ: I started out at Cornell undergraduate and then was accepted at Cornell Medical School, which is in New York City. There were only five women in our class. All of the students pretty much lived in the dormitory in New York right near Cornell Medical School, and all the women lived on the same corridor, so we became very close. Among the five women in my class I'm still in in pretty close contact with two others, so we were a very close-knit group and we did everything together, pretty much.

KN: Was it difficult? Did the male students accept you, or was there a lot of "Oh, you're taking away a spot from a man?"

EJ: No. The men were very accepting. We were close together, you know, the med students would eat together in the cafeteria. Actually, I met my husband, who's a lawyer, through one of my med school classmates. We were a group that spent a lot of time together.

KN: You didn't get a lot of sexism or discrimination?

EJ: No. I mean, I think they didn't quite know what to do with us. I started out at Cornell, and as I mentioned my husband was in law school and we got married after my second year, so I transferred to the University of Pennsylvania. So I did two years at Cornell and two years at Penn. When I was a third-year medical student at Penn, the medical students normally would take call and would sleep in the hospital when they were on call – you know, so they could see patients. They didn't know quite what to

do with the women. They didn't think it was right for the women students to sleep in the same on call room with the men so they would send us home at night.

KN: Oh, wow.

EJ: Yes, it's rather bizarre. Today that would be considered discriminatory, although at the time I'm not sure I minded so much going home at 11 o'clock at night rather than sleeping in the hospital.

KN: If you had a call in the middle of the night they'd call you on your home phone?

EJ: No, we were excused from that. I guess you could look back and say that that was discriminatory: we were not being provided the same level of education or exposure, but, you know, I didn't really think too much more about it at the time.

KN: What informed your shift from clinical medicine to the laboratory?

EJ: Before I go into that I should say that one more unique thing about my medical school education was that I actually had a child in my fourth year of medical school. That was during the Vietnam war, and my husband had a draft number that would put him at high risk for being drafted and sent to Vietnam. But at that time you could still get a deferment if you were a father, and so I got pregnant and my first child was born my fourth year in medical school, and he got his draft deferment.

KN: Sure. My dad got a draft deferment the same way.

EJ: Okay, so you know what those times were like.

KN: Oh, yeah. I mean I don't remember it very well because I was just a little bitty thing, but yeah.

Since you brought up the topic, it must have been unusual in that era to have a baby your fourth year of medical school and to be a new mother throughout your internship and residency. Did that have any impact on your decision to become a pathologist, where you'd – in theory -- be less back and forth?

EJ: I'd say theoretically yes, but I never really enjoyed patient care, I confess. I loved medical school and I loved learning about disease, but I really didn't enjoy interacting with patients, so it wasn't a sacrifice for me to go into something like pathology where there's less patient contact. Actually, we took pathology as second year students, and it was a full year course, and I really loved pathology. I was really excited by it, and it was at that point in my second year that I knew I would go into pathology, so it was not something that I wrestled with later in my career.

KN: After you had the MD, did you do a postdoc?

EJ: At that point I went directly into pathology and did what today would be called an internship or residency, rather than doing a regular clinical internship. I started my training in pathology, so I was a resident in pathology at Georgetown University Hospital here in town. I did one year at Georgetown and then I heard about the program at NIH. My husband had a cousin who was here as a research fellow during that time, and he knew about the pathology program and mentioned it to me, so I applied for the residency here at NIH and transferred here for my second year.

KN: Going back to being the mother of small children and being a full-time pathologist while your husband was working as a lawyer: how did that work out? Was it difficult? Were you lucky enough to have good childcare? Were the kids in school by that time?

EJ: It was stressful. I'd say childcare was always a challenge. When I was in medical school, we actually had someone who lived in with us in Philadelphia, and we had a large enough apartment that she could stay in our apartment and take care of the baby. When we moved to DC we hired someone, a kind of a nanny, who would come in the morning and leave in the evening, but there were always occasions where the nanny wouldn't show up and you were trying to figure out, well, what do I do now? I would say that my supervisors and my faculty were usually sympathetic if I had to cancel at the last minute. I confess that my husband never offered to stay home when the nanny didn't show up, so it was always in my lap in terms of what to do, but we got through it. It wasn't easy, but we got through it.

KN: Are your children scientists now as well?

EJ: No. My oldest son is a journalist right now. He writes for the *Washington Post*, and before that he worked for the *Wall Street Journal*. He's won a Pulitzer.

KN: Oh, wow.

EJ: Yeah, he covered the Obama White House and won the White House Correspondents [Association] Award (*note: Greg Jaffe won the White House Correspondents Association Aldo Beckman Award in 2017*) – actually one of the [awards] the year that [Donald] Trump was elected president. It was customary for the president to come to that dinner but Trump boycotted the dinner, so….And then my younger son is a law professor at the University of Virginia and teaches environmental law.

KN: I'd like to pivot to some of your research now. Can you explain what you're working on in layperson's terms?

EJ: My area of interest has always been hematopathology and in particular lymphoma. As a pathology resident I thought about several areas of specialization because most pathologists do specialize in one area or another, and I think the two areas that I considered most were hematopathology and GI [gastrointestinal] pathology or liver pathology. In a sense, those are both fields in which the pathologist works very closely with the clinical team and where the clinical features are a very important part of the diagnosis. It's not pure morphology, but you really have to integrate the clinical features with the diagnosis. So I was drawn to those areas.

I picked hematopathology and lymphoma because it was an era when we were at the beginning of the understanding immunology. We were first recognizing different types of lymphocytes – that there were T cells and B cells. Importantly, the field was developing tools and techniques that you could use to [differentiate] T cells from B cells. As a as a resident and as a fellow I started working with some of the immunologists here at NIH – Ira Green, Mike Frank, and Ethan Shevach, who still works here – and learning something about immunology and techniques to identify lymphoid cells and then use those techniques to identify lymphomas, which we understand today are neoplastic recapitulations of normal lymphoid cells, to characterize the lymphomas and relate them to the normal immune system.

KN: When you say that lymphomas are tumors of the immune system – which I see on your [laboratory's] web page – what does that mean? Does it mean simply that the lymphoid cells have gone

awry and they don't look like other cells or don't act like other cells?

EJ: What I mean by “tumors of the immune system” is that the malignant cells are caricatures of normal lymphocytes. Not only do they express some of the same surface receptors as normal lymphocytes, but they retain some of the functional attributes of normal lymphocytes, and then those functions impact the disease as we see it in the clinical situation. The clinical manifestations of the disease are closely related to what the function of normal lymphoid cells might be.

KN: What would you say was your first major discovery in this field?

EJ: My first major discovery was using fairly primitive tools – they were called rosettes – we used sheep erythrocytes which were coated with antibody and complement and looked at the surface receptors of B cells and T cells. I studied a disease which today we call follicular lymphoma – at that point it was called nodular lymphoma because the tumor cells were forming these nodules, but people didn't really fully understand what these nodules meant – and I showed that the lymphocytes in follicular lymphoma were derived from the normal lymphoid follicle. The lymphoid follicle is an important part of the B cell system. It's the part of the B cell system in which the immune system first encounters and reacts to an antigen and makes antibodies that are specific for that antigen.

That paper was published in 1974 in the *New England Journal [of Medicine]* – it was a lead article in the *New England Journal* – and it became a citation classic and is one of the most highly cited papers, so that was a very exciting time, for me and for the field.

KN: Did you [continue to study] follicular lymphoma, mostly?

EJ: I mean, I've continued to study all the lymphomas. I still study follicular lymphoma, and we know today that follicular lymphoma is not one disease but [rather] more than one disease, and that there are different lymphomas that are derived from follicular B cells and that these have a different clinical significance and are treated in different ways. So, for example, there's something called pediatric type follicular lymphoma, which is a very indolent disease. It usually presents just in a single site, Stage I, and these patients can be treated with just surgical excision. It's very important to [distinguish] that type of follicular lymphoma from other, more aggressive forms of follicular lymphoma, because the patients really don't need chemotherapy or radiation to manage their disease.

KN: So what you're talking about is identifying different types of lymphoma cells and determining how to tell what's different when you look through the microscope.

EJ: Yes. There are probably more than 100 types of lymphoma derived from B cells and T cells, and these look different under the microscope. They have different antigens on the cell surface of the malignant cells and different mutational profiles. Today, molecular biology is becoming much more important in terms of characterizing malignancies: the genomic profile of different diseases helps to characterize them and determine their clinical behavior.

KN: You really can't see that under a microscope.

EJ: You can't see the mutations on the under the microscope, but we learn enough by studying a group of lymphomas. For example, our group was one of the first to identify the BCL2 gene rearrangement in the most common form of follicular lymphoma, and we learned that what we see under the microscope

in many instances correlates very closely with what the genomic profile turns out to be, so you don't have to sequence every single lymphoma to understand it.

KN: Do you think that there is a finite number of lymphomas? You said there were over a hundred types of lymphoma. Do you think that's finite, or do you think that ultimately everybody's lymphoma is unique and will need its own [drug] cocktail?

EJ: Yes and no. No two tumors are exactly identical, but there are also common themes that dictate the clinical behavior.

There was an oncologist who actually questioned what we were doing early on, not at the NIH but somewhere else, who said, "You know, you're determining that every single tumor is different. That will make it impossible for the oncologist to know what to do," and, well, yes, every tumor *is* different, but there are common themes, and what's important is to identify what the common themes are for individual diseases that determine how they should be treated.

KN: I see that a research interest of yours is "gray zone" lymphomas. What are those and how common are they?

EJ: Historically, lymphomas were divided into what was called Hodgkin's disease and non-Hodgkin's lymphomas. Hodgkin's disease was sort of a mystery. The malignant cell in Hodgkin's disease – which is one of the more common types of lymphoma, particularly in young people – the malignant cell is called the Reed Sternberg cell, and for many years nobody knew what the Reed Sternberg cell was. People thought it might be a lymphocyte or a granulocyte or a histiocyte or a dendritic cell, so it was sort of a mystery cell. In our work we actually began to see that patients who had Hodgkin's disease also sometimes developed another lymphoma and that other lymphoma was often a B cell lymphoma, and so we thought that it was likely that the malignant cell of Hodgkin's disease, the Reed Sternberg cell, was a B cell. And that was ultimately proven to be the case. So what was originally thought to be two major classes of lymphoma – Hodgkin's and non-Hodgkin's – it turns out that they're much more closely related than was thought.

Gray zone lymphomas are tumors that sort of look somewhat like Hodgkin's and somewhat like non-Hodgkin's, so they're kind of in between. They're important because they help us try to understand how a malignant B cell turns into a Reed Sternberg cell.

KN: Just so I understand, was the Reed Sternberg cell the abnormal cell?

EJ: Yes.

KN: So [a patient would be diagnosed with] Hodgkin's disease and then later they would get this B cell lymphoma…was it a continuum of the same disease?

EJ: What we were able to show by looking at the immunoglobulin gene rearrangement was that the two tumors were clonally related. They were part of the same tumor, but the malignant cell had changed its appearance, changed its morphology, and changed its phenotype, so while they looked very different under the microscope you could show that it was actually a single neoplastic clone.

KN: What causes that to happen sometimes but not all the time?

EJ: Well, that's something we still don't know the answer to. There are many different theories that have been offered – mutations or changes in transcription factors, epigenetics – but there's no one theory that explains that fully. That's something that's still being studied.

KN: Is there any difference clinically? For example, if they're basically the same cell, do we treat the Hodgkin's and the Reed Sternberg cell lymphomas the same way?

EJ: Traditionally, what we now call Hodgkin's lymphoma rather than Hodgkin's disease (because we know it is a lymphoid malignancy) is treated differently from other B-cell lymphomas. Although they're similar in some respects, there are also differences that lead to different therapies.

KN: So they're two manifestations of the same process – is that fair to say?

EJ: Yes. Then in between them, their "cousins." Then, kind of in between them, is the "gray zone."

KN: When you're choosing a treatment for B-cell lymphoma, do you start with the Hodgkin's lymphoma, or do you start with the Reed Sternberg?

EJ: That's actually been the subject of a clinical trial. It was done here at NIH, led by Wyndham Wilson. Those tumors – "gray zone" lymphomas – are actually closely related to another tumor called primary mediastinal large B-cell lymphoma. Dr. Wilson showed that the therapy that's used for primary mediastinal large B-cell lymphoma is also very effective in these so-called "gray zone" lymphomas.

KN: That's really interesting! I know they're all lymphomas, but does that imply other similarities from a basic standpoint between Hodgkin's lymphoma, the Reed Sternberg, and the gray zone?

EJ: In fact, mediastinal gray zone lymphoma shares a lot of genetic aberrations with primary mediastinal large B cell lymphoma and also certain forms of classic Hodgkin's lymphoma, so there are certain characteristic mutations that tie all of those tumors together.

KN: But clinically they appear similarly enough that everyone with, for example, Hodgkin's lymphoma isn't necessarily going to need to be genotyped to choose the [best treatment].

EJ: Right.

KN: That's really interesting. I recently completed an oral history with Lou Staudt. Do you and he and Dr. Wilson work together often?

EJ: We work together constantly. We work very closely with Lou Staudt and the people in his Branch, and the clinical team. We have weekly conferences where we discuss patients. Lou Staudt initiated something called the Leukemia Lymphoma Molecular Profiling Project many years ago. It's a consortium that involves a number of centers around the world that study lymphoma, mainly in Europe and the U.S. We work together with the other members of that Consortium – and actually in February (2023) we had a meeting in Phoenix, Arizona, where the investigators met and discussed some of the ongoing projects.

KN: What are you working on right now?

EJ: There are a couple of areas that we're working on, sort of as a departure from conventional lymphomas. We're studying neoplasms of the histiocytic system. Histiocytes are immune cells that are distinct from lymphocytes. They have more of a role in the processing of antigen and presentation of antigen, but they don't make antibodies like B cells or mediate cytotoxicity like T cells, and I'd say that people have been slower to understand the spectrum of malignancies that are derived from histiocytes. For a long time now we've understood the different types of B cells and T cells. Neoplasms derived from histiocytes are more complex and less well understood, or at least haven't been as thoroughly studied. So now we're studying a lot of malignant diseases derived from histiocytes and cells called dendritic cells, which are a specialized type of histiocyte.

KN: I'm not familiar with histiocytes at all. What sorts of malignancies derive from those?

EJ: The most common, and one that's been recognized for the longest time, is something called Langerhans cell histiocytosis. I don't know if you've ever heard of that, but it's a disease that's relatively common in children – it can even present in infancy. It varies a lot in its clinical behavior, so some forms of Langerhans cell histiocytosis present just as a single lesion in a bone and you can cure the disease by going in and curetting out the tumor, while other forms are more widespread and involve many sites in the body and need systemic therapy. So again, that's a disease that varies in its clinical behavior.

KN: Forgive my ignorance, but is that considered a malignancy?

EJ: Yes. For many years, something about a lot of the things we now know are histiocytic malignancies is that a lot of them were not even recognized as tumors, so people really didn't know that Langerhans cell histiocytosis was a malignancy. They thought it maybe it was an unusual reactive process. We're now beginning to understand that these are neoplasms, and again, they have a characteristic mutational profile, so there are certain recurrent mutations that are associated with these diseases that led to their recognition as neoplasms.

KN: What about these histiocytes are you studying?

EJ: We're trying to characterize them as individual disease entities, and we're using next generation sequencing to look at the genomic profile and identify recurrent mutations that are associated with individual types of histiocytic tumors.

KN: Have you published anything yet or is it too early?

EJ: We've published a few things. One of my fellows is now working on a paper characterizing something called indeterminate dendritic cell histiocytosis. [That's] a tumor that actually looks a lot like Langerhans cell histiocytosis under the microscope but it's different at the genetic level. While Langerhans cell histiocytosis usually occurs in young children, this type of histiocytosis occurs in older patients with a median age in the 70s, so clinically it's very different.

KN: Does that imply that the treatment will also be different?

EJ: Again, it depends on the stage and the extent of disease, but some patients have a very indolent clinical course. Others are treated more aggressively using regimens that are similar to leukemia-type regimens.

KN: What do you think has been your greatest achievement at NCI?

EJ: Certainly the study I told you about identifying follicular lymphoma. That became a citation classic, and it was a significant achievement. I also identified something that we call in situ follicular lymphoma and described that. It was a cover article in *Blood*, and what we showed was that the earliest event that leads to follicular lymphoma is BCL2 gene rearrangement, where you have a translocation that involves BCL2 and the immunoglobulin heavy chain gene. What we learned was that translocation will lead to overexpression of BCL2, but those patients don't necessarily go on to develop clinically significant follicular lymphoma. We identified something that we called in situ follicular lymphoma in which you could find B cells within individual follicles that overexpress BCL2 and have that translocation, but they only have that first hit. They don't have subsequent hits, and so the patient actually doesn't need to be treated – less than five percent of those patients will go on to develop lymphoma.

I think this is a theme in cancer in general. We know that cancer is a disease of multiple genetic hits, and if you have just a single hit those cells don't necessarily become malignant. [In situ follicular lymphoma] is a disease in which the single hit has occurred – the cells have developed the BCL2 translocation, they overexpress BCL2, those cells traffic around your body, they settle in reactive follicles, they sit there, you can see them under the microscope – but those patients don't go on to develop lymphoma. That was an important thing to recognize because it has major clinical implications. And we now have identified other forms of in situ lymphoma that have this first hit but not the subsequent hits that lead to true malignancy.

KN: Is there any way to prevent that second hit?

EJ: Well, we don't really know what causes the second hit, but it's a rare event, luckily, for most patients.

Another discovery that I made, again related to follicular lymphoma, was that we saw that there were some patients with follicular lymphoma who developed histiocytic sarcomas. We talked about how histiocytes are different from lymphocytes, but these cells actually went through transdifferentiation, so you had a B cell and it became a histiocyte, and yet it's clonally related to that original B cell. That occurs in some cases of follicular lymphoma, and we don't fully understand what leads to that transdifferentiation. In some ways it's probably a block in some of the transcription factors. That was another significant discovery that is highly cited and recognized.

KN: Is it common among malignancies for one cell to convert to another cell, both of them diseased?

EJ: It's one neoplasm so it's one neoplastic event, but it’s been seen, for example, in carcinomas that cells are relatively plastic. I mean, if you think about it, we know you start out with a stem cell – start out with that fertilized egg – and it becomes all the cells in your body. Cells have enormous capacity to become different types of cells. In a way, the stem cell is the multi-potential cell that can turn into bone and lymphocytes and nervous tissue – and we can see that that actually happens in some tumors and also happens in some carcinomas. So, for example, in the hematopoietic system, in the lymphoid system, we know that in the bone marrow there's a stem cell and that stem cell can differentiate into a lymphocyte, it can differentiate into a histiocyte, it can differentiate into a myeloid cell or neutrophil or granulocyte, so there are stem cells in your bone marrow that have this great capacity to differentiate in many different directions.

KN: So it's different cells, but they all have different precursors.

EJ: Well, yes and no. If you go back to that certain fertilized ovum that was a single cell, but in the hematopoietic system, there's a stem cell in the bone marrow that goes in all these different directions, so your bone marrow stem cell will not become an intestinal cell or a cell in your stomach, but it can become many different types of hematopoietic cells.

KN: So they're all, like you said earlier, cousins.

EJ: Right.

KN: We're coming toward the end here, so I just have a few more questions. What was the biggest change in the NIH since you began here? What hasn't changed?

EJ: Honestly, I think the biggest change is probably security. I think, sadly, [before September 11, 2001] the NIH was much more open, obviously, to the public, and I think it sort of impacted our thinking. Certainly the pandemic has impacted the way we interact with people, but 9/11 had a huge impact just on how people came on campus, so I think unfortunately it's probably had some impact on our culture.

KN: How so?

EJ: There's less of a freedom and openness. I don't know; it may be subtle, but I think it somehow impacts our way of life.

KN: Yeah, I remember before 9/11 just driving up and parking in a parking lot and walking up, and kids sledding down the hill behind NLM. What hasn't changed at NIH?

EJ: I guess the excitement about disease and science. And I think we're very lucky in that we're sort of insulated from the need to apply for grants and so we have a certain independence and freedom to pursue our interests, and if we want to go in a different direction we don't have to apply for a grant to do that. For example, our work that I mentioned on the histiocytoses – that's something that we really started just the last couple of years. It's a new area of investigation, and I didn't have to go out and get independent funding to do that, so I think it's a luxury that that we're all fortunate to share.

KN: What would you tell a postdoc just beginning their career now if they wanted to come into a lab like yours, or even to your lab?

EJ: I think an important lesson is to finish what you start. I think the people who are most successful start a project, and [bring] it to completion, and get it to publication. I've seen a lot of people who come in and they may be very bright and have lots of ideas, but they get too diffuse in their thinking and their studies. They'll start one project and then they'll pick up something else and they never really finish what they start. It's something that I remind my postdocs and fellows: Stay focused. Make sure you pick a project that's worth doing and then finish it.

KN: What do you tell your postdocs if they've been doing the research and they want to finish, but they've hit a dead end and it's just not going anywhere? They don't think they're going to get anything out of it. How do you advise them then?

EJ: I don't think that happens very often, and our work is clinical and translational, so it may not turn out to be as important as you hoped, but you could tell a story and at least you can bring it to completion.

KN: It seems to me that discovery is incremental and those big jumps forward rest on the incremental stuff but don't happen all that often. Where do you see the field of pathology in 20 years?

EJ: Certainly molecular biology has had a huge impact. Today we rely a lot on molecular diagnostics and it's much more of our daily practice, so I think that it will continue to play a major role in identifying different types of tumors, including lymphoma.

Some people have [suggested] that maybe we could throw out our microscopes in 20 years and we'll just put it all in a sequencer and come up with a diagnosis, but I don't think that will happen. [For example,] we were talking about the histiocytoses – there are many genes and recurrent mutations that are associated with many different types of tumors, so for example BRAF is a gene that's commonly mutated in Langerhans cell histiocytosis, the disease I was talking about [earlier]. It's also mutated in malignant melanoma, and in some forms of lung cancer or colon cancer. So I think we're not going to be at a stage where you just get a sequence and have a diagnosis. I think we're still going to rely on the microscope and more traditional methods.

KN: It sounds like the possibilities are expanding, [but] it's not like the field is going to be completely different in 20 years than it was before.

EJ: You've still got to learn the basics. [But] then in 20 years molecular diagnosis may *be* "the basics."

KN: I there anything else anything else you'd like to add before we finish?

EJ: No. I mean, I've worked here since 1970, so it's going on 53 years, and I look forward to coming to work every day. I don't think I've missed a day of work during the pandemic! I think NIH has been a great place to work, and I have no regrets about coming here.

KN: Thank you. This has been really interesting.

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