



# BRIGHAM AND WOMEN'S HOSPITAL

JEFFREY GOLDEN

Interviewed by Peter Tishler, MD, September 2012

My name is Jeffrey Golden and I am the Chair of Pathology at the Brigham and Women's Hospital and I am the Ramzi S. Cotran Professor of Pathology at Harvard Medical School.

**Wonderful. Now I am going to ask you some questions of a personal nature. You have devoted your professional life to pathology, first by training at the Massachusetts General Hospital since graduating from the University of Pennsylvania School of Medicine in 1988. Why did you choose pathology?**

Well it was a very difficult decision for me. I knew I wanted to be in the neurosciences, and I am a trained neuropathologist. I was deciding between neurology, neurosurgery and neuropathology. What it came down to was that I enjoyed being in the lab, I wanted to have my own research lab, and I wanted to spend that time nonencumbered by other requirements of having to take care of patients and see patients regularly. I felt neuropathology would give me the best opportunity to spend that time in the lab, which is what I wanted to do.

**You completed a fellowship in genetics at Harvard after your pathology training. What did you acquire of lifelong value from this fellowship?**

This fellowship was a research postdoctoral fellowship and it was different from any aspect of my clinical training. It was focused on enabling me to develop the skills I needed in the laboratory, developing model systems, being able to formulate questions and to address them in using the scientific process. And that fellowship allowed me to do that, which really wasn't part of my clinical training.

**Who were your mentors either then and now?**

I've had fortunately quite a few mentors. At the Massachusetts General Hospital it was E.P. Richardson and Tessa Hedly –Whyte, particularly in the neurophysiology field. When I went on to do my postdoctoral work it was Connie Cepko who is still here at the Harvard Medical School, a phenomenal mentor; my postdoc time was fantastic. And then when I started my first job in Philadelphia, my main mentor was really Lucy Rourke, a pediatric neuropathologist who took me under her wing and provided me the opportunities to be able to advance my career. And that happened in multiple ways. She not only ensured that I had the protected time, which is so critical for junior faculty, to get my research lab going. She also made the right introductions and made sure that I was getting to and giving talks in certain places so that people in the field knew who I was.

**We welcome you to the Brigham as the new Chair of Pathology. Why are you back in Boston?**

I never thought I was going to leave Philadelphia. I had a fantastic position, loved it there and think it's an amazing institution. And it is a credit to the Brigham that it was able to provide an environment that I saw as a place in which to really grow and develop. As I started going through the recruitment process to come here, which I never anticipated even beginning, I was forced to think more about what I wanted to do with pathology and why I would want to take a position like this. And in thinking about the future of pathology and how I thought it needed to go or change, the opportunity to have a training program here, and the elite and storied department of pathology here at the Brigham is a platform that would allow me to think about and do those things that I find so exciting for the future.

**How wonderful. Are you currently happy at the Brigham since you've been here?**

I'm very happy at the Brigham. A little busy but very happy.

**I'm going to ask you some questions about your role in pathology here at the Brigham. You assumed this directorship early in 2012 following many outstanding leaders in pathology whom you may or may not know: Gus Dammin, Ramzi Cotran a personal friend of mine for many years, and Mike Gimbrone. Have you appointed individuals to assist you in leading the department?**

We're in that process of reorganizing the department. Previously the department, particularly under Ramzi and I was here under Ramzi, was a much different department because it was only anatomic pathology. It was much smaller. It was also a leading department in pathology, particularly in the development of clinician scientists. That tradition has continued and I certainly want to continue to promote it. Under Michael Gimbrone the department really expanded because it assumed the oversight of all the clinical labs: lab medicine, the blood bank, transfusion medicine, all these other areas, which previously had not been under Ramzi's purview. As that has grown, the leadership under Michael really remained very similar to what

it was under Ramzi: a very narrow leadership group that was truly exceptional. My plans going forward are to elevate a number who I think are outstanding individuals in the lab. We're in the process of bringing those people into the leadership domain. I've created an executive committee for the department -- what I've called Chairs' Council. The members are counseling me -- that's what they're here for. It is a group of about 10 of the very senior faculty in the department who on an annual basis will be providing me with strategic planning in specific areas. Each year we'll define 2 or 3 areas in which we want to come up with a roadmap on how we're going to do it for the department. We've started that this year. Once we've come up with a roadmap in these first couple of areas, we'll then do it in subsequent years in other areas. And we've selected already a number of areas to address.

**Are there names you would like to mention who have assumed a leadership capacity?**

Continuing in the leadership capacity here is Fred Schoen, who has been the Executive Vice Chair for many years and is continuing in that position. I've asked Michael Gimbrone, who brings quite a bit of wisdom, is very thoughtful and has a long history here, to be on the Chief's Council. I want to be inclusive of our very significant role at the Dana-Farber Cancer Institute and the Dana-Farber Brigham and Women's Cancer Center; and so Max Loda, who is a senior professor here is working with that group. I believe that genetics and cytogenetics are very important for the future of pathology, so Cynthia Morton is involved in that group. It really is to draw on the major areas and have representation of each of the major areas, so that we can examine how we interact and how we can better serve the department going forward.

**What clinical changes in pathology do you anticipate in the future?**

The major thing that's going to change in pathology and one of the big reasons I came here, is how we integrate very large datasets with all the other work we do in pathology. Today, if a patient comes in and is seen, it doesn't matter if it's in the realm of cancer, cardiovascular disease, pulmonary disease or GI. The clinician often orders a series of tests -- five, six, seven tests. They may be biopsies, chemistry tests, metabolic tests, or any domain of testing. That is all done here in this department, and what the clinician gets back is a whole series of different results. And those results don't always align, the clinician doesn't always know how to quite interpret them. And to me that's placing the burden of that evaluation analysis in the wrong hands. It's not putting it in the hands of the individual who's done the tests, who understands the nuances of the test. And it's not helping in terms of the best care of that patient. What we need to do in the future is to integrate all that into a single pathology report in which the clinician can go in and garner an understanding of what all the various testing is done on that individual patient.

This is becoming more and more important because as we move into metabolomics, proteomics, genomics, and all these things that we're actually doing now, the amount of data that's coming back is growing beyond exponentially. Trying to decipher all the test information and understand it, and know how you use external databases to be able to understand these data on an individual patient, are going to be beyond what any clinician is expected to be able to do. But we as the pathology department need to be able to convey that information that allows the clinicians here to best take care of those patients. So that's where we're going in terms of this pathology department and what we need to be doing in the future. It's not going to be a simple task and it's going to take a while to do this, but ultimately this will lead to the foundation of personalized medicine. This will allow us to take care of individuals.

Beyond that this will allow us to take care of populations of patients. One of the important things that this institution is looking at doing is how we manage populations of people. We are going to be able to pull from these very large datasets that we're assembling and start looking at a group of patients, such as asthmatics or those with congestive heart failure, and start making predictions. What are the biomarkers that tell us that this person is getting into trouble? How can we cut it off? How can we do things earlier? These are the kinds of things that are going to allow us to actually manage populations better.

**As a corollary, what do you anticipate in the training of your residents?**

So I think that - again this goes back to your question about why did I came here. As I think about where I think pathology needs to go, and I think I've just given you a little sample of how I'm thinking about it, the only way that's going to be able to happen is if we start from training people at the beginning.

**Yes.**

Right now none of us are prepared to do this kind of integrative reporting. And so we need to start at the very beginning with our trainees and get them used to, and thinking about how to do this integration. And that's why I think it's going to take at least a decade to really change this whole concept of what pathology is and how it participates and collaborates with our clinical colleagues in patient care.

**Your research, which you have brought with you, is similarly outstanding. Can you give us an overview of your research?**

So for many years my lab has been interested in very early development of the nervous system. We are particularly interested in disorders that result in individuals having epilepsy, intellectual disabilities, and some behavioral things such as it's described as autism, I'm not sure if that's

the right way to do it, but autistic spectrum disorder. And that's a wide variety of disorders and there's a whole lot of developmental neuroscience that goes into all of that.

What we're specifically interested in are how cells in the nervous system get to the right place – cell migration. One of the fundamental components of neurodevelopment is that the progenitor cells, the neuro stem cells, are in one location and the cells divide. But those cells after they're done dividing, they don't stay there. Where they end up in the mature brain is quite a distance away from there. So how do they get from where they're -- that immature progenitor cell, to where they're supposed to be in the mature nervous system and make all those connections, differentiate into the type of neuron they're supposed to be and that process from the molecular biology through the cell biology to the function is what my lab is primarily interested in studying. And we do it mainly through different animal models. And we have been modeling different human disorders by introducing the human mutation into the animals, recapitulating some of the phenotypes that are observed, and then trying to understand how these processes are perturbed in these animal models. With the idea that ultimately that's going to give us better biologically based mechanisms to go at for treatment and therapy.

**That's very exciting.**

Thank you.

**Would you care to comment on the research of any of our other faculty here?**

Oh that's a loaded question because there is so much and there's so many faculty. With well over 100 faculty and so many outstanding research projects that that would be hard to do on an individual basis. What I think I'd like to do is give you some kind of flavor of the kinds of research that exist within this department. So this department is very much engaged in understanding cancer. And so there's probably a couple dozen faculty or more that actually are studying various aspects of cancer that bridge the entire spectrum from the very basic science, understanding things like cell cycle and how genes are regulated and misregulated in cancer, up through translational science.

So taking those findings at the basic science level and actually applying them to understanding patients and understanding what drugs a particular patient should get or what prognosis they might get which changes what therapy they're going to actually be on. So that's a whole kind of area – a broad stroke of what is happening in the department. We have one of the premier, if not the elite vascular biology groups really in the, really in the world, and they're studying vascular biology dating back to when Ramzi Cotran and Judah Folkman were doing their pioneering work. But there's a whole group of individuals in the department understanding the basic biology of the blood vessels, and what's become very interesting is the kind of interplay

between vascular biology and immunity. And that's one of the big areas that are currently being studied in this department.

Another area is understanding genetics and genomics. Our department has been instrumental in understanding or identifying the genes that cause a whole variety of disorders including a number of deafness genes -- I mean it goes on forever. But beyond that at the genomic level it has been individuals in our department who have identified how genomic structure changes across populations and across individuals which has permitted literally hundreds of labs across the world to be able to further study associations of genes with disease. Actually beyond that understand how kind of people migrated out of Africa and into Europe and into different places so -- so much from an anthropologic standpoint have been discoveries that have started in this department have been imported into different labs around the world and into different disciplines. So that's just kind of a few examples of the kinds of things that are happening in the department. And again to pick out one or two individuals would be impossible because there's just so many outstanding areas right now in the department.

**You've joined quite a faculty.**

It's an impressive faculty.

**Let me ask you a few questions about the future. What do you predict for the future of pathology at the Brigham and nationally? You mentioned things about it but since there is going to be an effort to define and refine the amount of money that we are afforded or that we ask for, there may be differences.**

Yup. I think what we're looking at doing is going to actually make medicine more cost effective. And that's going to happen on several fronts. But one is just a -- having a common medical pathology record and one part I didn't tell you about is I also see it as dynamic. It changes over time. As more data comes in, it evolves, it grows, it changes. If that record is universally available, I'm going to come back to that in just one minute, what you will be able to do is have access to that patient's information over time.

So for example, let's just say, and I hope this isn't the case, you and I both come into the hospital tonight with pneumonia. We've come in, we're short of breath, we've got a fever, they diagnosis us in the ER with pneumonia. Based on your history, your genetics, your proteomic expression profile and mine, it may be that they're going to be able to look at that and actually sequence that organism that we each have right there on the spot and in the future they're going to send you home with an oral antibiotic for three days, that's all you're going to need. You don't need to come into the hospital. You won't have any allergic reactions to that drug and you're going to do absolutely fine.

But for me, because of who I am, you're going to admit me, and you're going to be able to prevent complications that would otherwise occur because of who I am. So we are going to be do much more effective, efficient medicine that will be far more cost-effective. I mentioned to you about the predictions. So we're hoping that by building these kinds of pathologic databases, we're going to actually construct algorithms through a division that I'm working at building, we don't have it, actually no one has it, called computational pathology. It's taking computational biology and applying it to these datasets to be able to understand what they mean for individuals and this is where we'll be able to do future tracking, future predictions about what happens to an individual in a population and how to manage that. All of that should actually reduce the cost of health care. And we think in a significant way.

The other part of it that I've become very engaged in is building a common labs information system across all of Partners. And this has become a very exciting initiative that was quickly bought into by all of the other Partners hospitals. And what this will allow us to do is have common informatics across all of the Partners systems so no matter where a patient goes, no matter where they are, we will be able to care for them and be able to do it more efficiently so that if a patient comes in and you need to look at their genome or look at just a hematocrit, if they had it done the day before at a center or a satellite, you can get that information, you don't have to repeat it. The amount of redundant testing that's done is a huge cost in the medical system and eliminating that will really improve what we can do for the cost of health care.