Life at the Forefront of Infectious Disease : An Interview with Dr. Andrew Henderson

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In his office, tucked away in a sixth floor laboratory in the Evans Biomedical Research Center, Dr. Andrew Henderson shared his non-linear path into a career researching infectious disease. Dr. Henderson is an Associate Professor at the Boston University School of Medicine and Assistant Dean of the Graduate Medical Sciences division. Between these roles, he has made significant contributions to the body of knowledge surrounding the integration and persistence of the Human Immunodeficiency Virus (HIV) in human cells (see his representative publications below. Emphasizing the need for mentorship in the sciences, Dr. Henderson sheds light on a life at the forefront of infectious disease.

Can you tell me a little bit more about your education and background?

My first research experience...I got into a program between my junior and senior year in high school where I went to UC Davis and measured photosynthesis in heat-stressed plants, and it was just part of this program to expose high school kids from all around California to research, and actually it kind of opened my eyes because...it was actually a lot of fun…

I went to UC Riverside, in large part because they had a pre-med accelerated program affiliated with UCLA, and I started off in that program and I think I very quickly...there were some family illnesses and so kind of experiencing that first-hand how a hospital environment is and how it made me feel, I think, some of the curriculum I was taking my first year, because it was a very rigid curriculum, I found some of the subject matter of the pre-med curriculum a little bit dry.

And I was 18 years old, relatively immature, away from home, I think that maybe also contributed to it, and I ended up playing sports in college as well. So I think a lot of those things made me think - I'm not cut out for a medical profession. Diseases didn't interest me as much as I got further along in my undergraduate training, as much as mechanisms. And so, probably at the end of my sophomore/junior year, I started taking classes like molecular biology, cell biology, and that's when I first realized: this is kind of me.

And the other thing I think was really good was the faculty teaching those courses presented from a more experimental design aspect...and I think it allowed me to appreciate the more creative process of science...At the time, this would have been in the 80s, so things like gene expression, how genes are turned on and off, chromatin, dynamics of turning on batteries in genes - we really didn't know a lot about. So it was also a very exciting time from that perspective.

My first research experience then, in college...came between my junior and senior year. I was going through this biology curriculum, and I kind of realized I had no idea what to do with this. I knew there were professors and I knew they had students and I knew there was biotech but I didn't quite know what people did in any of these environments and I didn't really have any experience with this.

So I ended up being shared by two companies. I just ended up writing to a bunch of biotech companies, and some academic labs. I was fortunate enough to be living in San Diego so there was...a bit of a boom of biotech. So I found two small companies and basically worked as a lab scut for those companies. But it was also my first chance of seeing what people do and seeing research where we're studying...So that was pretty exciting because it was the first time where I learned something in a classroom and we were kind of applying this. It was also the first time being in an environment with people, at different levels, doing science.

People were making a career. I was fortunate that at the end of that experience, they offered me a position...so I worked for them for about a year or so, and it was really rewarding because I had more responsibility, I did really well, they were promoting me…

I didn't quite know what graduate school was. She explained it that there was a stipend involved. But the other thing the company made me realize was that I did have ideas. And I kind of wanted to have a say in the science, work on some of my ideas and explore some of my ideas. And I kind of understood that there was a bit of a ceiling in small company with a Bachelor's degree, and if I was really going to come in and lead a group...I would probably need to [pursue a graduate degree].

So I ended up going back to Riverside. I did yeast genetics for a couple years, and what I realized there was that I just liked having the question, the creative part of it that was the scientific process, that you had this problem, you had these tools, you sort it out, you're building models, you're testing it out. I found that that was really rewarding.

So when I started thinking about what to do next, I started thinking about PHD programs, I was thinking a lot about developmental biology and immunology, and I'm not quite sure how it all worked but I ended up meeting someone on campus and he was

studying blood cell development (hematopoiesis)...and so I was able to switch labs and study B Cell development.

And not that I would ever recommend this for anybody, but I did my undergraduate, my Master's and my PHD all at the same institution. So that was my PHD training. My PHD training was a lot about how very early progenitors of B lymphocytes become immature...and a lot of what we did was try to understand phenotypic markers of that event…and as I mentioned this would have been in the 90s with better understanding of gene promotion, enhancers - those kind of questions were starting to be appreciated.

But I still had no idea what I wanted to do. I was probably going to go back to industry. I liked industry in that I felt like it was very directed. I felt like when companies were doing well... there were lots of resources to do experiments. Although, I also realized that there was a lot of turnover, people were dismissed with very little notice, and projects changed very quickly. So like everything, there are pluses and minuses. But I also kind of appreciated that if I wanted to lead a group in any environment, I needed additional training, and I wanted more biochemical and molecular biology training. So that is what I was looking for in terms of a post-doc. There is enough of a demand for post-docs where you can be somewhat proactive and say "I want to go here, I want to go there", which also allows you to potentially enhance your pedigree.

I think the other part that I was looking for, scientifically or career-wise...I wanted to challenge myself, and go to a more research-intensive, larger lab environment. And so I ended up doing my post-doc at Columbia. Also at a personal level, I felt that I grew up on the West Coast, I was very much Californian...I think I owned one pair of long pants…I owed it to myself to challenge myself and go out and explore.

So I moved to New York and that's where I did my post-doc. That was for about six years, and then got my first position at Penn State at University Park. I was there for about 10 years, and then I've been [at the Boston Medical Center] for about 10 years.

During my postdoc...I started off doing gene regulation in lymphocytes, in particular T-cells, and about half-way through, through a number of discussions and different projects going on in the lab, we realized that some of the factors and elements and questions that we were asking about T-cell receptor genes and tissue-specific gene regulation could be applied to HIV. And so we tried some experiments on the side, they worked really well, and that led me to turn my personal project into an HIV-based project to basically start building my career.

So what's sort of unusual about my career path...is that it was really kind of this switch through different collaborations. I didn't really go in and say...I wanted to work in an HIV lab. It was a little more grassroots and organic, where we were interested in certain questions that then seemed to intersect with HIV…I didn't seek out HIV as a disease.

So I guess that's the linear track of why you're talking to me right now."

In a couple sentences, what would you say is the main research focus of the Henderson Lab?

"We're interested in the biochemical mechanisms that establish and maintain HIV latency. And so the relevance of this is that there are reservoirs of cells that are harboring HIV; it's hiding from the immune response, it's not being expressed and so it's not being detected, probably in these quiescent cell populations, it's controlled during active treatment but once you interrupt the treatment regimens, you see that you get an immediate rebound of virus. So we want to understand that at a biochemical level with hopes that by understanding that, we can then come up with strategies to control it, whether that's targeting certain biochemical pathways, whether that's targeting cell functions and then manipulating the size of that reservoir."

What are a couple of the projects that you have going on right now?

"In general right now, we're very interested in this question of how latency is established, and what's happening at the time of acute infection. So we have a couple different systems where at the time that a cell is getting infected, we're challenging with either other pathogenic bacteria or viruses, or in addition, manipulating receptors on the surface of the cells, and asking, if we signal through these receptors, can we alter the fate of the virus -- does it become very robustly replicated or does it undergo latency? IF we then identify the spectrum of receptors and signals, obviously we want to look downstream and look at the molecular events those are triggering."

What do you think is a major recent development in the world of HIV research? What direction is the field headed towards?

"HIV is a disease we've been challenged with for a little bit more than three decades. And the fact that we can, in many populations, control that disease. The fact that we have a number of antiretroviral drugs, we can try these in different combinations, we can control the virus...It's been pretty amazing in terms of how much progress we've made in understanding this particular virus. I think we've made enough [progress] that people are talking about a cure. Some of those strategies may seem almost like fantasy right now. I think the efforts that people are putting into HIV and the cure agenda will have ramifications for other fields as well.

I think some of the major challenges [in the field]...are still a lot of public health issues - education, testing, adherence, and so I think those kind of efforts are very important especially in those nations that don't have resources that Western populations have. However, we're not too far from an injection every couple of months. So I think [technological developments in treatment] are the most exciting emerging developments in the field, as well as barriers to treatment."

What do you think your biggest challenges or obstacles have been in your research career? What do you think have been the best parts?

"I think the biggest challenge comes down to funding, and how we support academic research in this country. On one hand, there's a lot of support for research, and that's why we have some of the best institutions in the world and when you look at scientific achievements we're usually at the top of the lists. It's clear that, in terms of its impact in science, the United States is very very high. I think that the challenge is how universities use those resources and the availability of some of those resources. So, I think it's important that we have public-based funding of the sciences. I think it values advances in medical treatment. I think HIV is a fine example of where investment of federal dollars into this has led to a huge impact in terms of controlling the disease…

The freedom of being able to do my graduate research and work on problems that I thought were important because I was in well-funded labs was huge. I got into HIV research because I had my own funding, so nobody could tell me not to work on a project that I thought was important...it gave me a certain freedom to explore things.

The other thing that worries me as resources shrink and agendas try to align with outcomes, we undervalue science for the sake of science...and I do worry a lot about that because nobody can really tell you what the next 'hot' thing is going to be...nobody can tell you if we study this funny polymerase in these bacteria that grow in hot springs that we will revolutionize biology...so you need to have a system where you're funding more than five and twelve percent of science, because you have no error there. You have no diversity there. You need to have a system which is going to, to a certain extent, be based on failure in order to have those kind of successes that have a really high impact.

The challenge is how can we assure we support science at a level where you have a good balance of basic and applied, and you have a good spectrum that will let you not only discover, but validate discoveries. We're so fixated on novel discoveries, where sometimes we can just march right along and we haven't really validated with the rigor necessary that this is really a paradigm."

You are an associate professor of Medicine and Microbiology, a primary mentor in the Division of Graduate Medical Sciences and an assistant dean at Boston University's Division of Graduate Medical Sciences which has oversight at the . What would you say is the role of mentorship in research?

"To me, [mentorship] is one of the more important things that I do. I guess in many ways I am in academics because I enjoy teaching...and teaching also means training students in the lab...and using the lab to train people and get people excited about science and see the application of science and see how science works.

First off, I don't think anybody should have one mentor...everybody doesn't need the same type of mentor...I look at [mentorship] as my primary role or one of my more important roles when you look at my position. That's part of the reason I got involved with GMS [Graduate Medical Sciences] and took on that role to be more active and involved in graduate training. I think mentorship too is in large part the affirmation process...A lot of us come into school and we don't really have experience. I think a lot of us come in and we don't really have the sense for what a career path is...I went to college and I thought I would go to medical school, because there was just no context.

As we think about how education should evolve and if we want to have truly diverse institutions of higher education we need to think of ways to allow people to foresee that there are opportunities, there are careers. There's a creative process to this. That's a big part of mentorship as well.

I had good mentors as well, who said "I trust you, I believe you, take a chance" and that was a big part of it."

Do you have any advice for young people aspiring to enter the field of biomedical or infectious disease research?

"My advice is that it's actually fun. It's a lot more creative than people think. And I do think it is your education...and even if you're at a big institution, people want to help you, people will probably take up too much of your time telling you how they became what they became. There's always going to be lots of nos, but if you want to get a lab experience and if you're interested in something and you're sincere about it, you're going to be able to find it. But it is your education and you need to take charge of it."

DR. HENDERSON'S REPRESENTATIVE RESEARCH

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