Transcript of the December 2022 ASCI Perspectives video

Interview with Charles Dela Cruz, MD, PhD, Yale University (elected 2022)
Interviewed by Patrick Nana-Sinkam, MD, Virginia Commonwealth University (elected 2019)

Note: The text has been edited for readability by ASCI staff.

Patrick Nana-Sinkam: Good afternoon, everyone. I’d like to welcome you to this month’s ASCI Perspective. My name is Patrick Nana-Sinkam, and today I have the pleasure of interviewing Dr. Charles Dela Cruz from Yale University. Dr. Dela Cruz is Associate Professor of Medicine (Pulmonary Critical Care and Sleep Medicine, and Microbial Pathogenesis). He serves as the Director of the Center for Pulmonary Infection Research and Treatment and the Vice Chief of Clinical and Basic Research, as well as the Director of the Physician Scientist Training Program. To give you a little bit of Dr. Dela Cruz’s background: He completed his bachelor’s at the University of Toronto and then subsequently entered an MD-PhD program at University of Toronto, and completed his MD at Yale, followed by a residency program at Yale and fellowship at Yale. He actually entered the physician-scientist research track when he arrived at Yale. His laboratory is interested in studying the role of respiratory infection in the pathogenesis of acute and chronic lung diseases. Specifically, his work focuses on how lung infection and pneumonia contribute to inflammation, injury, and tissue repair in the lung. Among his many accomplishments, he’s been the recipient of several research awards throughout his career; has served as a chair of an NIH study section, which is very prestigious; and most recently, he was elected to the ASCI in 2022.

Congratulations, Dr. Dela Cruz, to being elected to the ASCI in 2022, and thank you so much for taking the time to join us today.

Charles Dela Cruz: Thank you very much, Patrick, for the opportunity.

PN: I’d like to start out with maybe just asking you to share a little bit about your background and, importantly, your path to becoming a physician-scientist. Why not a scientist or a clinician alone? Why did you decide to pursue both?

CD: Thank you for that question. So being a physician-scientist is very new to me and my family. I grew up in Canada. Both my parents are not physicians or scientists. In fact, I’ll be the first-generation person who has graduated from a professional school or a PhD degree. I grew up in a family where they’re in businesses or commerce or computer sciences. And so when I was growing up, especially in high school, I tended towards more in the field of sciences. I felt quite interested and fascinated about it. At the same time, I had some opportunities to volunteer in a local, nearby hospital, but was really impressed by the impact of that relationship with patients. I explored that as an undergraduate in the University of Toronto, where I focused on immunology, virology — in that field. And my first experience with research was actually an opportunity from a summer research internship in a laboratory where they were studying ribozymes against HIV infection. And I thought it was kind of fascinating: something really novel, new techniques — you test out your hypotheses, trying to figure out whether it works or not, and for a disease that people are still struggling now. And I further explored opportunities and balancing research and learning about sciences, both in classrooms and also the practical side of things. But I had no idea what a physician-scientist was all about. I actually didn’t even know they existed. And as I went along my undergraduate experience, I was exploring opportunities to help patients through medicine, but also was intrigued about the whole idea about scientific discovery and trying to figure out how that could work. To be honest, somebody told me about the MD-PhD program in Canada. There’s sort of only a few schools that provided that, and I think University of Toronto was one of the main ones. But I think it was a perfect opportunity for me at the time of my career to take a look back and really spend the time
through that more formalized program to study medicine, explore science, and really integrate both. And at least for me, it was the right timing — not because I wasn’t terribly decisive about what to go for initially, but it allowed me time to explore what I really wanted to do.

So I went through the medical school classes and then ultimately contributed to a PhD thesis work on vaccine design in the infectious disease realm. And shortly after I defended my PhD, I was provided some opportunity for some additional research at Yale, which is where I kind of transferred to Yale School of Medicine and matriculated with the MD class here in 2003. Here at Yale I was provided a lot of opportunities; I explored more research and really solidified the fact that I really wanted to be a physician-scientist, because I couldn’t give up one or the other — probably because I think the experience with patients really allowed me to understand what the needs are, especially in the area that I’m interested in. I rotated in an ICU as a medical student and later as an intern and really was fully interested in that field clinically: it would fit me perfectly clinically. I loved the interaction with the staff in the multidisciplinary rounds, the consultants, patients, patient families, taking care of really critically ill patients. And it was a decision I made that ultimately resulted in a fellowship in pulmonary critical care. I still tell my mentees and applicants that it’s really important to find your clinical niche and what you enjoy doing. And then that could easily be combined with your academic passion and research interests. And for that, I still was interested in infection. So specifically, it was pulmonary infection and how that causes pneumonia, how that causes lung injury, ARDS, how it causes chronic lung disease, for example. And so that has been the main focus of my research program and research career throughout my stay here, with a lot of support and wonderful collaborations.

Your question about why not just a scientist or a clinician: I think for some people, it was very hard to do one or the other, and I think that was for me — mostly because I get engaged both from a personal level, taking care of patients, understanding their needs, but also working in the health system, figuring out what is needed. And for me, for a while, I was studying pneumonia. And it was a disease that I know a lot of people take for granted. And thinking that it’ll cause you some cold symptoms, you’ll be fine after a few days if you take some rest, some antibiotics. But really it has affected a lot of people, not only in the US, but globally. And something very simple that could be addressed, could really save a lot of lives. I think as a practicing physician, I saw there’s a need not only for more advocacy, more attention to this disease, but also pushing the field to be more sophisticated, to really personalize how we approach pneumonia and to target a treatment for our patients. And I think becoming a physician and being a physician allowed me to see that as an opportunity and a need. And so throughout, I’m trying to balance what I’ve seen in the clinic, in the ICUs, to what we study. And for example, I couldn’t have envisioned a pandemic as large as COVID to highlight this importance and that infection can really cause a multitude of problems. And in a way, I think we’ve learned a lot. I think the academic medicine scientists and clinicians are ready for these kinds of challenges. But it’s unfortunate we had to wait for a pandemic to realize a respiratory infection can really cause major damage. I think these lessons have been learned from the past, and we really haven’t learned much from previous pandemics. And hopefully, I think, from this current experience, that we can learn a lot of lessons from it. So I can’t imagine, at least for myself and for many others, to separate those two experiences. And as a scientist and a clinician, I think it could be through a formalized MD-PhD program or physician-scientist training program — which we’re
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currently interviewing for candidates — or MDs who have a lot of research background who are physician-scientists. And many of my mentors who are physician-scientists are MD-only. And they’ve been wonderful mentors for me. And so I think it’s been humbling experience; it’s been a rewarding experience; and I think it allowed me to really explore a lot of things, both scientifically and what we can do for patients.

PN: Great. Well, I think that’s a perfect segue into my next question. And that really delves into some of the research that you’ve done. I had the opportunity to read through some of your work — not all, there’s a lot out there, but not all of it. Your group, certainly since the beginning of the pandemic, your group has been actively engaged, really focusing and trying to understand some of those underpinnings of the dysregulation of the immune response in COVID; and furthermore, how coronavirus seems to reprogram or alter the immune system in such a way that maybe it increases our susceptibility to secondary infection, particularly bacterial infections. Given the work that you’ve done over the last few years and even the work before that, how has what you’ve learned really informed your perspective on what the strategies should be moving forward to battling COVID — which as we know is not necessarily going away any time soon — and importantly, how it might inform the development of novel therapeutics down the road for coronavirus?

CD: Thank you. Great question. Our group in collaboration with others as well here at Yale, we’ve been studying respiratory infection using basic models as well as translational studies for many years now. I think through our center, we’ve had collaborations already in place, collaborators outside our section, other departments with diverse expertise. And we were also doing biorepository samples: a patient coming in our ICU with various respiratory infections. So we were, I think, poised for COVID-19. But we weren’t expecting the proportion, the extent of the pandemic, to be honest. But it really required a big-scale collaboration with all my collaborators and other faculties — from public health, immunobiology, department of medicine, from pathology, pediatrics even — to really work together and identify that this is a big need to really set up a biorepository to understand what is going on while we were all trying to figure out what this new virus is and what’s causing. This was actually kind of nerve-racking, because we had little understanding of how much this is transmittable; can we get infected doing this? what are the protections that’s needed and handling of specimens? And so I really commend all my collaborators and the team, and not only here at Yale, but other places around the country who really try to understand COVID for the purpose of pushing our understanding and also developing more treatment. We’ve learned a lot: we learned about the new tools to identify infections. Through some of the repository work, we were able to collaborate with individuals who wanted to study how we can use saliva as a detecting tool. And so now they have a way to protocolize this approach to detect infection in the saliva. We didn’t know a lot about saliva and respiratory infections in the beginning. In terms of the use of blood biomarkers and how cellular components are different in severe disease, try to phenotype that this immune response was really dysregulated at different phases of the disease, while you are trying to tap into, for example, these patients as they progress in the stages in their hospitalization. And this is what’s happening at the same time where the clinical team and treatment team were trying to figure out what’s the best treatment regimen. What are the antivirals? We’ve all had our experience and shares of different types of drugs that have been tried and that did not work. And ultimately came up with the idea that
you definitely need an antiviral treatment in the beginning, but if it’s too late in their disease course, maybe the immune response is dysregulated, and you might need some immunomodulators.

I was surprised that steroids work for COVID-19. Our experiences from a previous pandemic, the 2009 influenza pandemic, show that steroids do not work. In fact the guideline says steroids probably can cause more mortality than you think. And so the fact that globally, there are a lot of efforts to test the use of dexamethasone for certain types of patients in the hospital to calm down the immune response was really interesting, and it was probably quite helpful and really changed the course of the disease for the sick patients. And then, obviously, the significant, rapid advancement of novel vaccine strategies — and many are vaccinated — have really helped curb this infection in the various different waves. I think our own study from a basic science standpoint really found it intriguing that this SARS-CoV-2 coronavirus, when it infects cells, the macrophages, that really causes this lysosomal dysfunction — problems with deacidifications — and then really predisposes the cell for its ability to control bacterial infections. And we all know for maybe a third of the patients, after some viral infections — including influenza and now SARS-CoV-2 — that those patients are at higher risk for secondary bacterial infection because of what the virus did. And so this recent work sort of highlights that the viruses are pretty smart in terms of how they can manipulate the host. I think you mentioned earlier that these challenges for future viral epidemics and pandemics will come, and so hopefully, we’ll learn some lessons from this.

But what was impressive was how the academic, scientific, and medical fields all came together to really collaborate to find out what’s going on with COVID-19 — improving our understanding of the disease and trying to identify new treatments, novel treatments, including approaches to how to take care of our patients in the ICU on the ventilators, proning. We were doing also awake proning, even, for patients based on necessity, and we learned a lot from it, and now we know that it could work. But there are also things that — we knew that this was happening already even before COVID: that the tools we’ve learned so far, so much in the ICU to take care of these sick patients, still work. Proning was known to work before; ventilators, we know, help with low tidal volume. We know that that works. We also know that influenza virus can cause all these organ diseases outside of our lung. We just didn’t pay attention to it. COVID, because it’s one big infection globally, we saw all the different types of flavors of what it can do. And so it just really accentuated and really highlighted how a virus can cause all these different organ problems.

I think what it did was, hopefully, it made these collaborations much easier. I think initially it was by necessity, and people weren’t doing anything else other than COVID. But I think what it did was it sort of highlighted the importance of data sharing, large data uses, big team sciences, I think that’s the wave of the future in terms of where science is going to go. And I think our training of the next generation of physician-scientists will have to take that in mind, that they should be able to work with other people. They can’t be just working on their own labs any more. Those are the bygone days, I think.

**PN:** Yeah and it’s interesting: You talk about the future, and you mentioned there at the end about the future scientists and the importance of being part of a team. And that’s really going to be the most effective way, I think, to make any major discoveries. It’s no secret that over the last several years, we witnessed a reduction in the number of physician-scientists in our field. And I know that from your CV and just hearing you talk that, really, training that next generation is something that’s
CD: Yeah, I think that’s an important question, because that’s the foundation for what future medicine is going to look like. And so who will be the scientists, physician-scientists who are going to be doing the research, the training, and to move the field forward in any of our fields? And what I’ve learned throughout — and a lot of it is through learning as I go, because not so long ago, there’s less of a structure; there’s less of people understanding the right pathways to physician-scientist; opportunities for funding or collaboration — there’s less of those. I think now we have more of those, more people like yourself and others in the ASCI who have gone through this and are champions of this field. There’s no one path towards being a physician-scientists, as I mentioned earlier. I think MD-PhD, if it’s the right timing for you, that’s perfect. Some people say it’s too long — that’s fine. And some people: MD and a lot of research background — it’s perfectly fine, too — to be a physician-scientist. And some decide to do a formal degree later on; it could be a PhD or it could be a master’s in bioinformatics. I think there are many paths towards physician-scientist, and so there’s no one right fit for everybody. And everyone has their own special life experiences and circumstances that make one or the other more attractive. And so that’s what I’ve learned really is — what I’ve learned and what I’ve counseled people, essentially, is that there are opportunities if you want to be a physician-scientist. And for me, I was fortunate enough to have the right mentors, who looked out for me within Yale and outside Yale to let me know, “Oh, Charles, I think this would be great for you. You should look into this.” Or people who I collaborate with say, “Why don’t you have someone in your group work with us?” Looking out for the right mentors, I think, is important for future leaders.

The other lesson that I’ve learned is there’s no real rush to really hone in what field you want to get into. I think you really, really need to figure out: this is the right fit for you clinically. And then the hardest thing, to be honest, is figuring out what your academic passion is, and there’s no rush for that either. And so for me, it’s just so lucky that what I was interested in before, I’m still interested in now. And things can change, and so I adapt based on what’s going on, but I’m still interested in that field. And I think that’s quite important to make it sustainable to the life of a physician-scientist: pushing the discoveries, pushing your clinical work, and pushing your research program.

So I encourage a lot of the trainees to learn from their experiences, try things out, try rotations, clinical rotations, even lab rotations, and what makes you tick, clinically and academically, in terms of research. I think that’s the one that will sustain many people, including myself. Because when I attend the ICU, I love it. I’m there one week at a time, as you know. It’s really energizing. You know exactly: this is the field you want to get into. Sometimes the nurses would say, “Well, when do you come back?” I always tell them, “Well, I do this research thing on the side [chuckle], and won’t be able to come back any time soon, but hopefully.” We have to partition our time well. And that’s really, really an enjoyable and rewarding career, and I’ve been fortunate. I know my parents, who are not in the field, always ask me, “When do you stop training?” I think there was one point I stopped telling them I graduated from something [chuckle] — or be it a fellowship or something else. It’s a lifelong process. And so I think the way they’ve seen me going to the lab or working with a laptop here and there and sometimes, I think that’s part of the physician-scientist — I think with
the realization that you have to have a well-balanced work life. And I think that’s why it’s harder for people, and the purpose for why you’re doing this — it’s really important, And to have the right support system is even more important, I think.

**PN:** Well, I know I speak for everyone in saying that we’re fortunate to have you as a member of ASCI. And certainly, the fact that we’re in the middle of this pandemic, we’ll be looking to your lab and others in guiding us in terms of that next phase of how we’re going to manage COVID and other infections. I really, on behalf of all of the ASCI, I really want to thank you for taking the time. I know you’re very busy, and I appreciate you taking the time to be with us and, of course, wish you the very best in the future.

**CD:** Thank you very much for the opportunity.