IJMS INTERNATIONAL JOURNAL of MEDICAL STUDENTS

The AIDS Frontline, PhD Reformation and Our Definition of Scientific Rigor - An Interview with Professor Arturo Casadevall

Paul MacDaragh Ryan.[1]

The Interview

Professor Arturo Casadevall is the current Chair of Molecular Microbiology & Immunology at the Johns Hopkins Bloomberg School of Public Health and Johns Hopkins School of Medicine. Following completion of his MD/PhD at New York University and an internal medicine residency at Bellevue Hospital, he became a prolific physician-scientist who has made major contributions to the realm of infectious disease and host immunology. In addition, Professor Casadevall is the founder and Editor-in-Chief of the highly regarded open-access general microbiology journal *mBio*, a long-standing advocate for underrepresented minorities in science and a central figure in the promotion of scientific rigor, reproducibility and responsibility.

Professor Casadevall and his like-minded collaborator Professor Ferric Fang have published about the idea of scientific rigor, as well as on the central scientific process of grant peer review. The two have described the inequity of the grant review process and presented evidence indicating that there is no relationship between grant score and productivity. As a result, Professor Casadevall and his colleague shocked many by suggesting that the National Institute of Health should undergo a fundamental reformation in its grant system and implement a process in which funds would be allocated by a lottery, in which only meritorious applications would hold a ticket. This type of perpendicular thinking, along with an impeccably ethical mind and an outstanding medical research portfolio make Professor Casadevall an ideal role model for all trainees within the medical and scientific profession.

After finishing your bachelors in chemistry, what drew you to a career in medicine?

I had always been interested in medicine. Perhaps it was because my grandfather was a surgeon and he was a major formative influence in my early life. A career in medicine offered the opportunity to combine my interests in science and investigation in a field devoted to promoting human well-being.

In light of current discussion around the death of the modern clinician-scientist, what would you say to promising medics with research aspirations who are considering following the MD/PhD route that you followed?

I think the death of the modern clinician-scientist has been overplayed. Medicine needs clinician-scientists to make progress since clinical practice is a great observatory for new insights into the pathogenesis of human disease. Given this need, there will always be a route for physicians interested in investigation to develop successful careers. I admit that it is harder today to combine a career that includes clinical medicine practice with investigation given the enormous demands placed on clinicians. The MD/PhD approach is a natural route for physicians who are interested in investigation. However, other routes such as research residencies and post-graduate training programs can train aspiring clinician-scientists on the methods of investigation.

You came into your internal medicine residency at Bellevue Hospital at a pivotal moment in 20th century history. What was it like to be a junior doctor in the United States during the AIDS epidemic and did this inspire your choice in specialty?

The HIV epidemic was a formative experience for many of us who became physicians in the 1980s. Today, when an HIV infection is treatable, it is difficult to convey the magnitude of the calamity that became the AIDS epidemic and how it influenced medicine. Basically, you had a new organism emerge that destroyed the immune system. In retrospect, it is remarkable how much progress was accomplished so quickly. The syndrome was described in 1981, the virus was described in 1984, the first antiviral therapy was available in 1987 and the highly effective therapy became available in 1996. Although clearly a decade and a half is too long for those afflicted at the time, it is nonetheless remarkable how rapidly progress was made considering that we were dealing with a new agent. The progress with HIV has given me a lot of hope that science and human ingenuity can one day solve many of today's intractable medical problems.

While listening to a recent JAMA Network podcast entitled "Working on the Precipice: On the Frontlines of the AIDS Epidemic at the CDC", I heard Dr. David Auerbach reflect on the camaraderie and sense of greater purpose that he discovered while working on the AIDS epidemic (referred to at the time as Kaposi Sarcoma with Opportunistic Infections) for the CDC.[1] Although there may not be any directly comparable crises in today's terms, we are facing our own plethora of global and local health challenges. In what area do you believe the doctors of tomorrow may be able to contribute in a similar manner to health and society (i.e. vaccines/antimicrobial resistance/metabolic syndrome etc.)?

The AIDS epidemic in the 1980s was a terrible time and difficult times have a way of solidifying bonds between caretakers. I suspect similar experiences occurred during the recent Ebola outbreak in West Africa. I think every crisis is different and every generation of physicians faces their own trials. Although I do not have a crystal ball for the problems that doctors of tomorrow will face, I suspect that they will have to confront similar problems as those of the past. In every crisis, the answer to new challenges is to deliver the best care possible while also carrying out investigative work to push back the boundaries of science and improve medicine.

You have mentioned previously -perhaps in a tongue-in-cheek manner- that you are not sure that you would be able to get educated in New York today, as your alma mater (City University of New York) is now a fee-paying institute. As an open advocate for the underrepresented, do you think that the outlook is good for minority groups within science and medicine? If not, what can be done to rectify this?

It is true that we were so poor that the only place that I could have attended college when I finished high school was the City University of New York, which at the time guaranteed a place to every applicant and

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Editor: Mihnea-Alexandru Găman
Submission: Nov 11, 2018
Acceptance: Nov 19, 2018
Publication: Dec 20, 2018
Process: Not peer-reviewed

was free. Eventually, they were forced to charge tuition but even today, it remains modest relative to what other Institutions charge. I think the demise of free higher education in the United States was a terrible loss to society and I am a big proponent and supporter of public education. I think the road for the underrepresented and minority groups is rockier but I am encouraged by all the progress made in recent years. I am optimistic that things will continue to get better although improvements may be slow and incremental.

Do you believe that free-to-publish, open-access journals like IJMS are removing barriers for curious medical students and young scientists?
I think having a free and peer reviewed journal for medical students and young scientists is terrific because it encourages scholarship and investigation.

In 2016, you and Prof. Fang authored an editorial in which you produced a novel definition of scientific rigor.[1] Could you give us some insight into this definition and why you felt it needed to be explicitly outlined?
We were very surprised that despite all the talk and emphasis on greater rigor there was not a good definition for how to accomplish it. I think our major contribution was to argue that to achieve rigor one needs the five components that we identified. In other words, it is important to bring different approaches to test conclusions and results to reduce the likelihood that these are spurious or faulty.

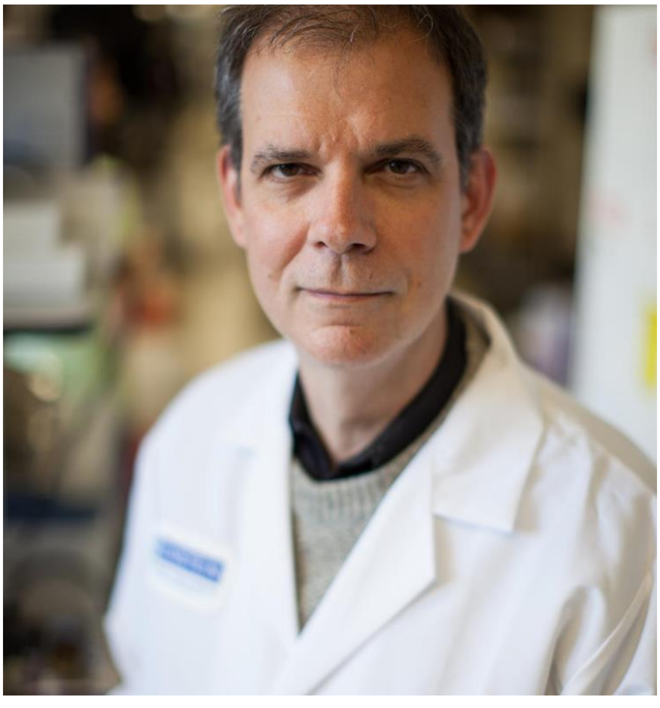
You have been doing some revolutionary work within the realms of PhD education and scientific training. Could you tell us a bit about the R3 programme which you developed and what you intend to achieve with it?
We (Ferric Fang and I) argued in 2012 in an article titled 'Reforming Science' that there was a need to improve the training of scientists.[2] Current PhD programs are excellent at teaching students how to do deep work and that needs to be protected and encouraged. However, current programs do not do a good job of teaching critical thinking or developing broadly trained scientists. The goal of the R3 program is to maintain the rigorous training in laboratory research while also teaching didactically the fundamentals of good science, rigor, communication, etc. The program was created at the Johns Hopkins School of Public Health and we have been very gratified by the interest and success of the initial efforts.

The R3 programme currently appears to be targeting PhD trainees; however, you have previously indicated that you believe it should be compulsory curriculum for researchers of all experience levels (including principal investigators), in a manner similar to continuous medical education. Do you foresee that a standardised continuous scientific education curriculum may become a global reality?
The R3 program is currently focused on PhD training but we hope that some of the principles that we are trying to develop, such as teaching critical thinking, could be applicable to other disciplines such as medicine. One of the problems in setting up the R3 program was there are few faculty who can teach it. However, if scientists make the effort to learn critical thinking, logical traps and the basis of good experimental design then many can become teachers and it may improve their own science. I believe there is a need for programs similar to continuing medical education for scientists that would provide continuing scientific education. These programs would allow them to keep up and remain current. We hope to take that on in future years.

As you outline, up to this point junior researchers have generally learned their trade from their mentor in a form of scientific apprenticeship. For those who do not yet have access to the R3 programme, what characteristics would you advise an early-stage researcher to look for in potential mentors?
I think all graduate students should ask their prospective mentors some basic questions like: 1) How do you plan to train me? 2) What is a PhD degree to you? 3) How do you know when a student is ready to finish to finish their PhD? Even these simple questions will encourage discussion between students and prospective mentors that would help the student understand what training is like in that particular laboratory and that could lead to better decisions in selecting laboratories.

Several years ago, you called for a reformation of the National Institute of Health grant review process and called for a system of funding by lottery.[3] Presumably, this concept consistently alarms and confuses your audiences, yet your rationale is in fact extremely compelling. Could you briefly explain this concept for our readership?
Current review panels tend to stratify applications based on their perceived excellence. However, we showed that scientists cannot stratify applications in the upper 20% range where most funding paylines fall. Hence, asking scientists to stratify grants is futile for identifying the best work and has the debit that it brings in conscious and unconscious biases. Although scientists are not very good at stratifying proposals they can certainly make two piles - meritorious and non-meritorious since most reviewers can discriminate between good and not so good proposals. We have suggested that funding in the meritorious pile is then allocated by lottery. Current review systems are already a lottery but without the benefit of It being truly random. The modified lottery system that we have proposed would preserve peer review and could result in more innovative work funded. This system is already used in New Zealand and by some European funding agencies. I believe it could one day be broadly used to distribute scarce research funds

Figure 1. Professor Arturo Casadevall, Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health



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Acknowledgments

The author wishes to extend his sincere gratitude to Professor Casadevall for taking the time to be interviewed and for his insightful responses.

Conflict of Interest Statement & Funding

Dr. Ryan has nothing to disclose. No financial assistance was sought for this article.

Author Contributions

Conceptualization: PMR. Writing – Original Draft: PMR. Writing – Review & Editing: PMR.

Cite as:

Ryan PM. The AIDS Frontline, PhD Reformation and Our Definition of Scientific Rigor - An Interview with Professor Arturo Casadevall. Int J Med Students. 2018 Sep-Dec;6(3):126-8.