Interview

Rheumatology, collaboration, and modern-day research: An interview with Dr. Proton Rahman

Ben Edwards, BSc Pharm¹

1. Faculty of Medicine, Memorial University, St. John's, Canada

ABSTRACT

An interview with Dr. Proton Rahman, a rheumatologist, genetic epidemiologist, and professor at Memorial University. Dr. Rahman has been working in the province for the past 24 years and in addition to his clinical work, has done an extensive amount of research with an interest in the genetics of spondyloarthropathies. He has received numerous awards in the field, including the Canadian Rheumatology Association (CRA) Young Investigator and CRA Distinguished Investigator awards. In addition to this, Dr. Rahman has made significant contributions in the development of the Newfoundland Genealogy Database (providing extended pedigree information for over 550,000 Newfoundlanders) and has led a COVID-19 pandemic analytics team for the Government of Newfoundland and Labrador. In this interview Dr. Rahman discusses his background, the clinician-scientist balance, and tips for learners interested in a career in research.

Could you tell us a little about yourself and your background in research?

I did most things here at Memorial University (MUN), I went through MUN medical school then did a rotating internship. I did my residency at Memorial and my subspecialty in Toronto in rheumatology. While in Toronto, I did genetic epidemiology (a combination of genetics and clinical epidemiology). I have been back since 1999, just working away in clinical rheumatology. I find the trainees nowadays are so much further ahead than we were, way back when. Research was certainly encouraged but now I think it is thought of more by the residents; it allows you to be more competitive for a residency position, faculty position, or to continue on with research. It adds a lot of flavour to clinical medicine if you do research along with it.

So, the benefit of clinical medicine is that you get to help people right away and that is a great feeling and privilege. Especially if you specialize, after a while you see similar things over and over again. The variety added by being able to answer your own questions that you actually see is really rewarding. To present to your peers, get feedback, then work at it again is quite good. I have a soft spot for researchers that are clinician scientists. I think that is something, respectfully, we are lacking a little bit in our university.

You can do clinical research or bench research as a clinician. Both are really important. The transition from being a clinician to a clinical researcher in, say,

clinical epidemiology, health economics, or qualitative studies is easier because it is more of a natural extension of what is being done in the clinic. It is highly relevant and adds a lot of value. Biomedical research is a more difficult transition, particularly if you are planning to be an independent investigator running a laboratory. When I went through, a master's degree was probably sufficient. Now, if you wanted to do any molecular investigative work, it would be tough for a lab to be funded unless you had a Ph.D. The first thing when I mentor someone, if they are looking towards a clinician scientist route, is to make sure they take the time to train appropriately. Otherwise, they would collaborate on studies but not independently lead them from their laboratories. To a certain extent, you must have a fire in your belly to do that because it takes a little bit longer, and, in some ways, it doesn't fit as well with your clinical work. You spend extra time learning to do things.

Having a molecular understanding has helped me tremendously in clinic, oddly enough. I got into genetics because I thought it would be neat to look at the genetic basis of rheumatic disease as they are highly familial. What I didn't realize when I got into it is how much my research would help me in the clinical realm. What happens when you take the time to understand disease pathogenesis, when it comes to choosing therapeutics, or trying to determine disease prognosis, having a deeper understanding of pathogenesis helps you make clinical decisions—translating to better care for the patients. Research doesn't necessarily have to be just

something that is only in the lab or only something that you publish but is something you can bring back to the clinic. It goes both ways.

The kind of work that I do fits into translational genetics. I got interested in that when I realized I was going to come back to work in Newfoundland and Labrador (NL). We have a higher prevalence of psoriasis, due to something called the founder effect. I thought it was very strategic to understand the genetic basis of why we have this founder effect. The extension of psoriasis for rheumatologists is psoriatic arthritis. I put some thought into what it was I wanted to get an expertise in, to a certain extent took advantage of the natural history or genetic history of our province.

My main interest is identifying different genes related to psoriatic arthritis. I've had a lab for about 20 years that have identified several genetic variants associated with psoriasis and a few with response to biologics in patients with psoriasis. Along with doing genetic studies, I also got into clinical trials. Not so much participating in clinical trials, which I have as well, but helping pharmaceutical companies think about post-hoc analysis, and secondary predictive analysis, searching for super-responders and those resistant to therapy. That itself has been very rewarding as it gives you insight into the steps from early product development to completion of phase 3 registrations studies - you then are aware of what it entails to get a drug to market and the rigor that is needed from the FDA and others to approve a drug.

The other thing with research is that every 4-5 years. you may need to re-invent or transform yourself so that your ideas or approach does not become stale. Obtaining funding is very competitive, so you need to develop new ideas rather than merely an extension of previous methods. My recent focus has been on working out of the lab and in real-world studies for various reasons. Much of this has been due to the availability of multiple sources of extensive data, such as the EMRs, along with advances in our ability to interrogate big data using artificial intelligence. The lesson I've learned here is not to get stuck with the same technique repeatedly for many years but instead strategically think about shifting focus. Once you have mastered certain key principles related to research, it is not as challenging to make these changes.

How do you find time to integrate your clinical and academic work on a daily basis?

It is a great question, and it is very challenging. The issue with doing rheumatology is that we have an

exceptionally long waitlist, so there is invariably pressure regarding seeing new patients follow ups, handling emergency cases, and doing call. For me, the patients always come first, so sometimes, despite my best efforts, it is difficult to secure research time as clinical duty can be disruptive. You have to be flexible and organized. The way I've survived securing grants and publishing manuscripts at a decent rate is to bring the research work home and spend time at night doing these tasks. If you were in a discipline with less clinical pressure, you might be able secure more protected research time. If you are committed to doing research exclusively as a clinician, there are research-intensive universities that may support you in this endeavor. However, this type of support is not necessarily available in all universities. Despite my keen research interest, just doing research without a clinical focus does not appeal to me. Seeing patients can be instantly gratifying, whereas, in research, there are very few 'Eureka' moments. So a combination of clinical and research duties is ideal, but finding the balance can be difficult.

Could you describe how a curious clinical finding, trend, or need you notice in clinic goes from an idea to a published paper?

Unmet needs are relatively easy to identify in the clinic, as you are faced with multiple questions when you are unsure about the next steps in managing patients. Once you have formulated a question, the most important thing is to see if someone else has answered it. So often, you get so excited about something, then you look deeply into it, and it has been adequately addressed. It is a good use of time to explore these ideas. You always want to be inquisitive; you always want to learn; you always want to follow best practices, which means going to the literature all the time. If your question has not been previously addressed, the next thing you have to do is explore the feasibility: can you answer this by asking yourself if you have the patients, resources, and funding? If you cannot answer this on your own, then seeking collaborators that are mutually interested in your question is important. This is the usual process that I run through. Once you are actively engaged in research areas, finding collaborators is not as difficult as you think, as the research community for a dedicated area of research is generally relatively small.

Do you have any advice for medical students or residents that are trying to get into research or who want to integrate medical research into their future careers?

Everyone should have a general idea of how evidence is generated and appreciate that research is essential in improving patient care. Only some people have to do research, but everyone should be "research friendly" in understanding how the data is generated. This will help you understand how to interpret studies that you are reading. Please be open to entertaining requests from researchers seeking patients for their studies.

As you progress in your clinical training, I encourage you to align your clinical and research interests. In other words, ideally, you should not have a research interest entirely unrelated to your clinical interest. You can get those aligned and bring the things you see in the clinic back to your research program and vice versa. It doesn't matter what comes first. Suppose you have extensive research experience in neurosciences. In that case, you may want to think about if you want to meld the two together by doing neurology or rehab medicine. Things are so competitive in terms of grants that a cohesive clinical and research package makes you a more attractive commodity to get funded. You would be surprised how people's research interests sometimes differ from what they do daily. Try and link them as much as you can.

The other thing is always to collaborate; if you want to do something quickly, you can do it yourself, but if you're going to do it for a long time, you have to do it with others. What you want to do if you want to do research is to work with a large group, sometimes, they will carry you, whether it is in regards ideas or funding, and sometimes you are the primary contributor to the group. Research is also quite multifaceted and having investigators with a slightly different perspective will only strengthen your program.

Can you describe the watershed moments of a career in research? What are the highlights and what are some of the downsides?

The highlight of any research is when you have conceived an original idea and your paper has been accepted. It is not so much about publication or subsequent citation. The concept of peer review is fundamentally important to me. This is why I am an Associate Editor for the Journal of Rheumatology. Completing a study and not sending it out for peer review does not sit well with me. You need to communicate your results and have your peers (experts in the field) say that your completed work contributes to the literature. This is the purpose behind peer review. So, the work being done with the MUN medical journal is very important — as the authors' will get their work appraised. Once your article has been peer-reviewed

and published, you feel you have contributed positively to the scientific process. Then if that study contributes directly or indirectly to improved patient care, that is the watershed moment for me. We have been fortunate in developing tests or identifying genes that have had a clinical impact; however, most of our research does not lead to that clinical translation that quickly.

The downside of research is when you think you have a good/great idea, but you can't get that idea off the ground because you can't convince your peers to fund that project. It is easy to get frustrated at this point, but you have to believe in what you are doing; please stay with it and find a way to address it.

In terms of doing research in NL, can you speak to doing research in a more remote centre with a more rural population?

You can get your research aligned with your population, but it depends on the research you want to do. There are certainly challenges to doing research when there is not a critical mass of investigators with similar or complementary interests to ours. For instance, more research-intensive universities will have shared laboratory space with state-of-the-art equipment and support staff to help with the analysis. So, when researching in NL, and if these resources do not exist, you need to seek out colleagues doing similar work outside your institution. You can overcome some challenges by strategically partnering with others outside Memorial. The more significant challenge to overcome is the need for adequate protected time compared to peers from larger centers. Working in smaller jurisdictions does have its benefits as well. As there are fewer researchers, you can expand your scope of research without interfering with other ongoing initiatives.

If you had a magic wand—are there two things you would like to change about medical research, either in the province or in the country?

I would revisit how research is funded and how researchers are acknowledged for their efforts. The success rate for a substantive research grant is quite dismal. We either need to increase the total research funding or be committed to funding researchers with an established track record for an extended period. Many good ideas are abandoned when funding an ongoing study or program is terminated. We need to have greater faith that a well-trained, motivated, and accomplished researcher will do meaningful research. In the present system, we are just cycling through the

researchers, deterring physicians from research training.

As research is more collaborative, multiple investigators are contributing substantively to completing a research project. Crediting only one host institution with the funds or just the first or senior authors for the manuscript does not seem fair to me. We need to think more carefully about how to acknowledge the actual contribution to a project. The present system fosters research silos than genuine collaborative efforts.

Can you please describe a 'day in the life' of a rheumatologist/clinical geneticist and any advice you might have for students interested in the field of rheumatology?

I am happy to chat with any medical student who wants to do research. Regarding advice for those interested in rheumatology research or, in fact, any research - identify a research mentor who has been able to navigate the system successfully.

Mentors help and will accelerate your progress. Mentors will guide you on how best to align your clinical work with research and maintain work-life balance. They will also

facilitate connections to their broader research network and work with you to identify optimal places to train if necessary. If you can get involved with some aspect of the research your mentor is doing, that would be ideal, as you can benefit from a somewhat mature project. It would be best to be patient as you develop your research expertise. Everything moves slowly at the start, from getting ethics, patient recruitment, or laboratory setup. You need to be realistic regarding your expectations and not get too frustrated. Everyone has a different step up, so resist the urge to compare your progress with others. Finally, enjoy the process and believe that these extra efforts in research will pay off in a more rewarding medical career and improved patient outcomes.

ACKNOWLEDGEMENTS

A thank you to Dr. Rahman for being so generous with his time and participating in this interview.