Interview with Dr. Vinod Chandran

UTMJ Interview Team (Happy Inibhunu and Jeff Park)

Dr. Vinod Chandran

Dr. Vinod Chandran MBBS MD DM PhD, a rheumatologist and clinician-scientist, is an Associate Professor of Medicine & Laboratory Medicine and Pathobiology at the University of Toronto, an Adjunct Professor at the Memorial University of Newfoundland, an affiliate scientist at the Krembil Research Institute, a member of the graduate faculty at the Institute of Medical Science, University of Toronto, a scientist with the Creative Destruction Lab, Rotman School of Management, University of Toronto and a staff physician at the University Health Network and Mount Sinai Hospitals. He co-directs the Psoriatic Disease Program at the University Health Network, Toronto, Canada.

Dr. Chandran's research interests lie in the genetic and molecular epidemiology of psoriasis and psoriatic arthritis (PsA), especially with regard to prognosis. His translational research program is focused on developing proteomics and metabolomics-based screening and prognostic tools for psoriatic arthritis. His bench research aims to identify mechanisms underlying inflammation and joint damage in psoriatic arthritis and develop novel topical and systemic anti-psoriatic therapies. He is also investigating the cutaneous microbiome in psoriasis and PsA and its relationship to psoriatic disease phenotype and genotype. He is a member of the executive committee of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis. He is an active collaborator in multi-centre research consortia such as the International Psoriasis and Arthritis Research Team and the Spondyloarthritis Research Consortium of Canada and aims to conduct validation studies of discoveries made at his program through these collaborations.

UTMJ: Can you tell us a little bit about yourself as a physician and clinician-scientist?

VC: I am a rheumatologist, who takes care of patients who have arthritis and other related diseases. I came to Canada many years ago to do my fellowship on psoriatic arthritis. In my field, you are always looking for reasons why some patients get arthritis. With psoriatic arthritis, people get skin disease first and then usually within 10 years, they develop inflammatory arthritis that affects the joints in their hands, feet and spine. So, I thought psoriatic arthritis would be a good model to study the early pathogenesis of arthritis. Most of my work during my PhD and fellowship involved studying immunity-related genes, especially the human leukocyte antigen (HLA) genes. I have since continued to work on identifying genes as well as proteins and metabolites associated with development and progression of psoriatic arthritis.

UTMJ: What is the current state of your research on the topic of HLA and its relationship with the onset of psoriasis?

VC: We have shifted our focus from not just looking at HLA, but genes outside the HLA region as well in an unbiased manner. We have conducted genome-wide association studies by developing a large research network, including our research team here at the University of Toronto, University of Michigan, Memorial University of Newfoundland, as well as University of Rochester, New York. We have a large cohort here in Toronto where patients have been carefully and systematically evaluated. We use their data to find genes and other markers that are the most relevant to psoriatic arthritis.

Subsequent to that, we started investigating other factors that may cause the disease. Psoriatic arthritis is a complex disease, which means there are multiple factors at play, genetic factors being just one. Early studies done by one of our colleagues showed that infections, especially the ones that require treatment with antibiotics, are more likely to result in psoriatic arthritis. The question was whether the infection or the antibiotic treatment (that may have altered the microbiome) triggers psoriatic arthritis. We still don't have a definite answer to this question.

The question is whether gut dysbiosis occurs before or after the development of psoriatic arthritis. A colleague of ours in New York is working on this at a large gut microbiome centre. We have not begun such a study here yet, but will do so soon, in collaboration with a large research team investigating inflammatory bowel disease (IBD) here in Toronto. The link between IBD and psoriatic arthritis is interesting. Psoriatic arthritis and psoriasis have been shown to be linked with Crohn's disease in familial studies. So, if you have psoriasis, you are also more likely to get Crohn's disease as well. Many of the genes are similar in these conditions, and treatments are also quite similar. Gut dysbiosis is another link between obesity and metabolic syndrome and psoriatic disease. So how these environmental factors cause inflammation in joints is a good question, and that is what we are trying to understand.

UTMJ: Can you shed some light on the current research you are working on related to the microbiome?

VC: There has been a lot of attention given to the gut microbiome. The other aspect of the microbiome is of course the skin, which is the largest organ in the body. My PhD student characterized the skin microbiome of healthy people, patients with psoriasis without arthritis, patients with psoriasis and arthritis in the hands and feet, and patients with psoriasis and arthritis in the hands, feet, and the spine. In addition, different HLA alleles have been associated with different manifestations of the disease; HLA-C*06 is primarily associated with skin diseases and -B*27 is with joint disease. Our hypothesis was that there would be differences in the microbiome based on the psoriatic disease phenotype as well as based on HLA genotype. Our results show that there were no differences in the microbiome of the patients with psoriasis and psoriatic arthritis, or different types of psoriatic arthritis. However, there were small, but statistically significant differences based on the type of HLA alleles. These findings are novel and will soon be published. We believe that there is a potential interaction between the skin microbiome and the susceptible genes in patients with psoriasis.

UTMJ: What happens when patients have both genetic risk and dysbiosis or metabolic syndrome?

VC: Most diseases happen due to interactions between genetic and environmental factors. Even AIDS develops due to the interaction between HIV and a genetically susceptible host; there are subjects who never develop HIV disease despite being repeatedly exposed. In autoimmune diseases, such as Crohn's disease or psoriasis, genetic factors alone may not be sufficient to cause the disease. Environmental triggers, such as smoking, infection, injury, or obesity are also important. At this moment, all we can say is that the individuals with both genetic and environmental risk factors are at a greater risk of developing psoriasis and psoriatic arthritis.

UTMJ: Are there any particular challenges that you have faced in your work?

VC: The challenge in skin microbiome studies is the amount of DNA that you get. The yield for microbial DNA from skin is quite low. Stool samples are easier to work with because you get a lot of DNA from them. Another consideration is which part of the skin are we going to extract samples from. When you are working with the gut microbiome, one usually obtains stool samples, but one can acquire samples, for example, from the colon or small intestine, via scopes. We are trying to do a similar approach with the skin, by taking samples from the extensor aspect and/or flexor aspect of the skin or the scalp. It has been shown that in healthy individuals, the microbiome is different in all these areas. We chose to sample the skin from the extensor aspects of the extremities because that is the most common site of psoriasis. We take samples from lesions using swabs, put it into solution, extract DNA and then sequence it. We also take control samples from the same patient from the opposite side, and also from healthy controls. Each step of the study has challenges that we have overcome.

UTMJ: What are the clinical implications of the work in psoriatic arthritis and the microbiome you have done so far?

VC: Nowadays, the treatment for psoriatic arthritis is trial and error, because we don't fully understand how each patient develops the disease. You try one drug and it often does not work, so you try something else. By identifying the disease factors that I already mentioned, we will hopefully know which drug will work for the patient and what treatment would be the most effective. For instance, it is possible that combining drug treatment with dietary interventions to alter the microbiome could be beneficial for some patients, especially with treatment resistant disease. Sometimes we see psoriatic patients, who after receiving bariatric surgery, need no treatment for psoriatic disease anymore. This may be due to a change in the gut microbiome. In the case of skin psoriasis, if certain bacteria metabolites drive psoriasis, we may be able to ameliorate it with novel topical medications.

UTMJ: Based on your tremendous experience in this field and collaboration with various experts, what advice do you have for medical students, who are trying to embark on a similar path as yourself, a rheumatologist and clinician-scientist?

VC: As a medical student, it is important to get as much exposure to clinical practice and research as you can. First off, become passionate about something and explore it. In the first year of medical school, as you are learning about different diseases and systems, see what piques your interest. There are some fundamental methods and approaches in medicine that will not change, but the understanding of certain diseases might. So find an area that you really care about and then explore and learn. Second, try to engage in positive interactions with physicians and clinician-scientists to understand how your chosen area of interest are handled in both clinical and research settings. Summer studentships and other opportunities throughout the year, here in Toronto, are excellent opportunities to figure out what you want to do while learning from world leaders. By second or third year, you start to get a fair idea of what you want to do or what areas interest you. Then, of course, if you are keen on becoming a clinician-scientist, it is strongly recommended that you do a PhD. This can be done in MD/PhD programs or even after residency. Take note, the journey is long. Therefore, try to get the exposure and opportunities to explore your passion early with different research programs, especially during the summer. You can also shadow physicians and scientists to see what actually goes on in a typical day. There is quite a lot of work to do in this journey, but it is ultimately a satisfying one.