Faatima Laher Interview

Our July Immunologist of the month is Faatima Laher from the Cape Town HIV Vaccine Trials Network (HVTN) Immunology Laboratory (CHIL). Faatima is a recent PhD graduate, and is currently a Scientific Officer at CHIL. Her research focuses on studying the cellular immune responses to putative HIV and TB vaccines. The immunopaedia team was very fortunate to interview Faatima, and learn more about her transition from academia to a clinical vaccines research centre.

Why did you become an immunologist ? "*It might take a year, it might take a day, but what is meant to be, will always find its way.*" This saying rings quite true for me, with my journey commencing as a curious undergraduate student in Biological Sciences at the University of KwaZulu-Natal. Despite being the recipient of the Best Honours student in Zoology, my interests shifted from plants and animals to what I had always had a deep fascination about, that is, human diseases and their impact on society. This interest led me to pursue post-graduate studies in Medical Sciences. I joined the HIV Pathogenesis Programme to pursue my Masters degree under the mentorship of Dr. Zaza Ndhlovu and Prof Thumbi Ndung'u. This move was rewarding and opened up incredible opportunities for me, with progression to PhD studies being an obvious decision. I became further captivated by the complexity of the human

body in maintaining good health and more so by the tremendous efforts and discoveries that have been translated in various diseases. These factors all contributed to me being able to call myself an immunologist today.

What is your research focus? My overarching research focus has been the role of CD4+ T helper cells in the immune response to clade C HIV-1 infection.

A major aspect that strengthened my resolve to continue in my post-graduate studies was the unique cohorts that I would have access to during my research, i.e. the FRESH (Females Rising through Education, Support, and Health) study. The program ties in the research aspect (identifying and analysing participants immediately after they are infected with HIV), together with a concurrent intensive empowerment, life-skills and job readiness curriculum that coincides with sample collection provided to the young women enrolled in this study. This was introduced in order to offer support to a community ravaged by the HIV epidemic. In addition, an excisional lymph node study cohort, where one of the major goals was to characterise immune responses in lymphoid tissue as compared to peripheral blood. Most of what we have learned regarding immune responses to HIV has come from studies of the peripheral blood, despite knowledge that lymphoid tissue harbours much higher levels of HIV following dissemination. Access to human lymph nodes allowed us, among other benefits, to gain pivotal insight into our understanding of the overall quality of defences against HIV in different compartments in the body.

My PhD study in particular focused on using these special cohorts in understanding the role of HIV-specific immunoregulatory cells in lymphoid tissue and peripheral blood, particularly during early HIV infection, where they are more likely to influence the evolution of adaptive immune responses.

HIV eradication efforts have been unsuccessful due to virus persistence in immune sanctuary sites within lymphoid tissues. High affinity antibodies and overall humoral immunity is dependent on interactions between B cells and T follicular helper (TFH) cells in germinal centres (GCs). The CD4+ T cell's helper function to B cells via secretion of cytokines and expression of costimulatory molecules is well characterised. The GC response is tightly regulated and requires adequate TFH and B cell interactions, however, the regulatory mechanisms underlying this process are not fully understood. Evidence suggested that a newly characterised subset of CD4+ T cells may play a role in this regulation; these are called T follicular regulatory cells (TFR). My study focused on understanding and providing insights into the biology, antigen-specificity, localisation and function of TFR and their role during very early ART initiation. As a whole, the results showed that TFR are important in contributing to the overall humoral response and could be interesting targets for therapeutic manipulation for an HIV cure.

Currently at CHIL my research focus is on studying the cellular immune responses to HIV and TB vaccines.

Who are HIV controllers ? Generally, if left untreated, HIV will typically progress to AIDS. However, there are a rare group of HIV-positive individuals who are able to control HIV and maintain undetectable viral loads in the absence of any treatment. These individuals are broadly and commonly referred to as "HIV controllers" or "long-term non-progressors".

> **What makes them an interesting cohort to conduct research on?** The exact reason and factors that go into control and non-progression of HIV are complex and not yet fully understood. These individuals make for an interesting cohort as understanding of the mechanisms associated with the natural control of HIV-infection is essential to achieve HIV-long-term remission (absence of viral rebound after ART interruption for an undefined period of at least

several years) or new insights in HIV cure strategies. There have been a few encouraging cases over the years that indicate a cure and sustained HIV remission is possible in the absence of ART.

How has your research contributed to understanding HIV immuno-pathogenesis in HIV controllers? Overall, my research work has highlighted the important contribution of CD4+ T cells to immune protection against HIV-1 infection. One of our studies, directed at developing tools to identify low frequency HIV-specific CD4+ T cells in the setting of clade C infection, demonstrated an association between the frequency of HIV-specific CD4+T cell responses targeting an immunodominant DRB1*11-Gag41 complex and HIV viral control, thus highlighting the important contribution of a single class II MHC-peptide complex to the immune response against HIV-1 infections. To our knowledge, this was the first study to demonstrate that CD4+ T cells directed against a single peptide-HLA class II specificity was associated with low HIV viremia. The data obtained further underlined the use of MHC class II tetramers as a sensitive tool for interrogating HIV- specific CD4+ T cells responses in natural infections, without relying on function and removing the bias associated with *in vitro* stimulation required for functional assays and the limitation associated with only detecting subsets of cells capable of secreting cytokines.

You completed your PhD last year, and you are currently a Scientific Officer at the Cape Town HIV Vaccine Trials Network Immunology laboratory.

What is a typical 9-5day for you ? As I have recently joined CHIL, my role is evolving, and every day is a new learning opportunity. However, my key responsibilities would be oversight of laboratory work and project management. During a typical day I am involved in design and overseeing of laboratory assays, data analysis and

troubleshooting of experiments. I am also involved in ensuring all work is conducted according to Good Clinical Laboratory Practice (GCLP), developing and managing relevant components of quality systems (documentation, training etc). In all of this, I work closely with laboratory management on project management and implementation to ensure success of overall study goals.

How is your current position different or similar to a Post-Doctoral Fellow? Upon completion of my PhD, I was quite enthusiastic about trying out something other than a conventional Post-Doctoral Fellowship. I was fortunate to have been able to join CHIL as a Scientific Officer where I can be involved in cutting-edge clinical laboratory research in support of the overall objective of the HVTN whose goal is to develop a safe, effective vaccine for prevention of HIV infections globally. I think this position is different to that of a post-doctoral fellow who are usually focused on further increasing expertise in a specialist subject, which is often considered essential to pursue a career in academia or research. In this position, I am more involved in overall processes that go into conducting clinical research which allows me to have a more holistic view in order to make better informed decisions on my career path.

Advice for grad students and early career scientists ? *Patience, passion and perseverance!* The path to becoming a scientist can be frustrating, with many challenges and all three of these qualities really go a long way in reaching one's goals. I think it is very important for one to know or have options of what they can do upon completion of a Masters or PhD degree. This will help in making the decision to pursue post-graduate studies. Many individuals pursue these studies without prior knowledge or at times unrealistic expectations of what opportunities are available once they are complete, which can often lead to disappointment.

If the decision is made and one wishes to follow this direction, don’t live in a bubble! I would strongly recommend to actively think about building your network – take advantage of the countless opportunities presented to you as a grad student (attending conferences, visiting other labs etc). The people one interacts with are invaluable resources in providing advice, mentorship and even possibly your next job! Become an expert in your own work – read extensively, take ownership of your project (this especially helps motivate oneself to push forward). Always be helpful and open to collaboration. Lastly, enjoy the process! Despite the many setbacks and challenges that come with being a grad student/early career scientist, the rewards of following your passion and pushing through are plentiful.

Interview by Cheleka AM Mpande