

Speaking Truth to Politics



After meeting Prof. Sandro Galea and Prof. Claire Gerada, we continue with our series of interviews with Maltese medics residing abroad. In this case, how did a young medical graduate from Żurrieq end up working alongside Dr Anthony Fauci, director of the US National Institute of Allergy and Infectious Diseases? Dr Ian Ellul catches up with **Dr Keith Sacco**, who works in the immunology field.

YOUR FATHER, DR RAY SACCO, HAS A BUSY PRACTICE IN ŻURRIEQ. AFTER GRADUATING, THE EASIEST OPTION FOR YOU WOULD HAVE BEEN TO JOIN HIS PRACTICE. NONETHELESS, IN 2015 AFTER YOUR HOUSEMANSHIP ENDED, YOU LITERALLY PACKED AND TRAVELLED TO THE MAYO CLINIC IN FLORIDA. HOW COME?

During my undergraduate years I reflected on the specialty which I was most passionate about and came to realize that it was immunology. In keeping with this, I was repeatedly advised that going to the US would be the wisest option since it would add value to such specialization. I thus took the leap and moved to the Mayo Clinic; its excellent clinical care proved to be an excellent launch pad for me.

BACK IN MALTA YOU WERE MUSICAL DIRECTOR OF THE ŻURRIEQ COUNCIL BAND, WHICH POSSIBLY STEMS FROM YOUR PASSION FOR EVERYTHING WHICH IS RELATED TO YOUR HOMETOWN. WAS IT DIFFICULT TO ADAPT TO THE US CULTURE?

I was socially engaged in Malta. I also formed part of the National Youth Orchestra. This yielded important cultural twinning opportunities which proved valuable since I got to meet people from all walks of life and learnt to adapt to their way of thinking. This was further strengthened through my participation in exchanges during my undergraduate years. Nonetheless, I admit that I faced a different culture in the US which contrasted greatly with the Maltese general laid-back attitude; the first few months proved to be a steep learning curve. The fact that few Maltese physicians reside in the US did not help much; I had no reference points to turn to. It would have been nice to draw from such experience. Suffice it to say that the last Maltese medic to venture here did so over ten years ago.

HOW DID YOU END UP AT THE NATIONAL INSTITUTES OF HEALTH, IN BETHESDA, IN 2018?

The US Department of Health includes the Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA) and National Institutes of Health (NIH). The NIH is the primary agency of the US government responsible for biomedical and public health research. It has 27 institutes. 90% of NIH funding goes to extramural activities and 10% goes to

intramural institutes (such as the main campus in Bethesda, which is within the Washington D.C. metropolitan area).

During my work experience at the Mayo Clinic I strengthened my conviction of specializing in immunology and it became increasingly evident that the NIH was the place to be. I was offered a fellowship (which is equivalent to the last few years of HST training in Malta) and moved there. It is a privilege to work at the NIH; suffice it to say that the NIH saw the first trials of chemotherapy as well as gene therapy in the world.

IS YOUR WORK CLINICAL OR MORE RESEARCH-BASED?

I mainly work at the NIH Clinical Centre which is on the intramural NIH campus in Bethesda, Maryland. This centre is the largest hospital in the US dedicated solely for clinical research. I see patients and carry out clinical work relating to research protocols. In order to get more clinical experience fellows also have the opportunity to go to the John Hopkins in Baltimore, as well as other hospitals. During my protected research time I then work at the National Institute of Allergy and Infectious Diseases (NIAID) which is one of the NIH's institutes. At the NIAID I carry out research on patient samples and also carry out pre-clinical animal modelling.

WE HEARD A LOT ON DR FAUCI, THE DIRECTOR OF THE NIAID SINCE 1984. INDEED, IF WE INCLUDE JOE BIDEN, HE ADVISED SEVEN US PRESIDENTS ON PUBLIC HEALTH ISSUES. DESCRIBE YOUR WORK EXPERIENCE, WITHIN THE NIH, UNDER THE ADMINISTRATION OF TRUMP.

On Monday, Wednesday and Friday the principal investigators carry out ward rounds (like the British system) and we fellows are like the consultants on the service, where we have the patients presented to us by the residents. Dr Fauci still sees patients during his monthly ward rounds. He invariably speaks to us on a first name basis whenever we seek assistance from him in relation to specific cases.

As explained, the NIH has a lot of institutes. The biggest is the National Cancer Institute. When Dr Fauci started in 1984 the NIAID was the 5th largest institute in terms of funding (\$319.6 million). Through his career, it is now the 2nd largest (\$4.7 billion government funds in 2020). Returning to your question relating to the Trump administration, his advice to us has always been to 'Speak truth to power'.

MOVING ON TO MORE TECHNICAL ISSUES, WHAT ARE YOUR VIEWS ON INTEGRATIVE OMNICS, INCLUDING THE MICROBIOME, IN ALLERGIES?

Our interaction with the microbiome is increasingly being placed in the limelight. We know that babies born via cesarean delivery

are at a higher risk of eczema because their skin does not receive the optimal microbial diversity during delivery through the vaginal canal. Also, infants who receive antibiotics early on, have a diminished microbiome diversity. In keeping with this, studies conducted by Dr Yasmine Belkaid, Director of the Metaorganism Immunity Section at the NIH, have demonstrated that certain species of bacteria grow in areas of eczema flares; this is due to a change in skin microbiota. Preliminary results have indeed shown that when specific microbes are topically transplanted to the affected area with a view to take over, the inflammation decreases.

WHAT ARE YOUR VIEWS ON AI AND MACHINE LEARNING?

The way we conduct research has not changed much along the years; we ask a question and we conduct experiments to validate a hypothesis. Through omics we now have access to big data, which is more than we can interpret. AI and machine learning are proving to be of great value in clinical work through their ability to integrate different data quickly.

One must appreciate that immunology-related data revolves around blood measurements, but many changes occur at the tissue level; one cannot simply conduct biopsies on a regular basis to validate a specific hypothesis, of course. AI together with computer modelling have an important role there.

Our microbiome changes in space and time. A person's microbiome in Malta will be different from that person's microbiome residing in the US. Circadian rhythms as well as psychosocial stress affect it as well. Through AI we can incorporate various variables in time and space to understand better such changes.

HAVE THERE BEEN RECENT DEVELOPMENTS ON THE ROLE OF BIOMARKERS IN ALLERGY?

Biomarkers are classically defined as measures which highlight specific changes in the biology of an organism. Allergologists and immunologists were among the first specialties to promote personalised medicine, since biomarkers guide us to the mechanism of the disease. Taking asthma as an example, when patients are not adequately controlled with high-dose inhaled corticosteroids and long-acting beta agonists, immunologists use biologics e.g. omalizumab. Omalizumab is an anti-IgE high-affinity monoclonal antibody. The biomarkers required to prescribe this are a high IgE together with evidence, through blood or skin testing, for sensitivity to perennial allergens such as dust mites. These two measures are biomarkers. Other biologics include anti-IL5 monoclonal antibodies such as mepolizumab, reslizumab and benralizumab which block either IL-5 or IL-5 receptors. Eosinophils thrive on IL-5 and these play an important role in allergic asthma. For these biologics you need to have 150-300 eosinophils/ μ L in peripheral blood.

WHAT ARE THE BENEFITS OF IMMUNOSTIMULATION VIS-À-VIS INFLAMMAGING IN OLDER ADULTS? I AM SPECIFICALLY REFERRING HERE TO MICRONUTRIENTS SUCH AS VITAMIN D.

In the Western world people tend to have more exhausted T cells. I like to draw the analogy of a broken car going uphill, which produces more fumes. Exhausted T cells are pro-

inflammatory and this seems to stem from overfeeding and a general lack of rest. Indeed, observational studies have shown that shift workers, who work regular night shifts have a higher relative risk of developing cancer, probably due to sleep deprivation. In fact the International Agency for Research on Cancer (IARC) classified night shift work as "probably carcinogenic to humans" based on limited research evidence. On the other hand, a daily fasting period of 10-12 hours - which allows the liver to rest and switch to glycogenolysis and gluconeogenesis - seems to decrease such inflammation and ensuing insulin resistance. These closely related mechanisms share common factors such as increased IL-6 and CRP.

Another related concept is autophagy which is one way to maintain cell homeostasis and could prevent development of dysplasia. Animal models have shown that a low-fat diet, with adequate fasting times and good sleep hygiene tend to promote autophagy.

Returning to your question, population-based studies indicate that for specific skin diseases a low vitamin D seems to predispose to a Th9 cell-type of inflammation which is similar to what we see in psoriasis (albeit this is a Th17 type of inflammation). Adequate serum vitamin D levels of 30-50nmol/L maintain an adequate skin keratinocyte turnover. This, of course, is not absolute. I personally do not advise patients to stop anything which does not cause overt harm, to avoid jeopardising the doctor-patient relationship. Notwithstanding this, I would not advise them to start any micronutrients unless I am absolutely sure of their benefit.

HOW DO YOU SEE YOURSELF IN TEN YEARS' TIME? BACK IN MALTA OR IN OTHER GREENER PASTURES?

I would never have imagined myself here ten years ago. However, my compass today is always directed to places where I can provide value to others. At the Mayo clinic I have been taught that if I am resourceful to others, opportunities will invariably come along. I am fortunate enough that immunology is a very dynamic and cellular science and thus will always keep up with the times. Most probably in ten years' time we would be dealing with other medical agendas. What I can say is that personally, geography is not a decision factor and I am open to any opportunity which may present itself.

WHAT DO YOU THINK OF OUR ONLINE CONTINUOUS MEDICAL EDUCATION PLATFORM CME.30?

CME.30 proves to be an excellent rendition of topical medical discussions aimed at healthcare professionals. It is a trailblazing initiative from your part and the reader engagement is behemoth. The Covid-19 online symposium which you organized had over 600 participants. Unfortunately medical expertise is not valued much on social media so **CME.30** is the perfect tool for us physicians to discuss ideas with peers, update our learning and, in keeping with this, continue to uphold the values outlined in the Hippocratic oath.

The views and opinions expressed in this interview are solely of the interviewee and do not necessarily reflect the official policy or position of the US National Institutes of Health or the US government.