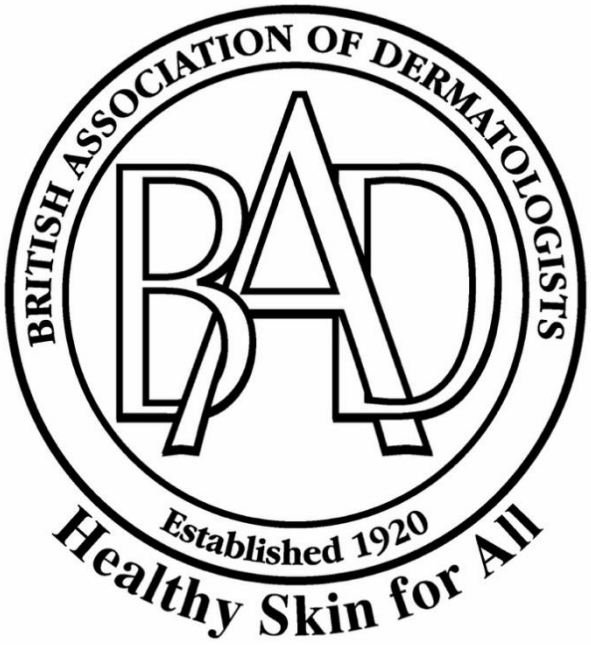


Elective prize / Project Grant Summer 2019

Philip Frost Department of Dermatology, The University of Miami

By Ferhan Muneeb

Introduction

For my elective I was fortunate enough to be able to visit The Philip Frost Department of Dermatology at the University of Miami. Over the course of my six weeks there, I participated in a variety of different dermatology clinics whilst also undertaking lab-based research. This project endeavoured to better understand dermal macrophage behaviour through an *in vitro* model of human skin re-innervated through culture with nerves harvested from dorsal root ganglia cells.

This combination of both clinical and lab-based work resulted in a thoroughly enriching experience, made possible by the generous elective bursary provided by the British Association of Dermatologists. I would like to thank them and my supervisors, Dr Ralf Paus and Dr Jérémy Cherét, for allowing me to experience both clinical and research dermatology in this new and exciting setting.

Photos of around the main university campus where I was living

Clinics and Surgery

Miami is best known for its sunny beaches and rich Latin culture, originating from a largely South American population prone to skin cancer from being fair skinned. Hence, it came as no surprise that general dermatology clinics consisted heavily of routine skin checks. It was particularly fascinating to see the hospital employ cutting edge technology to construct 3-dimensional avatars for patients with a genetic predisposition to skin cancer so as to map and track their lesions with absolute precision.

I also attended a number of subspecialty clinics focussing on chronic wound management and paediatric disease, allowing me to see the full breadth of conditions and age groups treated in dermatology. Moreover, The University of Miami was home to one of the few inpatient dermatology departments in Florida, giving me a comprehensive understanding of the extremes of dermatological disease such as severe exacerbations of psoriasis and erythroderma.

In addition to clinics, I regularly attended Mohs theatre where I observed the meticulous and complete removal of non-melanoma skin cancers followed by complex reconstructions. One of the most exciting procedures I witnessed was the reconstruction of a patient's ear following the removal of a basal cell carcinoma using a skin graft from the patient's arm. Additionally, I got to see the post-operative cosmetic follow up where the surgeon made use of lasers to reduce scarring or fillers to re-establish symmetry when lesions were removed from the face.

University of Miami Health System campus, consisting of a number of specialty hospitals and research centres, including the Philip Frost Department of Dermatology where I was working.

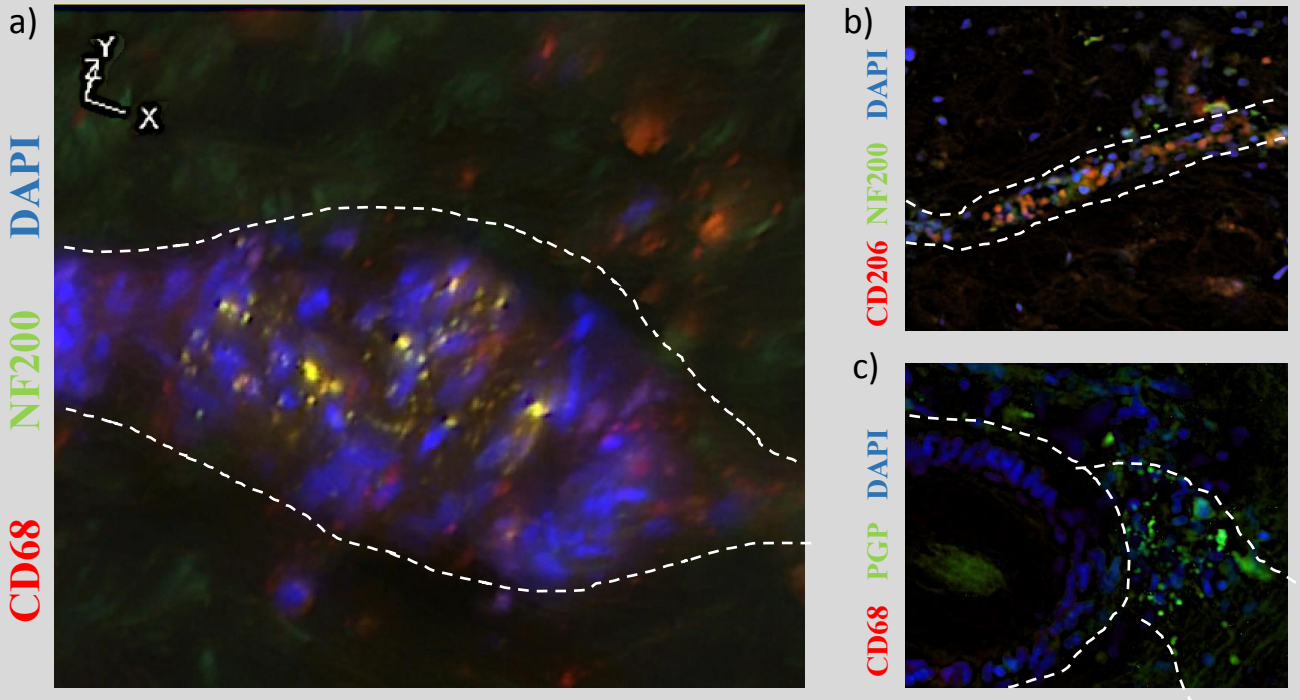
Planning Meetings and Grand Rounds

Every Wednesday morning, attendings (American Consultants) and residents (American Junior Doctors) would gather to discuss a small handful of complex patients, akin to our multi-disciplinary team (MDT) meetings. Unlike MDTs from other specialities, patients were seen prior to the meeting to allow everyone in the department to form an unbiased opinion. What followed was always an incredibly fascinating and in-depth discussion, resulting in a long list of differentials that comprised of diseases both regular and rare. A seemingly simple case of unexplained itch yielded every possibility from potential liver disease to carbon monoxide poisoning. These MDTs stood out to me beyond those I had experienced in other specialities as the endless list of pathologies encompassed by dermatology requires you to regularly exercise your thought process to keep a wide scope of differentials, making everyday practice intellectually refreshing.

These meetings were followed by grand round lectures where engaging topics not necessarily directly related to medicine were discussed by local and guest speakers. My favourite lecture was one on art in medicine, where a dermatology resident who minored in art history discussed how the study of medicine informed art and vice versa. She described how Leonardo Da Vinci, the master renaissance painter, began dissecting cadavers to be able to depict surface anatomy in perfect realism but later used his artistic talent to recreate his anatomical findings on paper for academic purposes. Moreover, she showed how individual artists work changed as they experienced illness, elegantly demonstrating the impact disease can have on one's outlook and creative process. This prompted me to reflect on how the patients I was seeing feel and perceive life once they leave our dermatology clinics and thus the importance of being holistic in our approach to patient wellbeing.

Research

For my research project, I investigated macrophages within the dermis using a re-innervated, *in vitro* human skin model created by culturing skin explants with primary sensory neurones harvested from dorsal root ganglia cells. This produces an afferent nerve supply that supports homeostasis within the skin model, resulting in increased epidermal skin integrity that far better reflects normal physiological conditions, thus making for an excellent research model. Our main aims were to establish dermal macrophage distribution/phenotype in our re-innervated skin and the subsequent effect this had on their distributions and progenitor cells when neurogenic skin inflammation was imitated using the neuropeptide Substance P. The figure below details some of our findings through immunofluorescence microscopy.



a) *A 3-D constructed image of a bundle of nerve fibres surrounded by clusters of macrophages in re-innervated human skin. NF200 binds to the nerve in between schwann cells, resulting in the dotted staining that can be seen travelling along singular nerve fibres. CD68 is expressed on the surface of macrophages, thus demonstrating the cell to coalesce around nerve fibres. DAPI counterstains any cell nuclei. Similarly,* ***b)*** *demonstrates this in 2-D but using CD206 instead CD68, a marker for a tissue repairing macrophage phenotype. Interestingly,* ***c)*** *demonstrates a bundle of nerves stained by PGP (similar to NF200) originating from a hair follicle in non-reinnervated skin but no corresponding macrophage staining. This suggests that dermal macrophages play a role in the re-innervation of skin within this co-culture model, suggesting perhaps a physiological role for these cells that may be manipulated for therapeutic utility in wound healing and peripheral neuropathy.*