

# Doctors in Training Grant

## PRELIMINARY REPORT

### Dr Mark Dowling

Research project – **Neurological complications in recipients of bone marrow transplants**

**Massachusetts General Hospital**  
Boston, Massachusetts, USA



In front of the Massachusetts General Hospital

My interest in haematological malignancies and bone marrow transplant began as a medical student on the wards meeting patients and sharing their journey through complex illnesses and treatments over many months and years. A diverse group of patients are affected, from young and previously well, to the elderly. Many are treated with an intention to cure, justifying the significant side effects of treatment and heroic measures to support patients through complications and difficult times.

This is a fascinating area of modern medicine that spans a broad range of disciplines from basic scientific research in immunology, haematopoiesis and genomics, through translational and clinical research. It is an area of medicine that is rapidly advancing with new treatments emerging almost weekly and a range of new molecularly-targeted and immunological therapies that are changing the course of these devastating illnesses. It is an exciting time to enter this field.

With the support of an MIGA Doctors in Training Grant, I am currently completing a three month rotation in clinical research at the Massachusetts General Hospital (MGH) in Boston, United States of America. I am working with the leukaemia and bone marrow transplant service, primarily supervised by Dr Karen Ballen, one of the leukaemia attending physicians. I previously completed a one month rotation as a medical student in the same department at MGH in 2013 and wanted to build on this relationship. For 2016, I have interrupted my basic physician training with the Royal Australasian College of Physicians to travel, to do locum medical officer work around Australia and to complete this clinical research project. My main goal in arranging this rotation was to gain experience in clinical research at one of the world's leading hospitals for academic medicine. I am planning to pursue advanced training in clinical haematology in Australia on completion of my basic physician training with a strong focus on research. I have a background in basic laboratory research in immunology, but as yet have not had the chance to participate in any clinical research.

My project focuses on neurological complications in patients undergoing bone marrow transplantation for haematological malignancies. Bone marrow transplantation is a curative treatment modality for patients with a variety of malignant haematological conditions, as well as, less frequently, non-malignant and non-haematological conditions. Myeloid malignancies such as acute myeloid leukaemia (AML) remain one of the indications for which bone marrow transplant can be offered with curative intent. Despite advances in supportive care, alternative donor sources, and conditioning regimens over the past several decades, its role remains limited by significant toxicity and transplant-related mortality.

*Neurological complications, such as seizures, encephalopathy, ischaemic and haemorrhagic strokes, intracranial infections, and peripheral neuropathies remain a devastating source of morbidity and mortality amongst bone marrow transplant patients.*

The study is a retrospective review of all consecutive allogeneic transplants performed at MGH between 2000 and 2010. My role is to collect the relevant data from electronic medical records, analyse the data with the help of a statistician, and to write up the results for journal publication and conference presentation. The study will be amongst the largest of its type assessing the factors leading to neurological complication.

*The results will inform clinical practice aimed at minimising the risk of these complications as well as serve as a basis for future prospective studies assessing specific interventions.*

The MGH is an impressive institution with a strong academic culture and focus on education of medical students, residents and fellows. The hospital clearly takes pride in its reputation for training the next generation of leaders in every field. Much of the history of modern medicine is associated with the MGH. Amongst many, a unique experience was visiting the "Ether Dome" – a small, traditional lecture theatre where the first public demonstration of anaesthesia took place in 1846. Few institutions can claim such significant contributions to medicine.

I have also taken advantage of my time at MGH to observe clinical practice, both on the inpatient wards and in outpatient clinics. There are many teaching and learning opportunities each day, on the wards and in formal lectures and seminars. As an example of the commitment to teaching, every day on the haematology and oncology wards there is a tutorial given by one of the attending physicians to the residents and medical students. There are also countless other research and educational seminars that happen every day, notably the weekly "medical grand rounds", often featuring the latest articles from the New England Journal of Medicine. The MGH Cancer Center has strong ties with the Dana Faber Cancer Institute in Boston, so there were also opportunities to travel across town for seminars, lectures and meetings.

Clinical and translational research form part of everyday practice on the wards and in outpatient clinics. Many of the patients are on clinical trials with novel agents and observation of this process was a valuable learning opportunity for me.

*I have gained insights into the role of clinical research and trials in advancing medical knowledge, as well as practical aspects of protocol writing, data extraction, requirements for enrolment in trials, safety aspects of trials, as well as limitations associated with retrospective analysis and single-institution reports.*

There is an upfront consideration of clinical trials for all new patients and following significant events such as relapse or complications (for example, graft versus host disease). The department aims to have trials open and available for the majority of commonly seen conditions. There is a large biotechnology sector in Boston, and the hospitals and patients benefit by having immediate access to early phase trials of the latest agents.

These experiences of state-of-the-art academic medicine will serve me well on return to Australia and especially on commencement of advanced training. The small study I am completing on neurological complications will contribute to knowledge of risk factors for these particular complications and the care of transplant patients. I believe my future patients and the community will benefit greatly from the experiences and perspectives I have gained by spending time at a world-leading institution. I would like to express my sincere gratitude to MIGA for making this rotation possible.

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**Email** [miga@miga.com.au](mailto:miga@miga.com.au)

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