ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

SCHOLARSHIP REPORT

This report should be completed by recipients of awards and scholarships from the Royal College of Physicians and Surgeons of Glasgow on completion of the activity for which they received their award or scholarship. Please complete all sections of the report form.

Please return your completed report via email to: **scholarships@rcpsg.ac.uk**

Or via mail to: **Scholarships Committee Administrator, Royal College of Physicians and Surgeons of Glasgow, 232-242 St Vincent Street, Glasgow G2 5RJ, UK**

Please use typeface when completing this form.

SECTION 1 | PERSONAL AND AWARD DETAILS			
Title	Mr	**PID**	63977
Surname	Ng	**Forename(s)**	Zhi Yang
Scholarship/award awarded	College Travelling Fellowship	**Amount awarded**	2000 GBP

SECTION 2 | PROJECT/VISIT DETAILS	
Name/Title	Research Fellowship in Vascularized Composite Allotransplantation
Location	Massachusetts General Hospital, Harvard Medical School, Boston, USA
Aims and objectives	1. To develop immunologic tolerance protocols in pre-clinical, large animal models of VCA 2. To further hone microsurgical competency 3. To prepare for a thesis submission for a PhD degree
Summary *Include methodology, results and conclusions if applicable*	INTRODUCTION: Tolerance in vascularized composite allotransplantation (VCA) remains elusive and patients are faced with a lifetime of immunosuppression and associated risks. Tocilizumab (anti-IL-6 receptor monoclonal antibody) is currently FDA approved for use in rheumatoid and idiopathic arthritis. It mitigates inflammation, reduces the incidence of GvHD, and is potentially pro-tolerogenic. We investigated the utility of a short course of tocilizumab in a non-human primate model (NHP) of facial VCA to achieve prolonged survival and/or tolerance. MATERIALS AND METHODS: VCAs were transplanted into MHC-mismatched NHPs (n=4) after induction with anti-thymocyte globulin. Post-operative maintenance consisted of triple immunosuppression (FK506, methylprednisolone, MMF) before further conditioning (irradiation, lymphocyte depletion) in preparation for co-stimulatory blockade-based donor bone marrow transplantation (DBMT) on POD 60. Tocilizumab was administered on the day of DBMT, and at weekly intervals thereafter for a total of 5 doses. Post-DBMT, the recipient was maintained on a tapering course of cyclosporine before complete withdrawal 28 days later. VCAs were assessed by serial clinical assessment and histopathology. Mixed chimerism in peripheral blood was monitored by flow cytometry and in vitro immunologic responses were assessed through mixed lymphocyte reaction (MLR) assays. RESULTS: Two recipients were euthanized within 2 weeks of DBMT due to neutropenic sepsis and post-transplant lymphoproliferative disorder but both VCAs remained viable up

	to experimental endpoint. M4515 (full MHC-mismatched recipient) has been off of all immunosuppression for 3 weeks without any evidence of rejection. M3815 (haplomatched) developed mixed chimerism transiently at 6 weeks after DBMT and corresponding MLR assays demonstrated decreased anti-donor responses; immunosuppression was then successfully withdrawn for a total of 5 weeks before rejection developed. Although the rejection episode could be reversed with steroid bolus and a tapering course of FK506, recurrence occurred after another 2 weeks off immunosuppression. CONCLUSION: As with the clinical experience with tocilizumab, vigilant monitoring is required following drug administration due to increased susceptibility to neutropenia and infections1. Tocilizumab appears to promote engraftment after DBMT to allow short-medium term immunosuppression-free VCA survival across haplomatched barriers in this NHP model. Continued follow-up is required to determine if similar results can be achieved across a full MHC mismatch. Further studies in our laboratory are focused on optimizing the current protocol to achieve stable engraftment and durable mixed chimerism for tolerance of VCA.
Learning outcomes *Detail here how the aims and objectives were met*	1. We have managed to withdraw all immunosuppression from MHC-mismatched, non-human primate recipients of VCA for short-medium term rejection-free survival using a delayed mixed chimerism protocol 2. I have participated in a total of 14 VCA surgeries so far and have progressed rapidly from assisting to becoming one of the main surgeons through donor flap harvest, recipient site preparation, and microsurgical anastomosis 3. The nature of large animal research makes it very unlikely for my PhD thesis submission to be ready by the end of this award. A more realistic date will be next year
Evaluation *How has this scholarship/award impacted on your clinical/NHS practice or equivalent?*	In addition to the phenomenal work in my laboratory, I have been very privileged to partake in the Harvard Plastic Surgery Residency program through grand rounds, clinic sessions, M&M conferences, observing in the OR and visiting professor talks. As well, I have met many colleagues from other institutions in the field of VCA by attending and presenting my work at key national meetings in the USA. Therefore, this award has enabled me to develop my academic career and network, while at the same time maintain and improve my knowledge base in plastic surgery at one of the foremost training programs. My experiences in Boston have inspired me, more than ever, to pursue an academic career in plastic surgery. I firmly believe that through academia, I will be uniquely positioned to (1) conduct ground breaking research with direct clinical relevance and applicability, which in turn will (2) improve the care of patients both within and beyond my normal practice, and (3) inform my fellow professionals of what is possible so that we can bring patient care to the next level. However, perhaps more importantly, my stint here has confirmed to me that it is the academic environment which is critical to the success of such endeavors. To build up a culture of academic medicine requires years of painstaking effort however and unfortunately, it cannot be "bought" like a simple commodity. Nevertheless, I will strive to maintain my commitment towards academic plastic surgery wherever I may end up practicing in future.

SECTION 3 | IMAGES

If available, please provide some images to support your report

SECTION 4 | EXPENDITURE

Breakdown of expenditures *Please demonstrate how the scholarship/award funding was used to support your project/visit*	Air Tickets from Singapore to USA - 800 GBP Visa Application Fees - 220 GBP Sublet Rental for Initial Period Upon Arrival to the USA - 980 GBP Total = 2000 GBP

SECTION 5| PUBLICATION

Scholarship/award reports may be published in College News. Please tick here if you agree to your report being published.	☒ I give permission for my report to be published in College News *If your report is selected for publishing, the editor of College News will be in touch to discuss this with you.*