



UNIVERSITY OF TORONTO
FACULTY OF MEDICINE



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MEDICAL ALUMNI ASSOCIATION AND CREMS-SPONSORED
DR. ELVA MAY ROWE FUND
INTERNATIONAL HEALTH SUMMER RESEARCH PROGRAM
2017 SUPERVISOR PROJECT INFORMATION FORM

If you wish to act as a Supervisor for a first or second year University of Toronto medical student wishing to conduct a research project abroad between June and August 2017, please complete the below form with as much detail as possible.

PLEASE PROVIDE A COPY OF THE ON-SITE SUPERVISOR'S CV. THIS IS REQUIRED FOR THE ADJUDICATION PROCESS.

****Submit this form to crems.programs@utoronto.ca by the deadline of Thursday January 5, 2017.****

PART A: Supervisor and On-Site Supervisor Contact Information

UofT Researcher:	Dr. Nancy Olivieri
Email Address:	nancy@hemoglobal.org
Telephone:	647-299-6935
Mailing Address:	Toronto General Hospital 200 Elizabeth Street, EN 13-222, Toronto, Ontario Canada M5G 2C4
Department:	Medical Oncology and Hematology
Degree (MD, PhD, MD/PhD):	MD, MA, FRCPC
SGS Appointment/where?:	Institute of Medical Sciences
Selected Publications (3 most recent and relevant to the project the student will be working on):	Premawardhena A, Fisher CA, Olivieri NF, de Silva S, Arambepola M, Perera W, O'Donnell A, Peto TE, Viprakasit V, Merson L, Muraca G, Weatherall DJ. Haemoglobin E beta thalassaemia in Sri Lanka. <i>Lancet</i> 2005; 366:1467-70. Olivieri NF, Thayalsuthan V, O'Donnell A, Premawardhena A, Rigobon C, Muraca G, Fisher C, Weatherall DJ., Emerging insights in the management of hemoglobin E beta thalassaemia. <i>Ann N Y Acad Sci.</i> 2010; 1202:155-7. Mettananda S, Gibbons R, Higgs D. α -Globin as a molecular target in the treatment of β -thalassaemia. <i>Blood</i> 2015; 125: 3694-701
Name of On-site Supervisor:	Dr. Anuja P Premawardhena
Location of placement (Name of Institution/hospital; City; Country):	Professor in Medicine, Department of Medicine, University of Kelaniya Sri Lanka; Consultant in charge: Adolescent & Adult Thalassaemia Care Unit, North Colombo (Teaching) Hospital Ragama, Sri Lanka
Email Address:	premawa@hotmail.com
Telephone:	
Degree (MD, PhD, MD/PhD):	M.B.B.S, M.D M.R.C.P (London) 2001 D.Phil (Oxon) 2002 FRCP (London) 2008 FCCP (Sri Lanka) 2010
Area of Medicine of the Research Project	Thalassaemia, Global Health



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(2 keywords):

PART B: PROJECT INFORMATION

Project Title (this can be modified later, but we would like to have working title from the start):

Evaluation of the effectiveness of therapy and frequency of disease complications in patients with thalassemia in Sri Lanka

Provide background information on the project and program/institution; max 500 words:

Thalassemia is an inherited blood disorder characterized by decreased production of hemoglobin, and one of most common monogenic disorders worldwide. Although thalassemia imposes a huge disease burden throughout Asia, the disorder was until recently rarely included in the health priorities of governments or international health agencies. In 2000, The World Health Organization acknowledged thalassemia as a major global health problem.

Since 1996, our research and clinical programs have worked in Asia, including Sri Lanka, where thalassemia is the most common inherited disease. Working primarily with thalassemia patients in two Sri Lankan cities, one urban (Colombo, the capital) and one serving a larger, relatively rural population (Kurunegala, about three hours north of Colombo), over two decades we have conducted three to four field visits every year, accompanied by students and trainees. We have provided consultations in management, screening, and basic and applied research in thalassemia, built a National Thalassemia Center for management of the increasing numbers of patients (in 2001), and in 2004 established a charity (Hemoglobal®) actively directed at raising awareness, and funds, to improve care for patients with thalassemia. Over these years, we have established strong collaborations with clinicians and researchers throughout the island.

The well-described complications of iron accumulation in regularly-transfused patients with thalassemia include cardiac disease, liver dysfunction, diabetes mellitus, and premature death. The magnitude of the body iron burden in the critical determinant for prevention of complications, with daily iron-chelating therapy forming the cornerstone of treatment for patients. The orally-active iron chelator deferasirox became available in Sri Lanka for the treatment of transfusional iron overload in 2010. Within two years, deferasirox had replaced the former agent deferoxamine (which required parenteral infusion and with which compliance was hence often erratic) in most patients. Although Sri Lanka's excellent socialized medical system enables most children to receive free essential medicines, we are still observing a complication rate in Sri Lankan patients with thalassemia that is higher than in richer countries. While deferasirox has been demonstrated as effective *in high-resource settings* -- where expert care is available -- and although the drug has been distributed widely throughout Asia over the past five years, deferasirox has not been evaluated in a lower-resource setting. Because the effectiveness of any iron chelating



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therapy depends on attentive, expert supervision, oversight, and monitoring of patient adherence and quality of life by a trusted health care professional, adequate social and medical support can make a difference in the effectiveness of a drug which must be complied with daily, over a lifetime. Centers throughout Asia, including Sri Lanka, differ widely in available resources for such support for patients. We propose to assess the effectiveness of deferasirox in two centers: Colombo (which is relatively supported in terms of expert, dedicated medical care) and Kurunegala (where patients are managed in a less supportive environment). If it is found that the management and effectiveness of deferasirox is different (substantially less in Kurunegala), we will develop additional approaches, including seeking additional governmental resources, to help these patients who are not benefitting optimally from this life-saving drug. We anticipate that this publication will lead to a major publication of great importance to public health including to the understanding of the need to support patients in low-resource settings who are dependent for survival on complicated drug regimens. Dr. Anuja Premawardhena is a talented clinician and researcher dedicated to his patients, and will provide a nurturing experience for medical student or students.

What, if any, second language is required for the student to successfully complete this project?
 Fluency/understanding of Sinhala or Tamil will be useful but not required.

Is this project for 1 or 2 students to complete?

1 2

Two students sharing the work has always worked well in similar projects. We have made a parallel application for Dr. Mettananda to co-supervise the student(s) to provide both pediatric and adult patient experience.

How long have you worked with the on-site supervisor and briefly describe your working partnership:

My clinical and research teams have worked in Sri Lanka for 21 years. My primary research partner in this work has been Professor Sir David Weatherall, FRS, the world’s leading authority in thalassemia, at the University of Oxford, UK, with whom I actively continue to work. Both proposed supervisors, Drs. Mettananda (and Dr Premawardhena; please see application submitted with this one) trained in basic and clinic research at the institution founded by Professor Weatherall (The Weatherall Institute of Molecular Medicine, University of Oxford, UK). There Dr. Premawardhena received his D. Phil in 2002, and Dr Mettananda his D.Phil in 2015. I have worked with and continue to work with both Dr. Premawardhena and Dr Mettananda before and following their staff appointments in Sri Lanka. We meet and discuss our work on each field trip to Sri Lanka, of which three were conducted in 2016.

Have you visited the city/town where the medical student will be placed? If yes, when was your last visit?

Yes, to both Colombo (Ragama) and Kurunegala. I have worked in Sri Lanka for 21 years. I lead at least three field trips per year to the country, the most recent in November 2016. I will be visiting Sri Lanka in summer 2017 (*estimated dates June 18 to July 5, 2017*) to work at which time I can help provide additional support to the students, if funded.

Student’s roles/responsibilities in bullet form (Please be as specific as possible):

- Students should during this time develop a deep and broad understanding of the clinical and laboratory aspects of thalassemia including the complications of iron loading and approach to treatment
- Students will accompany Dr. Mettananda and Dr. Premawardhena and participate in rounds and clinics with have daily interactions with thalassemia patients aged approximately 5-20 years
- The research project will be directed at evaluation of the effectiveness of treatment with the



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<p>iron chelator deferasirox in patients aged approximately 5-25 years in three thalassemia units (Colombo’s Paediatric Thalassaemia Unit, Colombo North Teaching Hospital, Ragama, Sri Lanka; Adolescent & Adult Thalassaemia Care Unit, North Colombo (Teaching) Hospital Ragama, Sri Lanka; and the National Thalassemia Center, Kurunegala). The total number of patients is approximately 1000 and a subset of patients may therefore be selected for study.</p> <ul style="list-style-type: none"> - Students will at both sites conduct chart reviews to record the primary endpoints which reflect effectiveness of chelation therapy (serum ferritin concentration; fasting blood glucose; cardiac ejection fraction; liver function tests and other endpoints to be outlined) 	
<p>Is this project for a specific student, or will you interview and select an interested student who would contact you directly for this opportunity? <i>Note: All supervisor/student applications will be adjudicated by a panel of faculty, given a score, and ranked based on the score given. Funding will be based on ranking.</i></p>	<p><input type="checkbox"/> For a specific student. <u>Name</u> of student:</p> <p><input type="checkbox"/> For whichever student is chosen after interview</p> <p>We would welcome any students for this project. We hope that two can be funded in parallel on this project.</p>
<p>If human subjects are involved, has Ethics been obtained? <i>(Note: Written proof or an email indicating protocol approval may be requested prior to the student’s arrival at on-site location)</i></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A</p> <p>Yes – documents to be provided.</p>

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