Call for applications for PhD studies for doctoral degree and post doc fellowship in Sweden within the Research Training Partnership Programme in the sub-programme of infectious diseases

Background

The University of Rwanda (UR) with its partnering Swedish Universities offers an opportunity to complete one doctoral degree (PhD) and two postdocs in infectious diseases areas, in the new partnership of five years (2021-2026) funded by Swedish International Development Agency (SIDA).

Infectious diseases constitute a heavy burden for Rwanda and other developing countries. In particular, improvements in the prevention, diagnosis and management of viral diseases are warranted. The objectives of the proposed projects for PhD research in sandwich mode within the infectious diseases sub-programme of the UR-Sweden Programme for Research are to conduct epidemiological studies on challenging infectious diseases in Rwanda, along with drug development and optimization for treatment of infectious diseases and propose solutions to alleviate the infectious burden in the country.

1. Postion of PhD degree

The PhD program will be in sandwich mode. The PhD student will make yearly visits to Sweden. The planning of these visits will consider the needs of the PhD student's education as well as the requirements of the UR Sweden program management. The PhD student will attend the PhD courses at Gothenburg University including the compulsory set of PhD courses, as well as elective PhD courses of interest.

The main supervisor is affiliated to Gothenburg University, Sweden and Co-supervisors are affiliated to University of Rwanda and University of Gothenburg University, Sweden

Title: **Cause and prevalence of megaloblastic anemia in Rwanda**

Background: Megaloblastic anemia is a condition where the patient's erythrocytes are dysfunctional and display a larger than normal mean cell volume (MCV). The most common cause of megaloblastic anemia is a deficiency in vitamin B12 (VB12) and/or folates, and previous studies have suggested that genetic variants of proteins related to VB12 uptake and circulation in blood may result in reduced VB12 levels (Hu et al, Blood, 2018).

Megaloblastic anemia has a slow onset and diffuse symptoms, such as fatigue. In a pilot study, we noticed that an unexpectedly high frequency of Rwandan patients for unknown reasons displayed erythrocytes with larger than normal MCV, and hence signs of megaloblastic anemia. The primary cause of hematopoietic cancers, such as leukemia and lymphoma, remains largely unknown although infections with HIV (lymphoma), HTLV-I (leukemia) and Epstein-Barr virus (EBV; lymphoma) may contribute to cancer initiation and development.

In areas where malaria is holoendemic, concomitant EBV infection and malaria (caused by P. falciparum) is closely linked to Burkitt leukemia/lymphoma (BL) (Moormann et al, Curr Opin Virol, 2016). In recent co-operative studies at University of Rwanda and Gothenburg (UGOT) we found evidence to suggest that also subtypes of acute lymphoblastic leukemia (ALL), where leukemic cells do not show morphological or genetic features of BL, may be caused by concomitant EBV infection and malaria.

Aims: The major aims of this PhD-project are:
i) to determine the frequency and cause of megaloblastic anemia in Rwanda, along with defining the symptoms that are accompanying this condition in Rwanda.
ii) to validate an EBV- and malaria-related subtype of ALL, distinct from BL, as a specific disease entity in Rwanda,
iii) assess the role of EBV and malaria in the pathogenesis of hematopoietic cancers other than ALL and BL

Work plan: Megaloblastic anemia: Blood samples from Rwandan blood donors (including healthy blood donors, and subjects with fatigue seeking medical attention) will be analysed for erythrocyte MCV using a Sysmex XS800i analyser. Serum samples will be analysed for VB12 levels and folate levels. DNA will be purified from whole blood and analysed for polymorphisms associated with VB12 uptake and circulation, including rs34530014 in TCN1.
The participants in this study will also fill in a questioner, that includes information regarding malaria episodes and nutritional habits. The PhD-student will, with help from Dr. Florence Masaisa and other supervisors, design the study, apply for ethical clearance, collect and analyze the samples and questioners. The majority of these tests will be performed at hospitals in Rwanda, while the SNP genotyping will be performed at UGOT.
Leukemia/lymphoma: For this project both previously collected and prospectively collected blood and lymphoid tissue samples from patients with hematopoietic cancers will be utilized. The focus of the study is to define subtypes of acute leukemia and lymphoma that are present in Rwanda by whole exome sequencing (WES) and by immunohistochemistry analysis. In addition, the possible connection of hematopoietic cancer and a recent or ongoing malaria and/or EBV infection will be investigated. Hence, blood smears from whole blood will be examined by microscopy for presence of malaria parasites. Serum samples will be analysed for presence of EBV-IgM, EBV-IgG, HRP-2 and SE36. Formalin-fixed paraffin-embedded (FFPE) tissue blocks will be analysed for signs of EBV and malaria infection both by immunohistochemistry and by PCR methodology following extraction of nucleic acid. This part of the project has been initiated by Belson Rugwizangoga, who at present is a post doc within the Infectious disease subprogram. The PhD-student will thus conduct this project in collaboration with Dr. Rugwizangoga, and will be responsible for analyses of the prospectively collected samples. Sample collection, extraction of nucleic acids, ELISAs and part of the immunohistochemistry analysis will likely be performed at UR, while the initial immunohistochemistry analysis, the serology and majority of PCR analysis will be performed at UGOT.

Outcome: Megaloblastic anemia is generally associated with severe fatigue and may also be an indicator of various disease conditions. At present the frequency of megaloblastic anemia in Rwanda is unknown, but our pilot studies indicate that a large fraction of Rwandan people suffer from this condition. With this study we may be able to define how common megaloblastic anemia is in Rwanda, which symptoms that are associated with this condition, and the cause of the condition. If the condition is caused by VB12 deficiency, it may be easily corrected by vitamin B12 supplements. Residents in sub-Saharan countries are highly exposed to infections, including those causing immunosuppression such as malaria and HIV. The availability of diagnostic samples from many Rwandan patients with acute leukemia and lymphoma provides the opportunity to determine unique infection-related genetic changes in malignant cells. The planned studies may thus point towards previously undefined links between infections and development of leukemia or lymphoma. Our recent identification of an unexpected association between recent or ongoing malaria and non-Burkitt ALL may clarify the occurrence of unique forms of ALL in malaria-holoendemic countries.

Rwandan supervisors: Florence Masaisa, Belson Rugwizangoga
Swedish supervisors: Kristoffer Hellstrand, Roberta Kiffin, Anna Martner

1. **Post doc candidates:**

Postdoc fellowship in a sandwich mode are expected to be part of a bigger research team at the Swedish university and spend 3 months per year in Sweden doing research full time, while in Rwanda they pursue their research part-time (depending on UR regulations) ideally also in a research team. The postdoc fellowship is for a duration of two years.

Post Doc Position1:

Title: Improving Rwandan Health by Implementing a One Health Perspective

Background

Annually, more than 70 million years of healthy living are lost to vector borne diseases such as malaria, dengue fever, and other arthropod-borne viruses. Even though the number of malaria cases are reported, other zoonotic diseases are either undiagnosed or underreported. The importance of zoonotic viral pathogens and the impact on public health in Rwanda has not been properly assessed. Changes in environments, climate, land-use systems and animal demographics, in the face of high pathogen and vector diversity, drive the rate of emergence and re-emergence of new and old infectious diseases. We hypothesize that zoonotic pathogens are present and circulating in humans, animals and vectors. We also hypothesize that they cause undiagnosed disease, which could be prevented. This would have a high impact and yield improved health, and prepare for preventive measures.

Aim. To investigate zoonotic viruses in an environment where multi-hosts (humans, livestock, wildlife, e.g. rodents) intimately interact with multi-vectors (mosquitoes, ticks).

Work plan. Through cooperation between Rwanda, Kenya (the Kenya part is financed through other sources, within the framework of a VR-supported project) and Sweden, we wish to apply a transdisciplinary and multi-sectoral approach under the One Health strategy. From Rwanda one postdoc fellow will be recruited. Sampling areas will be defined by using remote sensed data. Appropriate sample size, frequency and sampling locations will be defined prior to actual sampling from livestock, bats, rodents, mosquitoes, ticks and humans. All samples will be analyzed for a wide range of virus families.

Outcome. We will determine the prevalence, incidence and distribution of zoonotic viral diseases, aiming to improve preventive measures to increase general health. The study will facilitate transfer of technology and skills through practical experience exchange and training. The project will also further strengthen the scientific collaboration between researchers in Rwanda, Kenya and Sweden. Rwandan supervisors: **Eric Seruyange**, Nadine Rujeni; Swedish supervisors: Olivia Lwande, Magnus Evander (UmU).

Post Doc Position2:

Title: Drug resistance – an urgent threat to malaria control and elimination in Rwanda
Background: Falciparum malaria represents a major disease burden in Rwanda, especially for the children. Artemisinin-based combination therapy (ACT) is the main and in principle only efficacious treatment presently. The development of resistance/tolerance to ACT, which first developed and spread in SE Asia. There are now alarming signs that it is also emerging on the African continent, in Rwanda, Uganda and maybe Cameroun. The possible evolution of resistance to artemisinin represents an absolute public health emergency. Its potential spread and therapeutic strategies to control it must now be a top priority for Rwanda. This requires effective surveillance involving genetic markers of drug resistance. The genetic mutations associated with resistance to artemisinin have largely been identified in many locations of the PfKelch-13 gene in the falciparum parasite. Identification of resistance to ACT therefore requires new genomic sequencing techniques on top of the PCR technology.
Aim: To identify and determine the possible evolution of resistance to ACT in areas of Rwanda
Workplan: Collection of blood samples (e g on filter paper) from malaria patients and possibly from cross-sectional community-based survey(s). Determination of molecular parasite resistance profiles by a) sequencing parts of the PfKelch-13 gene and b) determining any possible mutations at genetic loci known to be associated with tolerance to the common partner drugs (lumefantrine, amodiaquine..).
Outcome: Developing the necessary capacity to study and monitor malaria parasite resistance to ACT, with special emphasis on the molecular techniques. Contributing to an understanding of any possible evolution of resistance to ACT in Rwanda
Rwandan supervisors: Dr. Eric Seruyange, **Swedish supervisors** Ass Prof Pedro Gil and Prof Anders Björkman, Karolinska Institute

The project is funded by UR Sweden Program (SIDA). Candidates are invited to submit their applications according to the process described below. Studies are expected to start in 2022 and last for 4 years for PhD program and 2 years for Post doc fellowship.

Candidates are invited to submit their applications according to the process described below.

General Eligibility criteria

The applicant must be:
i. Permanent staff of the University of Rwanda
ii. Citizen of Rwanda
iii. Holding a relevant MSc (for PhD program)/PhD degree (for Post doc fellowship);
iv. Ready to spend a minimum of 7 months every year (for PhD program) or 3 months in each year (for Post doc fellowship) in Sweden.

Ready to continue working at the University of Rwanda after completion of the PhD/Postdoc studies;
vi. The candidates must be prepared to return back immediately after receiving a letter confirming satisfactory completion of the degree to serve in Rwanda.
vii. For PhD scholarships, the candidate should be prepared to work full time on the project and not in possession of another fellowship for PhD studies.

Specific eligibility criteria:
1.Cause and prevalence of megaloblastic anemia: The applicant should hold a master's degree in Medicine, Pharmaceutical Sciences, Microbiology or a similar field, and having knowledge in the area of hematology are prioritized.

2. Improving Rwandan Health by Implementing a One Health Perspective
The applicant should hold a PhD in Medicine, Pharmaceutical Sciences or Biomedical Sciences and having general experience in biomedical technologies, e g within immunoserology, microbiology, is essential. Previous experience in molecular techniques such as PCR and possibly other genetic techniques is a clear advantage. Background in infectious diseases/microbiology, especially with zoonotic diseases is also an advantage but not a must.

2. **Drug resistance – an urgent threat to malaria control and elimination in Rwanda:**

The applicant should hold a PhD in Medicine, Pharmaceutical Sciences or Biomedical Sciences and having general experience in biomedical technologies, e g within microbiology, is essential. Previous experience in molecular techniques such as PCR and possibly other genetic techniques is a clear advantage. Background in infectious diseases/microbiology, possibly even malaria is also an advantage but not a must.

How to apply:

Interested applicants should submit the following:
i. An application letter for the position addressed to the Director of the CPGS, the subject should be **PhD/postdoc sub-programme name** and it must specify which of the positions the applicant is applying for.
According to UR Scholarships policy

ii. A personal motivation statement for the programme of study. This statement should demonstrate commitment, motivation and reasons for interest in the programme (max 2 pages).
iii. Recommendation letters from two academic or professional referees; In the case of a PhD, two recommendation letters from people who can comment on the candidate's intellectual curiosity and academic ability to pursue research, leading to a PhD in the specified thematic area: one of the recommendation letters should be issued by a previous academic supervisor, preferably the Master's degree supervisor.
iv. Applicants from a College at UR need to inform the Principal about applying for this position; and attach a confirmatory letter from the Principal, who received this information.
v. Applicants from collaborating government institutions much attach letter from employer ensuring the candidate gets study leave for the entire period if chosen for the scholarship;
Certified copy of the relevant highest prior degree (e.g. Master's degree for PhD applicants; PhD degree for postdoc applicants).
vii. Copies of valid identification card or passport
viii. Copy of the Master dissertation/ PhD dissertation;
ix. Current CV (maximum of 3 pages) with full name, e-mail, date of birth, sex, formal education at xx university, including full specification of the Masters' degree specialization, teaching
experience, previous experience relevant to the programme, present position, scientific publications and/or any other academic experience that may be relevant.
x. Additional written assignment if asked for (e.g. concept note,
research/project plan, literature review, other relevant documents);

An electronic version of application should be sent to: ur-cpgscholarship@ur.ac.rw and copy to team leaders: egide.kayitare@gmail.com,sofia.birgersson@gu.se,

Please name the application folder with your name and e.g: Egide Kayitare- Infectious diseases.

1. **Submission deadline**

The deadline for application: is **25th August 2022**

2. **Recruitment process**

Applications must be submitted by emails as specified above. The candidates will be notified if they are called for an interview.

The interviews are expected to take place at UR campus in Kigali in the first week of September 2022.
The recruitment team includes senior staff from both UR and Swedish universities. Successful candidates will be notified.

3. **Contact for more information**
- **UR-team leader email:** egide.kayitare@gmail.com, Tel: **0782 172 937**
- **Sweden Team leader:** sofia.birgersson@gu.se
- **CPGS scholarship officer:** Gashayija Gloriose , e-mail: gashayijagloriose@gmail.com, Tel: **0788 532 939**

Done at Kigali, 4th August 2022

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Prof. Nosa O. Egiebor
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