北海道大学
One Health フロンティア卓越大学院プログラム
One Health Allyコース
Student Free Design Activities報告書

Hokkaido University
WISE Program for
"One Health Frontier Graduate School of Excellence"
One Health Ally Course
Student Free Design Activities Report from

Student Free Design Activities (One Health on-site Training)
報告書 Report

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活動報告 [Activity Report]
※活動内容が判る様な写真や図表を加えて下さい。/ Provide photos, tables and figures that clearly show the activities during the period.

タイトル [Course Title]	One Health On-Site Training: Training on human clinical trials at CIDRZ
実施期間 [Periods]	1/12/2022-6/01/2023
共同実施者 [Other participants]	None
言語 [Language]	1/12/2022-6/01/2023
実施場所 [Location]	Center for Infectious Disease Research in Zambia (CIDRZ)

申請時計画の実施報告 [Report how you carried out your plan in the application form]

Did you follow the schedule you initially planned? Did you get the outcome(s) you expected? Please describe what you did during the activity period in detail.

Yes, the schedule that was initially planned was followed. The following are the details of the activities I participated in;

1. **Introduction to research at the Enteric Diseases and Vaccine Research Unit (EDVRU) and participation in weekly research meetings**

   At the beginning of the internship, I was given a comprehensive introduction to the research projects at EDVRU including their objectives, methodology, and projected outcomes. During the research meetings, I learned the specifics of each ongoing project, the progress, as well as challenges, faced such as delays in reagent procurement and the lengthy process of ethical approval, and how the researchers mitigated such delays.

2. **Participation in ongoing research**

   a. **Genotyping of Rotaviruses**

      We performed reverse transcriptase polymerase chain reaction (RT-PCR) to detect the NSP3 gene of rotavirus in stool samples of hospitalized children. dsRNA extracted from stool samples served as a

template for the RT-PCR using the Qiagen One-Step RT-PCR kit according to the manufacturer's instructions. VP4- and VP7-specific forward and reverse primers were employed for assigning P and G genotypes to the isolates, respectively. We also conducted RT-qPCR in samples collected from vaccinated individuals with rotavirus breakthrough infections for surveillance purposes. For this purpose, we used Merck's One-Step RT-PCR Master Mix Kit, and the RT-qPCR was run on the 7500 Fast Real-Time PCR system at CIDRZ Central Laboratory. Samples with low Ct values were further genotyped as described above.

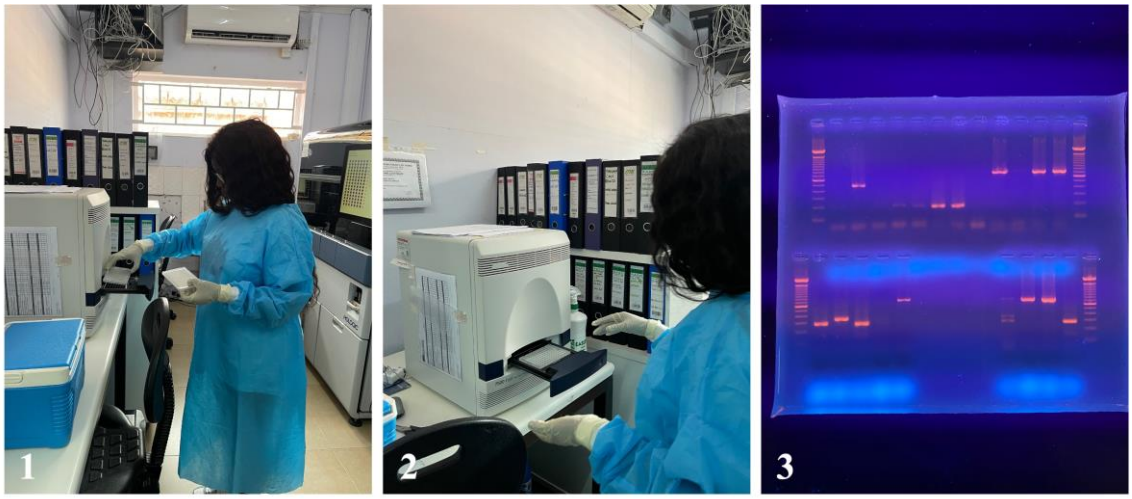

Fig.1 Rotavirus detection by RT-qPCR and genotyping. (1 and 2) Loading of samples for RT-qPCR, (3) gel electrophoresis image for genotyping of rotaviruses

b. ELISpot assay for measuring cellular immune responses

The purpose of this assay was to optimize a protocol for measuring the frequency of antigen-specific T-cells in children vaccinated against rotavirus. Briefly, we isolated peripheral blood mononuclear cells (PBMCs) from whole blood collected from a donor using Histopaque. The cells were cultured in the presence of stimuli of interest in a plate pre-coated with an anti-IFN- γ capture antibody. After overnight incubation, the cells were washed, and the secreted molecule was detected using a detection antibody. Using a precipitating substrate (AEC substrate in this case), the spots corresponding to each cytokine-producing cell were made visible and quantified using an automated ELISpot reader.

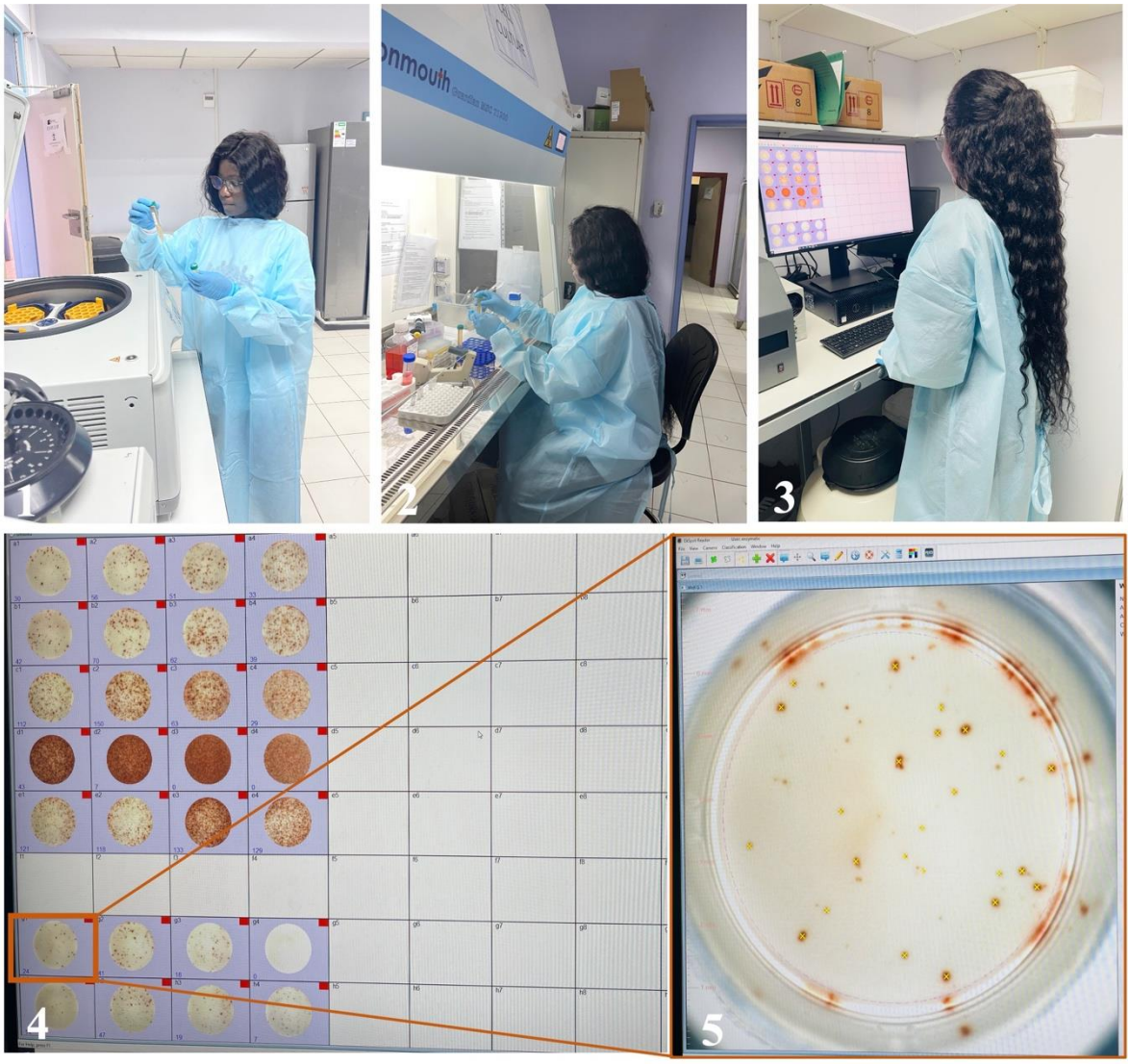

Fig.2 ELISpot assay for measuring Rotavirus-specific T cells. (1) Isolation of PBMCs, (2) Preparation of ELISpot plates, (3–5) Visualization and counting of spots

3. Training in the Collaborative Institutional Training Initiative (CITI) program

In order to understand the ethical and regulatory requirements of conducting human research, I enrolled in CITI program courses. I particularly found these courses invaluable for my future research in evaluating the safety and immunogenicity of vaccines under development in our laboratory in human populations and they also enhanced my professionalism in conducting research. While I have had exposure to ethical concerns in conducting animal experiments, these courses gave me an insight into the requirements for carrying out successful clinical trials and how to resolve ethical concerns that may arise during human subject research. Furthermore, the program allowed me to learn the concepts of good clinical practice and good laboratory practice which are cardinal for the effective efficient, and professional conduct of clinical trials.

4. Exposure to the clinical trial process

For the purpose of learning the clinical trial process, I visited Matero level 1 hospital; one of the sites that are actively involved in conducting clinical trials for EDVRU. My engagement with the different personnel in different departments allowed me to understand their different roles from recruitment of participants, consenting process, health examination, randomization, receipt of respective treatments, and follow-up of participants. In this setting, the research team comprised people with different backgrounds combining their efforts to achieve one goal mirroring a perfect application of the One-Health concept.

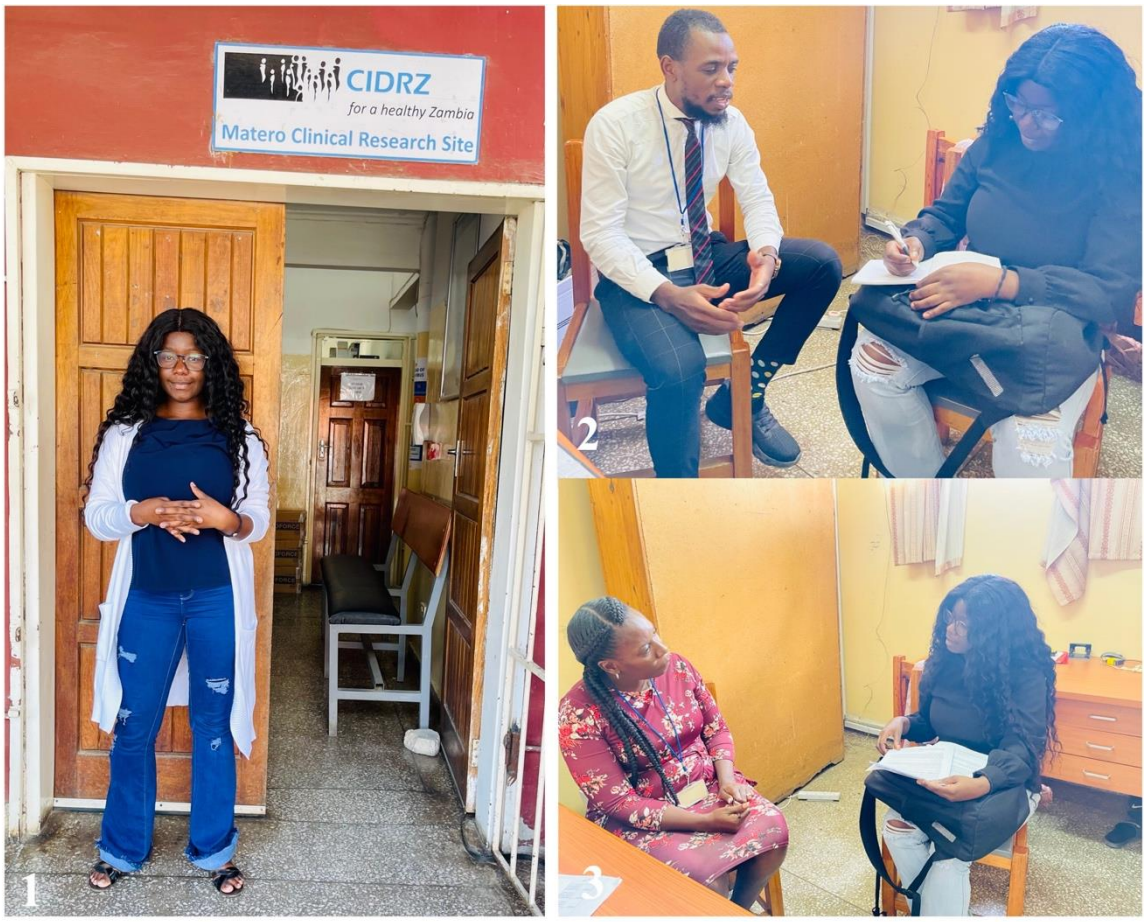

Fig.3 Visit at Matero Clinical Research Site for exposure to the clinical trial process. (1) Visit at Matero Clinical Research Site (2 and 3) Discussions of the clinical trial process

目的達成状況報告 [Report how you achieved your goal/objectives listed in the application form]

Did you achieve all the goals you initially planned? If not, please describe why you failed to fulfill your objectives.

I achieved some of the goals some of the goals planned.

The internship was an excellent and rewarding experience. I got an insight into the mission of CIDRZ particularly EDVRU. I met quality researchers as well as fellow PhD students who shared their research experiences and challenges over the years. I was able to identify my areas of weakness regarding vaccine

studies, especially clinical trials and related ethical concerns which I hope to improve through personal studies and engagement with specialists in that field. Being a vaccine researcher, I can't wait to apply this knowledge in my current studies and hopefully perform clinical trials in Zambia in collaboration with CIDRZ.

Why some objectives weren't fulfilled

One of the main drawbacks was the time limitation (1 month) which made it impossible for me to participate in other research projects and learn new laboratory skills. Secondly, the internship period coincided with a time when some reagents were undergoing shipment which took a long time considering the proximity of Zambia to supplying countries (mostly outside Africa). Thus, some experiments could not be carried out.

One Health Approach実践報告 [Report how your activity could link to One Health Approach]

Did you have a chance to experience One Health approach (collaboration with people from other academic areas)? Please describe some of the examples of One Health approach you implemented in your activity. Otherwise, explain the possibility(ies) how you could link this activity to One Health approach for your future.

Yes, I did.

As a veterinarian, I chose this organization for internship to experience the application of the One Health concept in human research. CIDRZ works in collaboration with various local and international governmental non-governmental entities that assist in financing research projects with the single aim of improving human health in Zambia. Also, through endorsement by the Ministry of Health in Zambia, CIDRZ carries out clinical trials at different phases in government clinics and hospitals while providing scientific evidence to the government for making informed decisions to improve human health.

Particularly I experienced the application of the One-Health approach in executing vaccine clinical trials as discussed hereafter. The initial process of the clinical trial calls for education and awareness of target populations through media platforms such as radio and television, social media (such as Facebook and twitter) and engagement with influential leaders like political leaders (such as ward councilors), church leaders (such as bishops and pastors) and traditional leaders (such as chiefs and headmen. Such an undertaking requires skilled individuals from social sciences and communication department for accurate and efficient dissemination of information. Interested participants are recruited based on set inclusion/exclusion criteria and undergo a consenting process describing in detail the study aims and objectives and the requirement of each participant including collection of samples and follow up visits. Individuals that consent to the study undergo a full physical examination by research clinicians (such as medical doctors) to ascertain health fitness. For most studies, blood (or other samples relevant to the study) is collected by laboratory technicians for measurement of baseline levels of parameters of interest. The research nurses then screen participant data collected during the recruitment, consenting and health examination after which the participants are randomly assigned treatment groups by data analysts. Finally, pharmacists prepare the

biologicals for respective participants which are then administered by medical doctors or nurses. Throughout the entire process, there is need for involvement of people with different skills and background highlighting a practical application of One-Health approach.
備考 [Remarks]

※ 報告書を作成後、担当教員に確認をお願いし署名をもらってください。PDFファイルとしてVetLog上の提出書類「Student Free Design Activities報告書」としてアップロードして下さい。

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