

Article

Application of Virtual Reality for PBMC Isolation

Somkiat Tangjitsitcharoen^{1,a,*}, Supranee Buranapraditkun², Purapat Rattanatraipop³, Phumin Wuthiprasit³, Tanawat Rattanagown³, and Thanaphat Norasettrakoon⁴

¹ Department of Industrial Engineering, Faculty of Engineering, Chulalongkorn University, Phayathai Road, Patumwan, Bangkok, 10330 Thailand

² Division of Allergy and Clinical Immunology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Rama IV Road, Patumwan, Bangkok, 10330 Thailand

³ International School of Engineering, Faculty of Engineering, Chulalongkorn University, Phayathai Road, Patumwan, Bangkok, 10330 Thailand

⁴ The National Board of Digital Economy and Society Office, 9 floor The Government Complex, Chaeng Watthana Road, Laksi Bangkok 10210 Thailand

E-mail: ^{a,*}somkiat.ta@eng.chula.ac.th (Corresponding author)

Abstract. This article presents the development of a virtual reality (VR) training program for the preparation of peripheral blood mononuclear cells (PBMCs). The VR training utilizes VR headsets and a two-touch controller to control the laboratory environment with all required equipment and tools. The developed software for VR training can reduce the medical training time for the science or medical staff who have to learn in the lab. An interactive training system is proposed which contains a timer and performance tracking system, ensuring that the progress can be understood by the user and performance can be evaluated. The program is designed to support conventional teaching methods and increase the efficiency of the teaching process. The virtual reality training is expected to minimize the cost required to perform PBMC isolation and positively enhance the environmental suitability by reducing the use of physical equipment. The developed VR training software can be used as a teaching medium for students and can also be used in any open space, serving as an efficient learning media for familiarizing with the whole experiment process. The experimental results are discussed including laboratory procedure, process tracking, and performance tracking. Moreover, the usability test and the virtual performance index are proposed to validate the application of VR for PBMC isolation. The testing results are accepted with the high scores of usability and virtual performance index.

Keywords: virtual reality, medical training, PBMC isolation, resource minimization, efficiency maximization

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1. Introduction

PBMCs, or Peripheral Blood Mononuclear Cells, are beneficial in the medical industry as they can be applied for multiple important purposes, including diagnosing the immune system's functionality and studying the toxicology of new vaccines. However, PBMCs are not individually found in the human body but are mixed with the blood, which requires an additional process to isolate them from the blood, and that process is called PBMC isolation.

The isolation process is normally done in the lab which requires special equipment and staff proficiency. To master these skills for PBMC isolation, the junior medical staff would have to go through a tremendous secondary study but will only have a few chances to genuinely experience a hands-on lab as the cost of the equipment is very high and the risk of damaging the sample could have led to serious consequences. Therefore, we decided to innovate a solution that would allow the user to have the closest experience to a real hands-on lab while eliminating the damage caused by the user. As a result, we came up with the idea of virtual reality training that would allow the user to train in this particular lab; however, to make this functional and different from the existing training resources, we must overcome 3 major challenges, to make the virtual reality training similar to the real lab, to enhance the training process allowing the user to improve their skills through this virtual reality training, and to use less resource compared to conventional teaching process.

To successfully overcome these challenges, we decided to implement VR technology in the virtual reality training to enhance the graphic visualization of the virtual reality training to be more realistic and similar to the real lab than conventional virtual reality training, add the timing system that will have the user to keep track of their performance, and lastly build the virtual reality training as an 'APK' file format which allows the user to run the virtual reality training along using oculus headset and its controller without needing any additional computer.

This study proposes a VR-based training system that introduces a structured procedural training framework, guiding users through each step in a controlled sequential manner. Second, it incorporates commonly used laboratory equipment and standardized workflows, enabling the proposed approach to be extended to a wide range of laboratory beyond PBMC isolation. Finally, this study proposes a quantitative evaluation metric, the Virtual Performance Index (VPI), which provides a normalized measure to assess how closely user performance in the virtual environment translates to real laboratory practice.

2. Designing Virtual Reality Laboratory

Peripheral blood mononuclear cells (PBMCs) are the type of immune cells that originate in the bone marrow and circulate in the peripheral bloodstream. PBMC plays a crucial role in the human body's immune response and encompasses diverse cell types, including lymphocytes,

monocytes, and macrophages [1]. These cells find extensive utility in various research and toxicology applications [2]. To isolate lymphocytes from PBMC, specific laboratory procedures and tools need to be employed.



Fig. 1. Acid citrate dextrose (ACD) blood

Advancements in technology have enabled scientists to maximize the utility of blood samples, such as ACD blood as shown in Fig. 1, for the analysis of diverse diseases, chronic disorders, and the overall health status of individuals undergoing testing [3]. According to a study conducted by Grand View Research [4], there has been a consistent rise in the demand for blood testing since 2017. It is projected that this demand will double by the end of 2028. Such a significant surge in demand will inevitably lead to an amplified requirement for the preparation of blood samples.

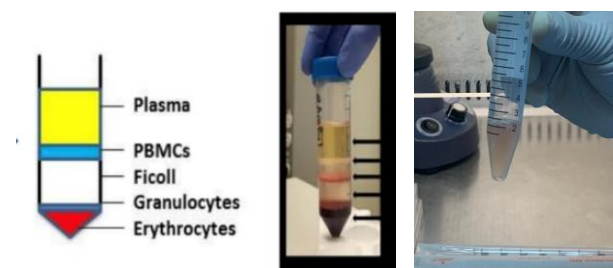


Fig. 2. PBMC preparation

The process of separating PBMCs requires specific laboratory tools and specific laboratory protocols as shown in Fig. 2. Even minor deviations in temperature, centrifuge speed settings, or the sequence of chemical additions can yield undesirable outcomes [5]. Consequently, medical and science students are required to thoroughly study the correct procedure and exercise utmost caution during the experimental process and testing phase. This resulted in not only substantial costs but also demanded considerable time and attention.

The conventional approach to training medical students in the blood separation process starts with initial instruction through lectures, followed by hands-on practice. However, a study conducted by the US National Library of Medicine suggests that medical students often experience anxiety due to the fear of making diagnostic errors [6]. To address this issue, the incorporation of medical case studies could prove beneficial, providing students with practical scenarios and enabling them to apply their knowledge in a realistic context. There is a potential to implement technology in the training process to enhance learning effectiveness while minimizing costs. Virtual Reality Technology (VR) emerges as an ideal choice for gamifying laboratory procedures, combining real-case training and document/video studying while remaining resource-efficient. VR's highly realistic training allows students to visualize the process with clarity and foster active engagement, facilitating learning by doing and enhancing their application of knowledge. Moreover, VR provides a safe space for students to learn from mistakes without any actual risk to samples or equipment [7]. By utilizing VR technology in the form of gamification, the training potential can be maximized, offering an effective and cost-efficient solution for medical students to master laboratory procedures [8]. Furthermore, the teaching process can be further enhanced by integrating 3D virtual reality technology and VRML (Virtual Reality Modeling Language), simplifying the learning process, and making it more accessible and comprehensible [9]. Providing students with a 3D environment for studying closely mimics the real-life laboratory setting, enhancing their understanding and familiarity with the procedures involved [10]. By incorporating medical case studies and leveraging 3D virtual reality technology, the training process for medical students in blood separation can be optimized, potentially alleviating anxiety, facilitating better comprehension of the procedures, and creating a more realistic learning environment.

The objective of this project is to optimize the efficiency of medical students and science students' training in the blood separation process by reducing the required study duration and associated costs. To achieve this, principles derived from process management and lean manufacturing will be applied. Specifically, an interactive, automated teaching system will be implemented, utilizing virtual reality technology. This system will provide medical students with a firsthand experience of the blood separation process, allowing them to comprehend the procedures before engaging in laboratory practice.

However, the developed application of VR for PBMC isolation will be examined by the validation processes including usability test [11-12], expert review, and performance check [13-14] and virtual performance index, which is proposed by authors.

The virtual performance index (VPI) is calculated by taking the ratio of virtual world score to real world score. The virtual world score (VWS) can be selected as the decimal number from 0 to 1 while the real world score

(RWS) is set as 1. The virtual performance index (VPI) is expressed as shown in Equation (1).

$$\text{VPI} = \text{VWS}/\text{RWS} \quad (1)$$

Hence, the result of VPI can vary from 0 to 1. If the VPI is close to 1, it is understood that the developed application of VR for PBMC isolation has the high performance which is similar to the real practice. On the other hand, if the VPI is lower than 0.5, it means that the developed application may not comfortable to be used for VR training for PBMC isolation.

Each VR training undergoes the usability and technical validation with target trainees including medical students, nurses, researchers and instructors. The developed VR training application is benchmarked against real lab activities and data on accuracy, completion rate, and user satisfaction were collected.

The system will include the laboratory room as shown in Fig. 3, which is equipped with essential tools such as a biosafety cabinet hood or laminar flow hood, a refrigerator, and a centrifuge. These tools represent a laboratory configuration widely used across biological and clinical procedures. Inside the laminar flow hood, there are various equipment including a pipette controller, a serological pipette, a freezing container, and reagents such as RPMI medium, Ficoll and freezing media for PBMC preparation as shown in Fig. 4. These components are not only specific to PBMC isolation but also fundamental to a wide range of laboratory protocols. Therefore, the simulation can be extended to other procedures by modifying task sequences while retaining the fundamental design. The project focuses on reducing training time from 1-2 hours to under 15 minutes while implementing validation and evaluation mechanisms. It also seeks to minimize costs and provide realistic virtual reality training that closely mimics the laboratory environment. Additionally, the virtual reality training must include all 15 required pieces of equipment at a close to 1:1 scale.

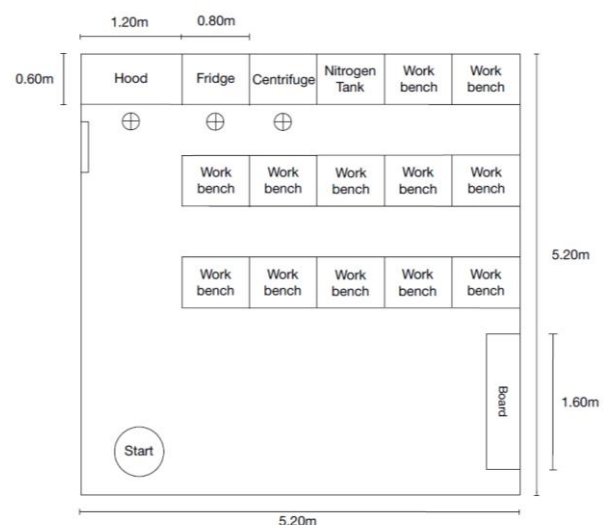


Fig. 3. Draft of laboratory room with important machines and workspace

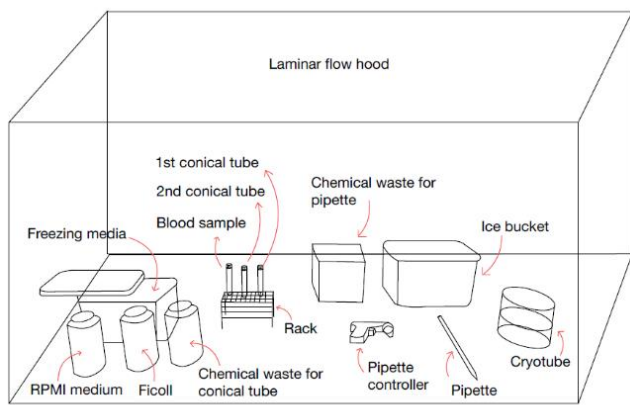


Fig. 4. Draft of equipment inside laminar flow hood with labels

The program runs on Android 10 with API level 29. It is made to be compatible with Oculus Quest 2. The user is required to download the APK file and launch the program before using it, therefore, the headset setting should be compatible with downloading files from unknown sources and developer mode must be turned on. This VR virtual reality training laboratory is a program designed for science or medical students to study the PBMC separation techniques. The program consists of a laboratory room with detailed controls and instructions provided around the room. The main laboratory equipment that the user will have to interact with is the centrifuge and laminar flow hood. Every piece of equipment required is in the hood and ready to be used. Only one pipette is available in the laboratory and it is assumed that the pipette is cleaned every time before using. Every equipment in the laboratory is designed to be interactable with two-touch controllers, whether it is grabbing, interacting, activating, or touching. Users can freely walk around the laboratory. In the scenario where the space in the room is limited, the user can also use the teleport command programmed in the controller to move instead of actual movement. The timer program will start when the user finishes reading the introductory message and clicks confirm and will end when all procedures are performed in the correct order and procedure. Detailed instructions are provided in the program and detect the user's progress. Any wrong step will not proceed the user to the next step and will instead prompt a message to tell the user to complete the process correctly.

3. Development of Virtual Reality Training

To ensure that the laboratory met the protocol in real life and that the visualization of the user was better when doing the real laboratory after finishing the virtual reality training program, the program was verified by an experienced professional as shown in Fig. 5. Throughout the process, every laboratory equipment was calibrated to mirror the scale of the real object and made to look as similar as possible as shown in Fig. 6. Any equipment that did not meet the requirement was improved until

approved. The controls in the simulation were also considered during this process to make them as similar to real-life actions as possible. The grab, activate, teleport, and cap on and off were implemented using the appropriate buttons on the two-touch controller as shown in Fig. 7. Furthermore, important functions including centrifuge activation, pipette activation, pipette connecting, cleaning pipette, and pouring chemicals were added.



Fig. 5. PBMC separation laboratory observation



Fig. 6. Equipment 3D models

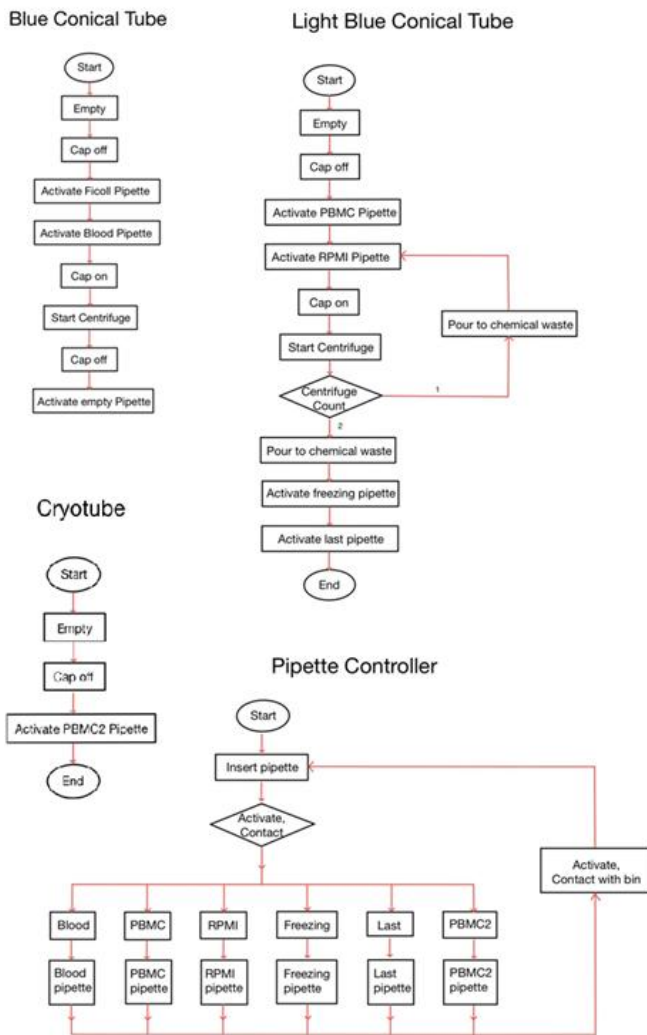


Fig. 7. Logic flow chart

4. Verification of Virtual Reality Laboratory

After the equipment had been identified and calibrated to the correct scale, the logic of object interaction was implemented. It was ensured that the user could not skip any step of the procedures and have to complete every step in the lab, as such action would not be deemed a realistic laboratory virtual reality training. The program would only conclude if every step had been completed in the correct order using the appropriate equipment. In the event of an incomplete step, the program would not progress to the next stage as shown in Fig. 8. The program meticulously tracked the progress of 5 steps throughout the virtual reality training. These 5 steps are paced to function as a checkpoint for each process of the laboratory.

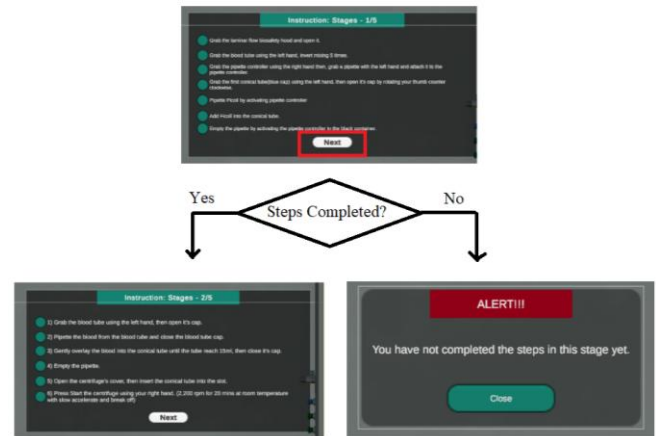


Fig. 8. Process tracking flow chart

When the user finishes the lab, the time the user had used will be displayed on the final interface which has been recorded from the start of the virtual reality training as shown in Fig. 9. The user can keep repeating the simulation to get more familiar with the lab and keep track of the time they used to complete the lab. Ideally, the time they use should get shorter as the user has repeatedly played the virtual reality training as they become more familiar with the lab and understand its correct process. These features significantly enhance the practicing experience for the user by not only allowing them to repeat their process anytime they want but also keep track of the time they used to see how well they have developed their skill for this lab.

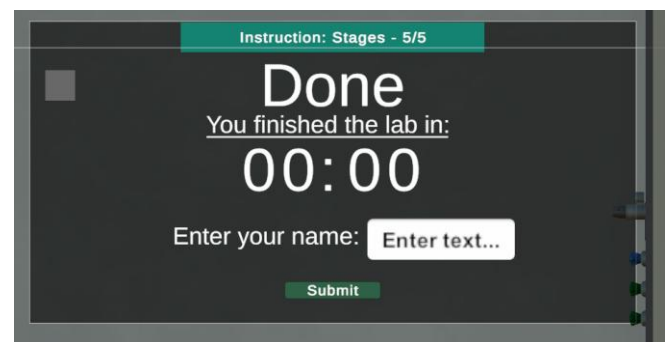


Fig. 9. Steps completed user interface

The developed application has been tested and verified by experienced users. It has been proved that the VR laboratory can help to improve the skills of users as the user can practice beforehand to get familiar before the real practice. The experimental results are discussed by following three methodologies including laboratory procedure, process tracking, and performance tracking.

For the laboratory procedure, we evaluated the realism of the simulation by surveying the feedback from the lab technician and monitored the tester's level of confusion to the graphical equipment when taking the simulation. As a result, the lab technician who has an extensive experience with the real equipment was expressed satisfaction with all of the 8 graphical

equipment and approved it is realism as to be used for the simulations. The graphical equipment is all built on 1:1 scale in the real lab to make it as accurate and realistic as possible.

Usability testing, which is evaluated by 30 trainees as shown in Fig. 10, results in positive with a high score over 80, exceeding the acceptance threshold which the generally average score of System Usability Scale (SUS) is 70. It indicates that the practice of developed application of VR for PBMC isolation pass an acceptable level.



Fig. 10. Example of usability testing on the developed application of VR for PBMC isolation.

For the performance tracking, we integrated the timing system that allow the user to record the time they used to finishing the simulation and having an opportunity to repeatedly train in the simulation. As a result, 75% of the sample group have significantly improved by reducing the time they used to finish the lab by 200% from 15 mins to 7.5 mins, and the rest 25% of the sample have moderately improved by reducing the time they used to finish the lab by over 150% from 15 mins to 10 mins as shown in Fig 11.

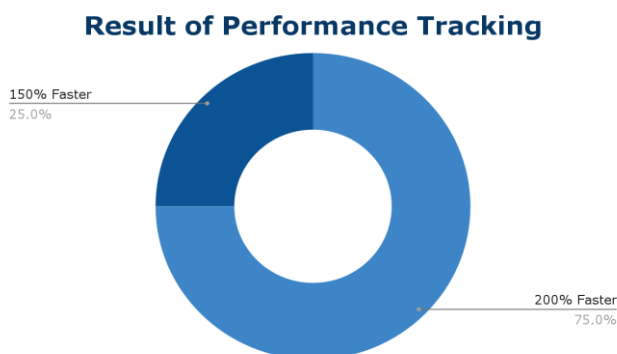


Fig.11. Illustration of experimental result of performance tracking chart.

For the process tracking, we developed the logic that follow the chronological steps in the real laboratory. To ensure its accuracy, we conducted a test and recorded the number of testers that experiencing the difficulty to follow the correct steps comparing to total sample. This number

represents a quantitative indicator to how accurate the tracking process is. As a result, 80% of the sample could successfully follow instructions while 20% were facing a minor difficulty during simulation but are able to process to the last steps as shown in Fig. 12.

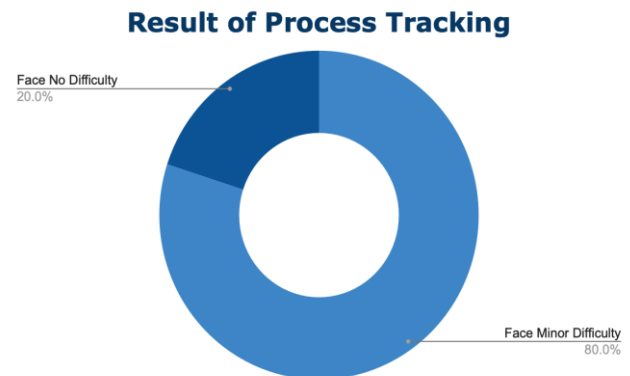


Fig.12. Illustration of experimental result of process tracking chart.

Moreover, the virtual performance index (VPI) for each VR training exceeds 0.5 and the average results of VPI are approximately 0.8. It implied that the developed application of VR for PBMC isolation can be employed to practice and train the users to get used to the real practice.

It is understood that the developed application of VR for PBMC isolation could successfully deliver the important aspects of this research including offering realistic simulation, incorporating an accurate tracking process, and providing an efficient training environment. There still some limitations in term of regulations and resources that contributed to the quality and adoption of the simulation; however, its current functionality could successfully delegate the conventional training materials and enhance the laboratory training aid. However, this research will be improved and developed using haptic gloves to feel more comfortable and realistic. The sound system will be added for further research to help users not be distracted from reading the procedures appearing in the VR application by using the voice command.

For future development, incident and accident cases could be added to procedure to enhance learning outcomes. These scenarios would simulate common mistakes or unexpected situations, allowing user to response to errors and improve decision making in the unexpected situations.

For more complicated laboratory procedures, sub-step practice modules can be introduced to allow users to focus on specific stages of the workflow, enabling repeated practice on specific steps, improving understanding and skill acquisition.

5. Conclusions

This research aims to improve the medical students and science students' training process, especially during the first-time laboratory in the blood separation process by reducing the required study duration and associated

costs. The laboratory focuses specifically on PBMC separation techniques. This newly implemented virtual reality training program is a result of laboratory procedures, process tracking, and performance tracking. The end program is a virtual reality training capable of accurately simulating the real laboratory environment with all required equipment and tools and a performance tracking system to ensure that the user has improved performance from the training process.

Another benefit from using the developed application of VR for PBMC isolation is that the learning process could be done anywhere, not limited to just in lecture space or laboratory room. As any user can download the software on a compatible device and begin learning immediately. This makes the learning process significantly more accessible to people. It represents the first innovative application of VR technology for isolating PBMCs in the laboratory. By addressing gaps in traditional learning methods with VR technology, the whole learning process is more optimized and efficient, spending fewer resources and lowering the time people take to master the laboratory. Finally, the usability test and virtual performance index are proposed to undergo the developed application of VR for PBMC isolation, and the obtained results run satisfactory.

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Somkiat Tangjitsitcharoen completed D.E. degree in Mechanical Engineering from Kobe University, Japan, in 2004. He is currently the head of Advanced Manufacturing and Precision Engineering Research Center at the Industrial Engineering, Chulalongkorn University, Thailand. His research interests include in-process monitoring and optimization of manufacturing processes, micro-machining and micro-assembly, high precision cutting, and intelligent manufacturing systems and machine tools.



Supranee Buranapraditkun's current research focuses on an acute HIV infection cohort (RV254) to study earliest immune response in the periphery and lymph node. She is interested in T and B cells involved in immune responses to acute HIV-1 infection in order to better understand the mechanisms of the responses and to enhance vaccine design and development. Buranapraditkun completed a postdoctoral fellow at the U.S. Military HIV Research Program (MHRP) with Dr. Hendrik Streeck's laboratory in 2014-2015. She focused on how T follicular helper cells communicate with B cells and how their interaction drives the development of broadly neutralizing antibodies that may be protective when induced prophylactically. She graduated with a PhD in Molecular Biology and Immunology from the Interdisciplinary Medical

Microbiology Graduate School at Chulalongkorn University in 2012. She was a coordinator of the NIH contract #NO1-A1-30024 at the Thailand site focusing on "HLA Typing and Epitope Mapping Relative to Vaccine Design" (2004-2008) with Professor Todd M. Allen. She has been involved in the previous phase I: DNA/rfawlpox vaccine trial related to intracellular cytokine staining assays. Here, she is a medical technologist at Chulalongkorn University's Vaccine and Cellular Immunology Laboratory since 1995.

Purapat Rattanatraipop, photograph and biography not available at the time of publication.

Phumin Wuthiprasit, photograph and biography not available at the time of publication.

Tanawat Rattanagown, photograph and biography not available at the time of publication.

Thanaphat Norasettrakoon, photograph and biography not available at the time of publication.