

Strengthening infectious disease surveillance and control through long-term international collaboration: Insights from the Ghana-Japan partnership

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Abstract: West Africa remains a global epicenter for emerging and re-emerging infectious diseases, yet data on pathogen diversity and transmission dynamics remain fragmented. This communication summarizes 21 years of longitudinal research collaboration between the Institute of Science Tokyo (formerly Tokyo Medical and Dental University) and the Noguchi Memorial Institute for Medical Research (NMIMR) in Ghana. Our integrated surveillance framework encompasses: *i*) defining environmental virulence factors for *Mycobacterium ulcerans* to refine Buruli ulcer risk assessment; *ii*) uncovering the "masked" circulation of Dengue and SARS-CoV-2 through molecular epidemiology; *iii*) investigating biological determinants, including gut microbiome profiles, of reduced Rotavirus vaccine efficacy in low-income settings; *iv*) characterizing the environmental reservoirs and fitness costs of carbapenemase-producing *Enterobacteriaceae*; and *v*) analysis of the interaction of malaria parasites between symbionts in vector mosquitoes and vaccine development. By aligning basic research on infectious diseases with clinical data and human resource development, this partnership provides a scalable model for strengthening global health security and addressing the unique infectious disease challenges of the "post-viral" era.

Keywords: Infectious disease surveillance, international collaborative research, molecular epidemiology, vaccine efficacy, West Africa (Ghana)

1. Introduction

West Africa is the region most affected by emerging and re-emerging infectious diseases in the world, and the types of pathogens and the number of affected individuals are outstanding compared to those of other areas. In Ghana, which is located in the center of West Africa, infectious diseases are severe and variable, and they account for about 1/5 of all deaths. Malaria and diarrhea are particularly severe in children, and overcoming them is a significant public health issue. In recent years, dengue virus has invaded West Africa and is expanding its distribution through repeated small outbreaks. Furthermore, drug-resistant bacteria, which are exploding around the world, are being investigated in detail in Western Europe and Asian countries. However, their types and frequency in Africa are not accurately understood. Buruli ulcer is a disease of high focal prevalence mainly in children in West Africa, including in Ghana, but the number of cases has been increasing in Japan in recent years.

Dr. Hideyo Noguchi, the eminent Japanese microbiologist, died of yellow fever in 1928 in Ghana.

In commemoration of Dr. Noguchi's achievements, in 1979, the Japanese government constructed the Noguchi Memorial Institute of Medical Research (NMIMR) in the University of Ghana as a symbolic research facility for medical support for Africa. For the past 40 years, NMIMR has been conducting activities aimed at controlling local infectious diseases through joint research with Japanese research institutes (universities and research institutes). A research collaboration center between former Tokyo Medical and Dental University (TMDU) and NMIMR has been established since 2008. Our research collaboration started in the program of West African Centre for International Parasite Control (WACIPAC) from 2004, and subsequently the Science and Technology Research Partnership for Sustainable Development (SATREPS) project, and 3 phases (1st to 3rd phase) of the Japan Initiative for Global Research Network on Infectious Disease (J-GRID) project in Ghana. In 2020, our collaborative research has been started in the Japan Program for Infectious Diseases Research and Infrastructure for research on emerging and re-emerging infectious diseases with the support of the Japan Agency for Medical Research and Development

(AMED). Our collaboration has been ongoing for 21 years, which is more than one-third of NMIMR's 40-year history. Through this long-term development of collaborative research, we have built a scheme to carry out joint research with local researchers with strong trust. TMDU has been merged with Tokyo Institute of Technology in 2024 to become a new Institute of Science Tokyo (ISCT), and the research activities are unchanged. Figure 1 shows a schematic diagram outlining the structure and framework of the international collaborative research, including the participating institutions.

In this correspondence, we overview our collaborative research projects between NMIMR and its current challenges, and also highlight the importance of our contribution to infectious disease issues in Ghana.

2. Infectious disease research in Ghana

2.1. Study on life stage and transmission of Buruli ulcer-causing bacteria

The causative agent of Buruli ulcer is *Mycobacterium ulcerans*, a type of acid-fast bacterium (1). The infection originates from an environmental source, but the mode of transmission to humans remains largely unknown. In environmental surveillance in endemic countries, IS2404 sequences which are thought to be a specific marker for *M. ulcerans*, have been detected in various environmental samples such as river water. However, it may be unlikely that the pathogenic bacteria to humans inhabit

all environments. In fact, IS2404 has been detected in other *Mycobacterium* species (2). In this study, we have made a new hypothesis that only bacteria having specific virulence factors among *M. ulcerans* living in the environment are able to be infectious in humans. The purpose of this study is to identify virulence factors from isolated bacteria (or nucleic acids) and verify them to elucidate the route of infection. The identified virulence factors are expected to dramatically improve the accuracy of environmental surveillance and to be useful for risk assessment of infection as new markers for the detection of Buruli ulcer-causing bacteria.

2.2. Research on the spread of virus infection in Ghana

Dengue virus (DENV) infection is spreading worldwide, but effective vaccine and therapeutic drugs have not yet been developed. Current possible measures will be to identify epidemic risk factors and utilize them to prevent the spread of DENV infection (3). To date, it has not been reported that Ghana and many other West African countries have a large-scale outbreak of dengue fever. However, our molecular epidemiological study of DENV in Ghana revealed that DENV is already widely spread in Ghana (4,5). In this study, we presume that there exist some factors that could prevent or mask the dengue epidemic from becoming apparent. We have been working to identify those factors by determining the DENV serotype-specificity of serum antibodies in febrile patients and evaluating the virus transmission

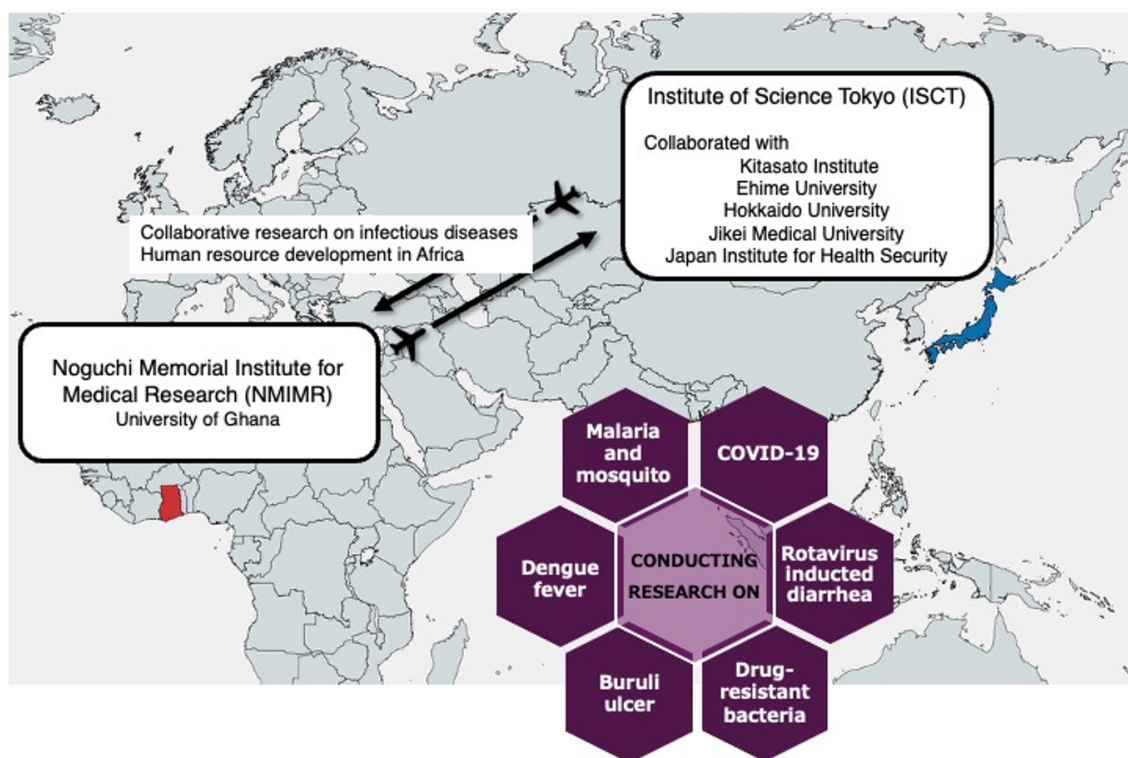


Figure 1. A schematic diagram outlining the structure and framework of the international collaborative research, including the participating institutions.

susceptibility of the vector *Aedes* mosquitoes (6,7).

Ghana has reported fewer cases of the COVID-19 infection than other countries. We detected anti-SARS-CoV-2 antibody in febrile patients reported prior to the COVID-19 pandemic in Ghana. We presume that some similar viruses may have been circulating before the COVID-19 outbreak, and that its antibodies may be related to the low levels of COVID-19 infections.

2.3. Comprehensive molecular study on viral diarrhea

Rotavirus A (RVA) is the leading cause of acute gastroenteritis in young children worldwide and is associated with many deaths each year (8). More than half of the cases of RVA-related diarrhea occur in low-income countries in Africa and Asia. Currently, RV vaccines are in extensive use globally and have made a demonstrable impact on the burden of disease, but the efficacy of the RV vaccines is not the same across all countries. RV vaccines demonstrated very high efficacy in high-income countries, whereas the efficacy was much lower in low-income countries where the burden and mortality are highest. Up to now, the exact reasons for RV vaccine underperformance in low-income countries are unclear. In this study, we are continuing to examine the genetic background of RV strains (9), and analyzing gut microbiome, and fecal antibody titer from children less than five years old in Ghana, where RV efficacy is low (around 50–60%) despite high vaccine coverage (> 95%). The results will tell us how different RV strains, gut microbiome, and immune response of Ghanaian children are from those in high-income countries where RV efficacy is high. This understanding may shed light on why RV vaccine efficacy against severe RV gastroenteritis is lower in low-income countries.

2.4. Study on characteristics and dynamics of antibiotic resistance gene

The rapid emergence and spread of drug-resistant bacteria have become worse in developing countries, including Ghana, due to the absence of a national antimicrobial policy, weak public health strategy including environmental improvement projects, frequent direct contact between animals and humans, and non-adherence to infection control practices. Carbapenemase (CP)-producing bacteria are a major healthcare issue now because of their resistance to carbapenems, which are one of the last resort antibiotics for the treatment of infectious diseases caused by multidrug-resistant bacteria. In this study, we determine the prevalence of CP-producing *Enterobacteriaceae* and *Acinetobacter baumannii* strains from different sources of specimens to understand the reservoirs of CP-producing clones (10-12). Besides, we will identify their bacterial host characteristics such as environmental adaptability and fitness by using CP-producing *E.coli* and *A. baumannii*

strains isolated in Ghana. The results will contribute to clarifying the mechanism of the occurrence and maintenance of CP genes in bacteria.

2.5. Molecular epidemiological study of malaria parasites and vector mosquitoes

West Africa including Ghana is a globally endemic region for the most virulent malaria species, *Plasmodium falciparum* (13). In malaria-endemic areas of Ghana, we investigate the types of vector mosquitoes carrying malaria parasites and the infection rate. Furthermore, we will analyze the symbiotic bacteria, viruses, and parasites in the mosquito's intestines to identify factors that promote/suppress malaria infection. In Ghana, where the first infection-blocking vaccine, RTS, S, was introduced early, we conduct genetic analysis of parasite strains derived from patients in Ghana to clarify whether vaccine-escape strains are prevalent there. In a new study, we will investigate whether infection-blocking antibodies are present in the serum of adults in endemic areas, in an attempt to identify new infection-blocking antibodies.

3. Important collaboration in the development of human resources

Collaboration between ISCT and NMIMR plays an important role in the development of human resources in Japan and Ghana. ISCT runs an educational program for medical or health sciences students who want to gain experience at medical institutions overseas. Under this program, undergraduate students stay to carry out short-term research projects at NMIMR. The visiting students worked with young Ghanaian scientists in the laboratory and field. They conducted their own research at NMIMR. ISCT accepts young, talented researchers as Ph.D. students under the scholarship program supported by MEXT. In 2025, three Ph.D. students from University of Ghana are enrolled in ISCT. They joined the parasitology, virology, bacteriology or biomedical departments in ISCT and started a "new research life". They are expected to bridge ISCT and NMIMR moving forward, contributing to collaboration between the two institutions.

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