



Lassa Fever in Nigeria

Lassa-Nigeria – Development of Sequencing Capacities

Duration

2019–2021

Budget/year

approx. 350,000 EUR

Partner country

Nigeria

Challenges addressed by the project

The Irrua Specialist Teaching Hospital in Irrua (ISTH), Edo State, Nigeria, witnesses yearly Lassa fever outbreaks of public health concern. In accordance with another of its projects, AfroLabNet Project – Stationary Lab, the Bernhard Nocht Institute for Tropical Medicine (BNITM) aims at addressing an important gap with this project by implementing a sequencing pipeline at the ISTH. This is not only to support Lassa Fever outbreak control efforts, but also of other diseases with epidemic potential in Nigeria. This sequencing pipeline enables the monitoring of Lassa virus epidemiology by detecting the potential occurrence of novel Lassa virus strains or any increase in human-to-human transmission of the virus. Moreover, Lassa viruses are highly variable and only the timely sequencing of strains can ensure that diagnostic procedures are up to date and detect all circulating strains. Finally, this platform will also ensure the detection of any unknown circulating pathogens.

Objectives

- » Implement a MinION sequencing pipeline at the ISTH to track Lassa viruses: expansion of the partner laboratory capacity of AfroLabNet – Stationary Lab
- » Train ISTH staff to independently operate the sequencing platform: onsite know-how
- » Support the Ministry of Health (MoH), the Nigeria Center for Disease Control (NCDC) and the World Health Organization (WHO) in monitoring circulating Lassa viruses within the country
- » Identify other or new pathogens that are causing an outbreak

Overview of activities

Based on the success of the 2018 pilot mission aiming at evaluating the feasibility of using MinION (Oxford Nanopore) metagenomics sequencing at ISTH (Kafetzopoulou et al., Science, January 2019), sequencing missions were carried out in 2019 and 2020 during the peak of Lassa fever outbreaks.



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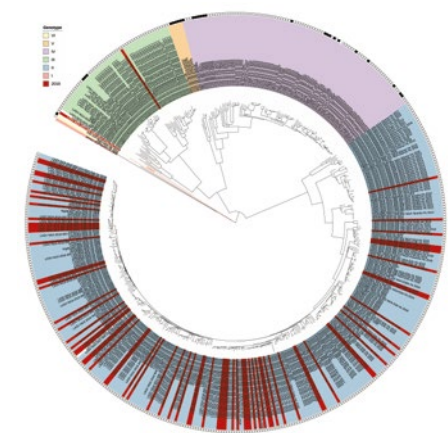
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Sequencing training of ISTH scientists at the BNIT



Adding the sequencing library into the Nanopore sequencer (MinION, Oxford Nanopore) which has a size of a chocolate bar



Phylogenetic tree of the S-segment of the 75 Lassa viruses sequenced during the 4-week sequencing efforts. Additional information about Lassa virus consensus can be found on virological.org

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Teams of BNITM staff deployed to Irrua and, together with ISTH scientists, successfully:

- » Supported the MoH by sharing all sequencing results in real-time (i.e. the sequences of circulating Lassa viruses are comparable to those seen the previous years)
- » Evaluated the upgraded MinION sequencing pipeline
- » Identified potential gaps to fully implement a sequencing laboratory at ISTH in the future, and
- » Trained local scientists in sequencing

Overall, a total of 130 samples were fully sequenced and analysed at ISTH. All results were shared in real-time on the virological.org platform and to NCDC. Results showed rodent-to-human spill-over events rather than human-to-human as the main driver of transmission. Remarkably, one outlier Lassa virus sequence, which did not match Lassa virus lineages II and III known to circulate in Nigeria, was found. Efforts are ongoing to investigate this further. ISTH sequencing capacity is under development and it remains the focus of the collaborative work.

Additionally, local scientists have been trained at the BNITM to independently perform MinION sequencing and the preliminary steps of data analysis.

These works are crucial to reassure communities and help delivering adequate messages about rodent controls.

Partner institution/Contact

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Lassa Fever in Nigeria

Lassa-Nigeria – Capacity Building for the Realisation of Clinical Trials

Duration

2019–2021

Budget/year

approx. 300,000 EUR

Partner country

Nigeria

Challenges addressed by the project

Together with the Irrua Specialist Teaching Hospital (ISTH), Edo State, Nigeria, capacities are being built in Nigeria and clinical trials will be initiated. The WHO has added Lassa fever to its Research and Development Blueprint priority disease list, which includes diseases with a potential to cause public health emergencies for which there are currently no vaccinations or safe treatment solutions. The case mortality of Lassa fever reaches up to 30%. As a WHO Collaboration Center, the Bernhard Nocht Institute for Tropical Medicine (BNITM) is working on medical countermeasures to contain Lassa fever outbreaks, as outlined in the WHO Research and Development Roadmap. The goal is the establishment of clinical sites and capacity building to conduct clinical trials, in which existing therapeutic options can be reviewed and new therapeutic candidates evaluated. Improving the treatment of Lassa fever in endemic regions will contribute to the reduction of mortality. In collaboration with the ISTH capacities are being built in Nigeria and clinical trials initiated.

In 2020 a second study site for the conduct of the interventional clinical phase II study for the treatment of Lassa fever was established with the help of the collaboration partners Inserm (Institut National de la Santé et de la Recherche Médicale) and ALIMA (Alliance for International Medical Action). The Federal Medical Center of Owo (FMCO) in Ondo State is like the ISTH one of the three major Lassa fever case management centres in Nigeria.

Objectives

Strengthening national capacities in outbreak and crisis situations by:

- » Establishment of clinical study sites
 - » Setting up a study centre at ISTH
 - » Setting up a study site at FMCO
 - » Training of study personnel
- » Realisation of collaborative clinical trials to improve the treatment of Lassa fever in endemic regions



Supported by:



Federal Ministry
of Health

on the basis of a decision
by the German Bundestag



Training of an investigator from ISTH at BNITM on the establishment of a quality management system



ISTH study investigator draws blood from a study participant



Presentation of the Principal Investigator to the study team during the initiation of the observational study at ISTH



Group picture during the initiation of the observational study with employees of ISTH and BNITM

Photos ©BNITM

Overview of activities

Current capacity building activities to conduct clinical trials:

- » Establishment of a GCP infrastructure at both sites in Nigeria
- » Equipment of the ISTH clinical research facility with the necessary IT infrastructure and the required medical equipment as well as additional interior equipment
- » Establishment of a quality management system and preparation of essential study documentation for human clinical trials in close collaboration with field study staff on location
- » Establishment of trial submission procedures for clinical trials to relevant ethics committees and authorities
- » Successful initiation of an observational pharmacokinetic study on the treatment of Lassa fever at ISTH
- » Continuous and efficient recruitment of study participants and clinical implementation of the study
- » Laboratory analysis of study participants' blood samples in parallel to the study conduct
- » Preparation and set-up of the second study site (FMCO) together with our collaboration partners Inserm and ALIMA

Partner institutions

- » Irrua Specialist Teaching Hospital (ISTH), Nigeria¹
- » Federal Medical Center of Owo (FMCO), Nigeria²
- » Institut National de la Santé et de la Recherche Médicale (Inserm), France
- » Alliance for International Medical Action (ALIMA), France
- » Institute of Pharmacy, University of Hamburg, Germany

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1 ISTH is a referral hospital serving 19 local governmental areas in a Lassa fever endemic area and is one of few hospitals in West Africa with the facilities for diagnosis, research, and treatment of Lassa fever.
2 FMCO is located in a hyperendemic area for Lassa fever. Since 2019 diagnostics with RT-PCR (reverse-transcription polymerase chain reaction) can be performed in the BSL three laboratory which is located directly on ground.