# JOINT CLINICAL RESEARCH CENTRE

## 40 YEARS OF THE HIV EPIDEMIC: JOINT CLINICAL RESEARCH CENTRE (JCRC) CONTRIBUTION TO THE EPIDEMIC CONTROL

Joint Clinical Research Centre administration block on Plot 101 Lubowa along Entebbe Road

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Executive Director

The Joint Clinical Research Centre (JCRC) is a limited liability company not for profit, which was established in 1991 by HE President Yoweri Museveni as a scientific intervention in the HIV epidemic, which was at its peak in Uganda at the time. It is a collaborative effort of the Ministries of Health, Defence and Makerere University Medical School (currently Makerere College of Health Sciences).

It specialises in HIV/AIDS research, care and treatment, with an expanded mandate on other health problems in the region including Tuberculosis (TB), sickle cell disease (SCD), cardiovascular diseases (CVDs) and more recently COVID-19. Since its inception spanning 30 years to date, the centre has been part of landmark studies that have informed policy and best practices in HIV prevention and treatment. This work has been done collaboratively with the national and international organisations, including research institutions, universities, non-governmental organisations (NGOs) and pharmaceutical companies, with funding

from various partners including Government of Uganda.

## FROM PIONEERING ANTIRETROVIRAL DRUGS (ARVS) IN SUB-SAHARAN AFRICA TO UNIVERSAL ACCESS UNDER PEPFAR

JCRC pioneered research on the use of ARVs in Uganda and sub-Saharan Africa in 1992. The Centre was also the first organisation to import generic ARVs in the region at a time when only a handful of patients could afford to buy these life-saving drugs. This enabled for the first time a public servant and employers to afford buying ARVS for themselves and employees respectively. JCRC continued to carry out operational research on expanded use of the drugs as it opened new Centres around the country to bring treatment closer to the people who needed it. We were involved in other HIV treatment research projects to provide proof of the concept that antiretroviral programmes are possible in developing countries. The experience JCRC obtained from this clinical and operational research was instrumental in providing evidence to the US Government that ARVs could be provided successfully in developing countries. The Centre then became one of the 2 case studies that informed the approval of the US President's Emergency Plan for AIDS Relief (PEPFAR) from 2003. JCRC received the first PEPFAR grant in the world in December 2003 to scale up HIV treatment in the region and save lives. The program established infrastructure and set up antiretroviral therapy (ART) clinics in the public and faith-based health facilities and NGOs under the JCRC TREAT program.

## PIONEERING HIV PREVENTION STRATEGIES IN THE REGION

The Centre pioneered research in sub-Saharan Africa on the use of preventive vaccines for HIV in collaboration with Makerere University and UVRI for adults and Makerere University-Johns Hopkins University Research Collaboration (MU-JHU) for paediatric participants. At the time, candidates for HIV vaccines were developed based on the HIV subtype B circulating in developed countries, yet the worst hit area by the epidemic had different circulating HIV subtypes. After overcoming political, social, regulatory and infrastructure issues, the pioneer studies were successfully implemented and this stimulated international organisations to start mobilising resources to address development of vaccines based on HIV subtypes circulating in Africa and other developing countries. Several such products have now been evaluated in the region and the research is ongoing to find an effective HIV vaccine. JCRC is now working on utilizing long acting antiretroviral drugs to prevent HIV infection in high risk populations

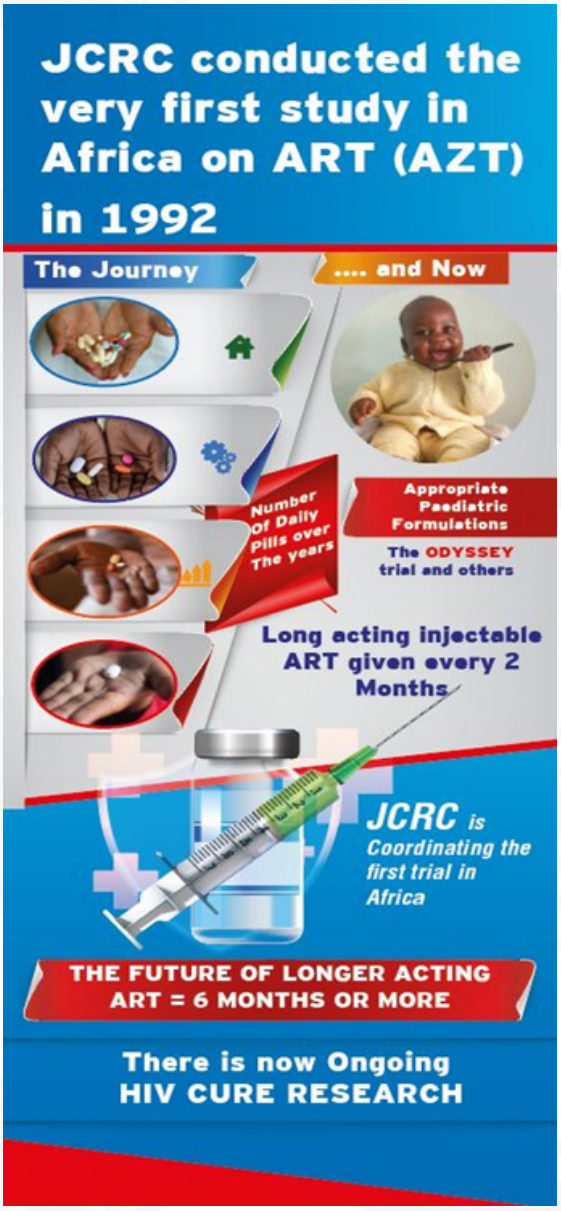
## SIMPLIFICATION OF HIV TREATMENT OVER THE YEARS; MOVING TOWARDS LONG-ACTING ANTIRETROVIRAL DRUGS

JCRC has conducted over 100 research projects in the past 30 years of its existence which have translated into over 500 publications in peer reviewed journals.

Many of the research findings have contributed to policy at both local and international levels including WHO. JCRC has informed policy and guidelines to inform practice in HIV care and simplification of HIV treatment over the years. Registration clinical trials undertaken have provided data for regulatory approvals like the US Food and Drug Administration (FDA) and European Medicine Agency (EMA) of new formulations, drug combinations, fixed dose combinations and treatment boosters for both adults and paediatric patients to enhance efficacy, acceptability, reduce side-effects and costs and increase time to developing resistance. The most recent regulatory approvals by FDA in June 2021are for the use of Dolutegravir in paediatric populations to optimize their HIV treatment.

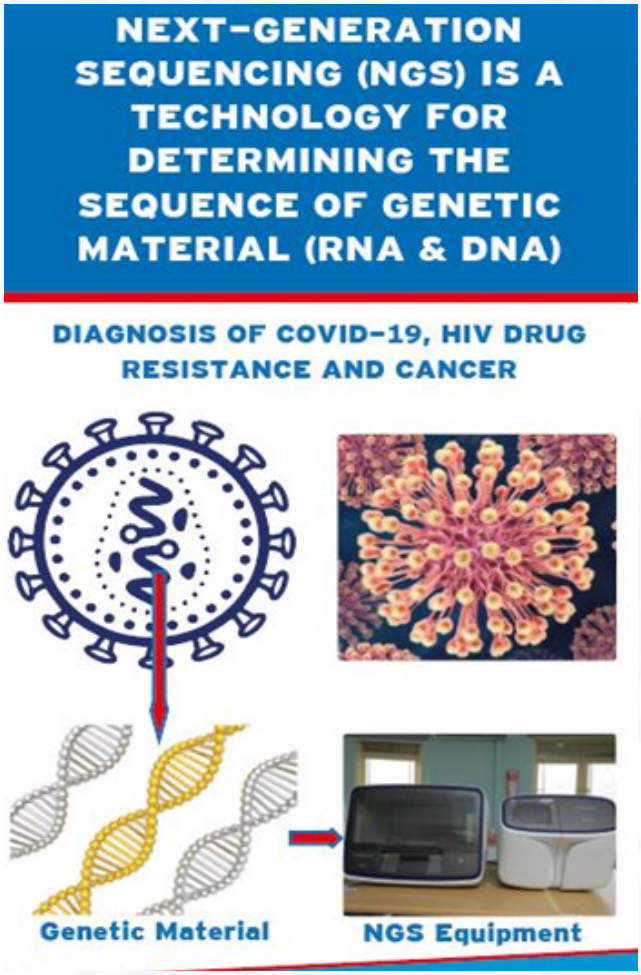
Further effort at HIV treatment simplification has culminated into JCRC coordinating the first trial in sub-Saharan Africa evaluating the use of long-acting ART given as injection of two drugs every 2 months

instead of taking a pill a day as per the current practice. This research is taking place at 8 sites in 3 countries that include Uganda, Kenya and South Africa and is being coordinated by the JCRC. Results of this study are anticipated to bring more hope to persons living with HIV and contribute to improved adherence to treatment which is one of the major challenges in HIV management.




## HIV DRUG RESISTANCE

As we expanded access to ART and reaped its many benefits, we noted the risk of developing resistance to the drugs that we used. Patients who have resistance have high viral loads and can spread HIV if they do not use protective measures. In turn, they spread HIV drug-resistant strains, which may not respond to the first line drugs we provide to patients presenting to the clinic as ART naïve patients. Consequently, we were part of a 6 African countries study to monitor the development of HIV drug resistance in patients who present to the clinics to start ART and those who are failing on their ART. The data generated from this work showed Uganda as having the highest level of drug resistant HIV in the region and contribution evidence to WHO to eventually change the HIV treatment we are currently using. Next Generation Sequencing introduced at JCRC in 2021 will allow for detection of HIV drug resistance as soon as it develops to enable institute timely prevention measures.




## CANCER RESEARCH AND DIAGNOSIS

The Ion Gene Studio S5 will be a game charger in the management of cancers in Uganda. Cancer associated mutations within the genetic material can be monitored through NGS platforms such as the S5. A number of patients will be benefit from this new technology which has only been available in developed countries only

and even at a limited scale. Introduction of this technology by JCRC will see improvement in management cancers as below:

### Hereditary Cancer risk assessment:

Early identification of individuals with such genes associated with different hereditary cancers so as to provide measures for prevention (if no cancer as yet) or provide treatment early in time.

Identification of pathogenic cancer mutations that could later result into cancer. Detection of Somatic mutations for disease prognosis and to predict response to treatment.

## GENE THERAPY FOR CURE OF HIV AND SICKLE CELL DISEASE

The future for HIV management and SCD is CURE and proof of concept has been established. However ongoing Gene Therapy for CURE does not include regions like Africa with highest burden of HIV and Sickle Cell Disease. JCRC will leverage existing facilities – like collecting selected cells from patient using the Apheresis machine that can be genetically modified to manufacture Gene Therapy cells applied to CURE studies of diseases that are currently considered incurable like HIV. JCRC has catalysed the formation of the Global Gene Therapy Initiative (GGTI) to enable access Low- and middle-income countries access Gene Therapy for HIV/SCD CURE initiatives. Preparations for these research initiatives is in process at JCRC.

## APHERESIS

Having acquired the apheresis equipment in 2017 as part of HIV CURE research, the equipment has also supported in the management of sickle cell disease (SCD) for several clients. A special clinic was established for SCD clients in 2019 and currently has over 140 clients some of whom are currently participating in a clinical trial that is assessing the efficacy of a new SCD drug. The apheresis machine has been used to save lives of SCD patients and other diseases by enabling efficient exchange of Red Blood Cells or Plasma. In July of 2021, the clinic also received a novel point of care test for Hb electrophoresis from Hemex Health® known as the Gazelle™ Microchip Electrophoresis platform to identify a client with sickle cell disease or a client with the sickle cell trait (a carrier). It is convenient and easy to use with sample preparation and results are ready in less than10 minutes compared to traditional method of Electrophoresis that takes >5hrs. We are going to use this system to collect plasma from individuals recovered from COVID-19 and concentrate the Antibodies for future use to treat COVID-19 as well as other research on the disease.

## JCRC DEVELOPS UGANDA'S FIRST RAPID PCR-BASED DIAGNOSTIC KIT FOR COVID-19

The Centre was among the first 12 Laboratories that were approved to support Ministry of Health in COVID-19 Testing a service it has offered since 2020. All the kits in the country used for testing were imported making the test very expensive. This led the Government of Uganda (GoU) to prioritize testing those at highest risk and performed limited community monitoring testing.

Scientists at JCRC building on their work on simplifying how to measure the HIV viral load in the body set out to develop COVID-19 diagnostic tests and platforms that are reliable, simple, fast, high throughput, affordable, with readily available reagents and can be deployed as both point of care tests or run in centralized molecular biology laboratories. This was termed the Rapid AirJump Amplification Assay (RARA).

The developed assay is a dramatic simplification over traditional PCR test methods and takes 30 minutes to run a plate of 96 samples compared to 7hrs 30 mins on the conventional Abbott Platform.

The other two assays we are developing will be used for massive community testing to monitor the COVID-19 epidemic and detect emerging new strains of COVID-19. These assay will employ a newer and more advanced technology, the Next Generation Sequencing Technology (NGS) which has the ability to screen and monitor evolution of the virus within the community even when it is at very low levels. Equipment for this work has already been obtained.

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