Uganda National Council for Science and Technology

(Established by Act of Parliament of the Republic of Uganda)

Our Ref: HS936ES **9 November 2020**

Matthew Cotten
MRC/UVRI & LSHTM Uganda Research Unit, Entebbe,
Uganda
Wakiso

Re: Research Approval: Local sequencing of SARS-CoV-2 from Uganda COVID-19 cases

I am pleased to inform you that on **09/11/2020**, the Uganda National Council for Science and Technology (UNCST) approved the above referenced research project. The Approval of the research project is for the period of **09/11/2020** to **09/11/2022**.

Your research registration number with the UNCST is **HS936ES**. Please, cite this number in all your future correspondences with UNCST in respect of the above research project. As the Principal Investigator of the research project, you are responsible for fulfilling the following requirements of approval:

1. Keeping all co-investigators informed of the status of the research.

2. Submitting all changes, amendments, and addenda to the research protocol or the consent form (where applicable) to the designated Research Ethics Committee (REC) or Lead Agency for re-review and approval **prior** to the activation of the changes. UNCST must be notified of the approved changes within five working days.

3. For clinical trials, all serious adverse events must be reported promptly to the designated local REC for review with copies to the National Drug Authority and a notification to the UNCST.

4. Unanticipated problems involving risks to research participants or other must be reported promptly to the UNCST. New information that becomes available which could change the risk/benefit ratio must be submitted promptly for UNCST notification after review by the REC.

5. Only approved study procedures are to be implemented. The UNCST may conduct impromptu audits of all study records.

6. An annual progress report and approval letter of continuation from the REC must be submitted electronically to UNCST. Failure to do so may result in termination of the research project.

Please note that this approval includes all study related tools submitted as part of the application as shown below:

No.	Document Title	Language	Version Number	Version Date
	Project Proposal	English	1.1	
1	Approval Letter	English	1.1	2020-04-16
2	Administrative Clearance	English	1.1	2020-04-16
2	Ministry of Health Support letter	English	1	10 March 2020

Yours Sincerely

Hellen Opolot
For: Executive Secretary
UGANDA NATIONAL COUNCIL FOR SCIENCE AND TECHNOLOGY

LOCATION/CORRESPONDENCE

Plot 6 Kimera Road, Ntinda
P.O. Box 6884
KAMPALA, UGANDA

COMMUNICATION

TEL: (256) 414 705500
FAX: (256) 414-234579
EMAIL: info@uncst.go.ug
WEBSITE: http://www.uncst.go.ug

UNCST/RC 1/02

REPUBLIC OF UGANDA

UGANDA NATIONAL COUNCIL FOR SCIENCE AND TECHNOLOGY

APPLICATION FOR RESEARCH APPROVAL IN UGANDA

(N.B. Read the instructions in Annex 1 before completing this form. Please, note that incomplete applications will not be received)

FOR OFFICIAL USE ONLY

<table>
<tr><th colspan="2">Registration</th><th colspan="2">Authorization</th></tr>
<tr><td colspan="2">Field of Research:</td><td>Reviewed:</td><td>Internally [ ]

Externally:
[ ]Peer review
[ ]Task Force
[ ]UNCST Specialized Committee</td></tr>
<tr><td>Research Registration No.</td><td></td><td></td><td></td></tr>
<tr><td colspan="2" rowspan="5">Date of registration

Stamp</td><td>Rejected:</td><td></td></tr>
<tr><td>Reason for rejection</td><td></td></tr>
<tr><td>Approved:</td><td>……
Executive Secretary
Uganda National Council for S&T</td></tr>
<tr><td>Date:</td><td></td></tr>
<tr><td>Research ID No.</td><td></td></tr>
</table>

SECTION A: PARTICULARS OF APPLICANT

1. Full Name: Matthew Louis Cotten
   (Underline Surname)

2. Male [x] Female [ ] (Please tick)

2. Date of Birth: 17 October 1957

4. Place of Birth (e.g. Kampala, Uganda): Grundy Center, Iowa, USA

5. Nationality: USA

6. Marital Status: Single

7. (i) Home Address: Plot 51-59, Nakiwogo Road, Entebbe

Telephone: +256 701 509 685 E-mail: matthew.cotten@lshtm.ac.uk

(ii) Organization of affiliation in Uganda
MRC/UVRI and LSHTM Uganda Research Unit.
Address: P.O Box 49 Entebbe, Plot 51-59, Nakiwogo Road, Entebbe
Telephone: +256417704000
E-mail: mrc@mrcuganda.org

8. Current Emigration Status:* Uganda visa with work permit ID 250389857
(If already in Uganda) *Refers only to foreign applicants.

9. Employment:

(i) Employer: **MRC/UVRI and LSHTM Uganda Research Unit.**

(ii) Position: Professor

10. Education

	University	**Qualification**	**Year**	**Field of Specialization**
1	Iowa State University	B.Sc.	1981	Biochemistry
2	University of Iowa	Ph.D.	1986	Biochemistry
3				

11. Research experience, with list of publications, if any (list no more than 10 publications) see also attached C.V.

Summary
I am a virologist who has worked in academic, clinical and industrial laboratories in the United States, Africa and Europe. My research has focused on describing virus-host interactions and the patterns of virus transmission. I have led independent research groups and have teaching experience at both undergraduate and postgraduate levels. I have wet-lab experience in growing and manipulating viruses. I have established high throughput viral next generating sequencing (NGS) methods with a special focus on large sample clinical studies. I have Python coding skills, and I am familiar with the bioinformatics tools for analyzing and extracting useful information from viral NGS data. I have a strong interest in supporting and training collaborators throughout the world.

Current post (from April 1 2019):

Professor of Pathogen Genomics and Bioinformatics

MRC/UVRI & LSHTM Uganda Research Unit, Entebbe, Uganda
and
Part-time Professor in Viral Genomics
MRC-University of Glasgow Centre for Virus Research

Previous posts:

- 2016- 2019: Senior Research Scientist, Department of Viroscience, ErasmusMC, Rotterdam, Netherlands. **Description**: 1. Established a core NGS process (clinical samples to complete genomes) for Morbilliviruses, Flaviviruses. 2. Developed novel analysis and machine learning tools for viral data. 3. Established viral sequencing for global sewage sequencing project within the COMPARE consortium.

- 2010- 2016: Senior Staff Scientist, Wellcome Trust Sanger Institute, Hinxton, UK. **Description**: 1. Set up and ran NGS methods for the Wellcome Trust Strategic Award project "VIZIONS" (Vietnam Initiative on Zoonotic Infections). 2. Provided sequencing and bioinformatics analyses support for the KEMRI/Wellcome Trust unit in Kilifi, Kenya. 3. Developed high-throughput NGS methods for full genome sequencing of MERS coronavirus directly from clinical samples. 4. Helped run a local real-time Ebola virus sequencing facility in Makeni, Sierra Leone, July-September 2015. 5. Assembled and analyzed >550 full genomes from the 2014 Ebola virus outbreak. 6. Developed novel methods for full genome next generation sequencing of other RNA viruses (norovirus, rotavirus, hepatitis C Virus, HIV-1, respiratory syncytial virus) directly from clinical and field samples.

2005-2010: Senior virologist, Medical Research Council Laboratories, Fajara, The Gambia

2000-2005: Group Leader, Axxima Pharmaceuticals, Munich, Germany

1992-2000: Group Leader, Institute for Molecular Pathology, Vienna, Austria

1990-1992: Staff Scientist, Institute for Molecular Pathology, Vienna, Austria

1987-1990: Postdoctoral research fellow, Institute for Molecular Pathology, Vienna, Austria

1986-1987: Postdoctoral research fellow, Vanderbilt University, Nashville Tennessee, USA

Cotten selected publications

1. Barry M, Phan MV, Akkielah L, Al-Majed F, Alhetheel A, Somily A, Alsubaie SS, McNabb SJ, **Cotten M**, Zumla A, Memish ZA. Nosocomial outbreak of the Middle East Respiratory Syndrome coronavirus: A phylogenetic, epidemiological, clinical and infection control analysis. Travel Med Infect Dis. 2020 Jun 26:101807. https://doi.org/10.1016/j.tmaid.2020.101807

2. Phan, M. V. T., Tue, N. T., Anh, P. H., Baker, S., Consortium, V., Kellam, P., and **Cotten, M**. Identification and characterization of Coronaviridae genomes from Vietnamese bats and rats based on conserved protein domains, Virus Evolution. 2018 Dec 15;4(2):vey035.https://doi.org/10.1093/ve/vey035

3. Kiyuka P.K., Agoti C.N., Munywoki P.K., Njeru R., Bett A., Otieno J.R., Otieno G.P., Kamau E., Clark T.G., van der Hoek L., Kellam P., Nokes D.J., **Cotten M**. Human Coronavirus NL63 Molecular Epidemiology and Evolutionary Patterns in Rural Coastal Kenya. J Infect Dis. 2018 May 5;217(11):1728-1739. https://doi.org/10.1093/infdis/jiy098

4. Dudas, G., ... **Cotten M**..., Rambaut A. Virus genomes reveal factors that spread and sustained the Ebola epidemic, Nature. 2017 Apr 20;544(7650):309-315. https://doi.org/10.1038/nature22040

5. Phan, M. V. T., Anh, P. H., Cuong, N. V., Munnink, B. B. O., van der Hoek, L., My, P. T., Tri, T. N., Bryant, J. E., Baker, S., Thwaites, G., Woolhouse, M., Kellam, P., Rabaa, M. A., **Cotten, M**., and Consortium, V. Unbiased whole-genome deep sequencing of human and porcine stool samples reveals circulation of multiple groups of rotaviruses and a putative zoonotic infection, Virus Evolution 2016 Oct 3;2(2):vew027. https://doi.org/10.1093/ve/vew027

6. Arias, A.,... and **Cotten, M.** Rapid outbreak sequencing of Ebola virus in Sierra Leone identifies transmission chains linked to sporadic cases, Virus Evolution 2016 Jun 22;2(1):vew016.https://doi.org/10.1093/ve/vew016

7. Memish, Z. A., **Cotten, M**., Meyer, B., Watson, S. J., Alsahafi, A. J., Al Rabeeah, A. A., Corman, V. M., Sieberg, A., Makhdoom, H. Q., Assiri, A., Al Masri, M., Aldabbagh, S., Bosch, B. J., Beer, M., Muller, M. A., Kellam, P., and Drosten, C. Human infection with MERS coronavirus after exposure to infected camels, Saudi Arabia, 2013, Emerg Infect Dis. 2014 Jun;20(6):1012-5. https://dx.doi.org/10.3201/eid2006.140402

8. **Cotten, M**., Watson, S. J., Zumla, A. I., Makhdoom, H. Q., Palser, A. L., Ong, S. H., Al Rabeeah, A. A., Alhakeem, R. F., Assiri, A., Al-Tawfiq, J. A., Albarrak, A., Barry, M., Shibl, A., Alrabiah, F. A., Hajjar, S., Balkhy, H. H., Flemban, H., Rambaut, A., Kellam, P., and Memish, Z. A. Spread, circulation, and evolution of the Middle East respiratory syndrome coronavirus, MBio. 2014 Feb 18;5(1). pii: e01062-13. https://dx.doi.org/10.1128/mBio.01062-13

9. **Cotten, M**., Watson, S. J., Kellam, P., Al-Rabeeah, A. A., Makhdoom, H. Q., Assiri, A., Al-Tawfiq, J. A., Alhakeem, R. F., Madani, H., AlRabiah, F. A., Al Hajjar, S., Al-nassir, W. N., Albarrak, A., Flemban, H., Balkhy, H. H., Alsubaie, S., Palser, A. L., Gall, A., Bashford-Rogers, R., Rambaut, A., Zumla, A. I., and Memish, Z. A. Transmission and evolution of the Middle East respiratory syndrome coronavirus in Saudi Arabia: a descriptive genomic study, Lancet. 2013 Dec 14;382(9909):1993-2002.https://doi.org/10.1016/S0140-6736(13)61887-5

10. **Cotten, M**., Lam, T. T., Watson, S. J., Palser, A. L., Petrova, V., Grant, P., Pybus, O. G., Rambaut, A., Guan, Y., Pillay, D., Kellam, P., and Nastouli, E. Full-genome deep sequencing and phylogenetic analysis of novel human betacoronavirus, Emerg Infect Dis 19, 736-742B.https://dx.doi.org/10.3201/eid1905.130057

12. Co-investigators* Details

	Name	Sex (Male/Female)	Qualifications	Nationality	Organization of affiliation *
1	Pontiano Kaleebu	Male	MB ChB, PhD	Ugandan	MRC/UVRI
2	John Kayiwa	Male		Ugandan	UVRI
3	Henry Mwebesa	Male		Ugandan	MoH
4	Julius Lutwama	Male	BSc, MSc, PHD	Ugandan	UVRI
5	Jonas Lexow	Male			MRC/UVRI
6	Deogratius Ssemwanga	Male		Ugandan	MRC/UVRI

*Co-investigators includes co-principal investigators and any member of the core research team.

SECTION B: MAIN FEATURES OF THE RESEARCH PROJECT

13. Title of research project:

Local sequencing of SARS-CoV-2 from Uganda COVID-19 cases

14. Objectives of the research project

To document the transmission dynamics of COVID-19 in Uganda using full viral genome sequencing.

15. Brief outline of research study design/methods

Study design: The study will be nested within the national COVID-19 outbreak surveillance which will be supported by MRC/UVRI & LSHTM Uganda Research Unit.

Laboratory methods: As part of the COVID-19 diagnostic process, real-time polymerase chain reaction is used to identify the presence of the COVID-19 virus SARS-CoV-2[1]. If positive, additional information on the virus can be obtained by determining the viral genomic sequences. This information is important for determining the source of the infection, for monitoring changes in the virus and as a validation of other diagnostic tools. The sequence data will be added to international open source collections (GenBank[2], GISAID[3], NEXTStrain[4], CoV-GLUE [7]) to help investigators globally track the virus movement and changes.

Once a sample is identified as SARS-CoV-2 positive by PCR, extracted nucleic acids will be converted to double-stranded DNA, amplified using PCR with SARS-CoV-2 specific primers and then ligated to sequencing adapters and subjected to MinION sequencing to determine SARS-CoV-2 genomic sequences [9]. The laboratory and computational methods required for these processes are well established with more than 1100 SARS-CoV-2 sequences currently available from the outbreak, many using the MinION sequencing method.

16. Briefly state the key ethical issues in carrying out the research project and how they will be addressed:

Ethical clearance will be obtained from the Uganda Virus Research Institute Research Ethics Committee, Uganda National Council of Science and Technology and the London School of Hygiene &Tropical Medicine Ethics Committee prior to undertaking the study, as applicable.

Confidentiality will be ensured by not capturing personal identifiers such as name, date of birth or telephone contacts during the research process and all collected data will be used for the purposes of this study. The research component is working with anonymised viral samples only.

We will protect the identity of the patient providing the sample in the following methods. Samples and the resulting sequence data will bear only a unique identifier numbers. Essential metadata collected as part of the diagnostics (patient age, gender, travel history, disease symptoms, outcome, date of collection, sample collection location) will be linked to a sample identification number, however these data will be stored separately and securely.

During the sequencing a small amount of human sequence data may be detected. This is minimized by using SARS-CoV-2-specific amplification primers during the sequence process. Finally, any human sequences present in the final raw read data will be removed computationally before public release of the data. Established methods of identifying and removing human sequences from next generation sequencing data are available and will be used [11].

Previous studies, UNCST has required that for samples collected as part of surveillance, sample sources must be traced to provide consent for use of their samples in research. We would like to request a waiver of this requirement for the following reasons. 1. No human biological samples will be analysed. The sequencing/research component will focus solely on viral RNA obtained from prior diagnostic efforts. 2. All human identifying sequences will be removed from the data before public release. 3. Upholding this requirement will expose the study team to COVID-19 infection risk. 3. The attention associated with revisiting positive patients may risk stigmatizing the patient.

17. Research type (Please tick ( ):

[ ] Academic Award [√] Non-Academic Award
(If Academic, state type of Academic Award e.g. BA, MSc or Ph.D, Fellowships, Post-Doctoral Studies, etc, and the awarding Organization)

.....N/A.....

18. Districts of Uganda in which research will be carried out

The study will be carried out in Uganda and samples will be analyzed at the diagnostic and research laboratories at the Uganda Virus Research Institute and MRC/UVRI & LSHTM Uganda Research Unit in Entebbe.

19. (i) **Estimated research budget (in USD**): $ 661,185 to MRC/UVRI and LSHTM Uganda Research Unit

(ii) **Sponsor (s):** Wellcome Trust

(iii) **Duration in months:** 24

20. Breakdown of Expenditure:

Summarised Budget for

No.	Item	Total Cost (USD)
1	Personal Costs (Job title)	255,310
2	Equipment	72,325
3	Approval & other regulatory fees	969
4	Laboratory Costs	39,450
5	Sequence SARS-CoV-2 positives	141,494
6	Travel Costs	57,214
7	Research Management Costs	94,422
	Grand total	661,185

21. Briefly state your plan to disseminate research results to study participants, communities or stakeholders.

Our full genome SARS-CoV-2 sequences (including raw data) will be made publicly available on our project website, in GenBank, GISAID, Virological.org or CoV-GLUE as soon as the data have passed our quality controls. The GLUE SARS-CoV-2 website is currently available at [10] for public use and will be extended with new analyses and tools as they become available during the project. We will use social media (institute websites and twitter) to communicate new findings

SECTION C

22. Names and addresses of two referees:

1. Charles Masembe (BVM, MSc., PhD),
   Associate Professor, Wellcome Trust Fellow, Makerere University, P.O. Box 7062, Kampala, Uganda
   Email: cmasembe@cns.mak.ac.ug, cmasembe@gmail.com
   Tel: +256 712 455 987

2. David Kateete
   Makerere University · Department of Microbiology
   B.Vet.Med, MSc, Ph.D.
   Email: davidkateete@gmail.com

23. I undertake to submit:

    i. Annual progress reports of my research project

    ii. Final report on completion of the research project

    iii. Copies of any publications arising from the research project

24. I hereby certify that to the best of my knowledge and belief, the particulars given in this form are true and complete in all respects.

Date 7 Sept 2020 **Signature of Applicant** 

ANNEX I

1. This form is to be submitted to the Executive Secretary, Uganda National Council for Science and Technology together with the following;

    1. A copy of the stamped research proposal
    2. A copy of stamped data collection instruments
    3. A copy of stamped informed consent documents, where applicable
    4. Approval letter from Research Ethics Committee or Institutional Review Board/Committee (for research involving humans as research participants only)/Uganda Wildlife Authority/National Biosafety Committee or other Lead Agency
    5. Letter of introduction/recommendation from the organization of affiliation in Uganda (for foreign investigators only)
    6. A copy of the admission letter for academic researches
    7. Three (3) copies of RS 6 forms for the principle investigator and the core research team
    8. Four (4) recent passport size photographs for the principle investigator and the core research team

    Additional information

    1. The proposed research project should at the minimum have a title, introduction, objectives, study design and methods, budget and the estimated duration.

    2. A researcher or any other person, who wishes to export plant or animal specimen for further investigations abroad, must obtain special export permits from the UNCST.

    3. The Uganda National Council for Science and Technology reserves the right to reject any research proposal.