H3Africa Kidney Disease Research Network
A U54 H3A Collaborative Clinical Center Award

The University of Ghana & The Noguchi Memorial Institute for Medical Research, Accra, Ghana
The H3Africa Kidney Disease Study
(U54 HG 006939-01)

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H3Africa Kidney Disease Research Network (U54): Research Objectives

1. Comprehensive phenotyping of the first ever kidney disease cohort of 8,000 cases and controls in four African countries
2. Conduct four genetic and translational research projects of CKD and childhood onset nephrotic syndrome
H3Africa Kidney Disease Research Network (U54): Infrastructure/Capacity Building

1. Two genomic research laboratories in West Africa using sustainable, low capital-intensity laboratory technology platform (Dr. David Burke)

2. Develop mechanism for high throughput whole genomic sequencing in collaboration with overseas institutions (Dr. Rob Lyons, Dr. David Burke and Dr. Michael Boehnke)
H3Africa Kidney Disease Research Network (U54): Training & Career Development Goals

1. Implement training programs genetics and genomics science for laboratory technicians, research scientists and research coordinators in Africa with use of sandwiched approach as appropriate

2. Implement genomics science training and career development program for African scientists in tandem with the Michigan Predoctoral Training Program in Genetics (Dr. John Moran) and the U-M Genome Science Training Program (Dr. Michael Boehnke)

3. Develop system biology training through U.S. platform extension to Africa (Dr. Matthias Kretzler)
## H3A Kidney Study Expanded Recruitment Goals

### Recruitment goals for each Clinical Center

<table>
<thead>
<tr>
<th>Clinical Center</th>
<th>Number of Participants</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Kidney Disease</td>
<td>Controls</td>
</tr>
<tr>
<td>Addis Ababa University</td>
<td>250</td>
<td>250</td>
<td></td>
</tr>
<tr>
<td>Kwame Nkrumah University of Science and Technology</td>
<td>500</td>
<td>500</td>
<td></td>
</tr>
<tr>
<td>Obafemi Awolowo University, Ile-Ife</td>
<td>500</td>
<td>500</td>
<td></td>
</tr>
<tr>
<td>University of Abuja</td>
<td>250</td>
<td>250</td>
<td></td>
</tr>
<tr>
<td>University of Ghana</td>
<td>750</td>
<td>750</td>
<td></td>
</tr>
<tr>
<td>University of Ibadan</td>
<td>925</td>
<td>925</td>
<td></td>
</tr>
<tr>
<td>University of Ilorin</td>
<td>500</td>
<td>500</td>
<td></td>
</tr>
<tr>
<td>University of Nairobi</td>
<td>250</td>
<td>250</td>
<td></td>
</tr>
<tr>
<td>University of Nigeria, Enugu</td>
<td>500</td>
<td>500</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>5,175</strong></td>
<td><strong>5,175</strong></td>
<td></td>
</tr>
</tbody>
</table>
Research Projects in the H3Africa Kidney Disease Research Network

H3Africa Initiative

H3Africa Kidney Disease Research Network

- Monogenic Disease Childhood Onset NS (N=50 families)
- GWAS (N=2000)
- Renal Candidate Genes (MYH9, APOL1, etc) Studies (N=8000)
- Ancillary Studies
# Study Subgroups

<table>
<thead>
<tr>
<th>Diagnosis-specific eligibility</th>
<th>Age</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid resistant nephrotic syndrome&lt;sup&gt;1&lt;/sup&gt;</td>
<td>&lt;18</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>FSGS/MCD &amp; MN</td>
<td>18-70</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>HIV nephropathy</td>
<td>18-70</td>
<td>500</td>
<td>500&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Sickle cell nephropathy</td>
<td>18-70</td>
<td>500</td>
<td>500&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hypertensive non-diabetics with CKD</td>
<td>18-70</td>
<td>800</td>
<td>800</td>
</tr>
<tr>
<td>CKD due to diabetic nephropathy</td>
<td>18-70</td>
<td>800</td>
<td>800&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>CKD – Unknown etiology</td>
<td>18-70</td>
<td>1,000</td>
<td>1,000</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>4,000</td>
<td>4,000</td>
</tr>
</tbody>
</table>

<sup>1</sup>Includes 50 families with index cases and affected family members
<sup>2</sup>Patients with HIV and no nephropathy
<sup>3</sup>Patients with sickle cell disease and no nephropathy
<sup>4</sup>Patient with diabetes mellitus and no nephropathy
H3A Kidney Disease Study: Timeline for Research Studies

Phase I
Case-Control Genetic Studies 2013-2015

Phase II
Cohort Studies (“CRIC” & “NEPTUNE”) 2014-2019

Recruitment

Follow up

07 / 2012 Grant Award & Protocol Dev.

01/2013 - Accra, Ghana Centralized Staff Training & Investigators Meeting

05 / 2013 Commence Enrolment

04 / 2016 Complete Phase I Enrolment

04 / 2017 Complete Phase II Enrolment

End of Phase I 06 / 2019

Phase II: Not yet funded
Case Report Forms (CRFs)

11 Participant CRFs (640 phenotyping variables)
- 640 phenotype variables on 11 CRFs:
  - Medical History
  - Blood Pressure Form
  - Concomitant Medications
  - SF 12
  - Environmental History
  - Kansas City Questionnaire
  - Physical Assessment
  - Symptoms List
  - Medical Events Questionnaire
  - Renal Replacement Therapy – Primary Survey
  - Renal Replacement Therapy – Follow-up Survey

11 Administrative CRFs
PHYSICAL ASSESSMENT

Participant ID: 

(Example: Site 04 Participant 0001 Enter: 040001)

CRF Date: 

(dd-mm-yy)

CRF Version V1.0.20130805

RC ID: 

______________________________________________________________________

ANTHROPOMETRY:

1. Date of measurement: 

(dd-mm-yyyy)

2. Time of measurement: 

(hh:mm)

A. Height and Weight: Height and weight are measured at follow-up clinic visits only. (Baseline height and weight are measured at screening visit and recorded on the Eligibility Assessment (ELIG) case report form.)

3. Standing height: (measured in cm) 

(cm)

4. Weight: (measured in kg) 

(kg)
BIOSPECIMEN COLLECTION Adult - 57 ML

Participant ID: (Example: Site 04 Participant 0001 Enter: 040001)

CRF Date: (dd-mm-yyyy)

CRF Version V1.0.20130805

RC ID:

1. Type of specimen(s):
   - Blood
   - Urine
   - Both
   - Unable to collect blood or urine

2. Date of birth: (dd-mm-yyyy)

2a. Gender:
   - Male
   - Female

3. Does the participant have a diagnosis of diabetes mellitus?
   - Yes
   - No

3b. Is the participant on dialysis?
   - Yes
   - No

Blood Specimens:

4. Collection Date: (dd-mm-yyyy)
REDCap: Data & Computing Environment Security

- Web-based clinical research data management system
- Developed at the Vanderbilt University & used by nearly all CTSA
- Interactive tools for:
  - Participant registration
  - Data entry and verification
  - Repository of all study forms
  - Individual participant calendars
  - Cumulative site calendars for expected study activities
  - Calculator of creatinine-based e-GFR
  - Access to the National Drug Data File (NDDF) in the Medication Reference
  - Link to the Network website
  - Generate individual participant and investigator-specific reports
  - Seamless data downloads to common statistical packages (SPSS, SAS, Stata, R)
University of Michigan
Michigan Institute for Clinical & Health Research

H3Africa

Data Entry

You may view an existing record's response by selecting it from the drop-down list. To create a new record's response, type a new value in the text box below and hit Tab or Enter. To quickly find a record without using the drop-downs, the text box will auto-populate with existing record names as you begin to type in it, allowing you to select it.

Total records: 0

Choose an existing Participant ID: -- select record --

Enter a new or existing Participant ID:

Data Search

Choose a field to search (excludes multiple choice fields) -- select search field --

Search query

Begin typing to search the project data, then click on an item in the list to navigate to that record.

⚠️ NOTICE:
This project is currently in Development status. Real data should NOT be entered until the project has been moved to Production status.
Phenotyping and Specimen acquisition resources

- Digital Blood Pressure Monitor – Omron HEM 907XL IntelliSense
- Blood Pressure Monitor Mounting Stand - Omron Floor stand Kit for 907XL
- Digital Floor Scale - SECA 813
- Centrifuge – BD Clay Adams Compact II Centrifuge
- Freezerworks Label Printer - Zebra GX420t
- Freezerworks Hand held barcode label scanner - Symbol 6707
- Portable EKG machine - GE Medical Systems MAC 1200
- Anthropometric Tape Measures - Gulick II Plus G7019
- Bioelectrode Body Composition Analyzer – RJL Systems Quantum II BIA Analyzer System
- Laptop - HP EliteBook 8470p Notebook PC
- Desktop Scanner - HP Scanjet N6350 networked
- Ultrasound Probe – Summit L250 Display Hand Held Doppler (Probe: SD8 8 MHz Vascular)
- Standiometer - SECA 216
### Biospecimen Collection Scheme – H3A Kidney Disease Study (Total phlebotomy = 57cc/adult)

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Tube</th>
<th>Overnight ship (cold pack) from CC to MDS Lancet Laboratory</th>
<th>Store in Freeze -80 at MDS Lancet Laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>10ml SST (Yellow Top)</td>
<td></td>
<td>(A1, A2, A3) Light sensitive aliquots (A4, A5, A6) Serum aliquots Stored for future testing</td>
</tr>
<tr>
<td>B</td>
<td>5ml SST Yellow top</td>
<td>(B1) Serum aliquot-- Serum creatinine. Serum aliquots stored for Hepatitis B &amp; C, HIV antibody</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>5ml SST Yellow top</td>
<td></td>
<td>(C1, C2, C3) Serum aliquot Stored for future testing</td>
</tr>
<tr>
<td>D</td>
<td>5ml SST Yellow top</td>
<td></td>
<td>(D1) Serum Creatinine</td>
</tr>
<tr>
<td>E</td>
<td>3ml Purple (EDTA)</td>
<td>(E1) FBC</td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>6.5ml orange top (DNAgard)</td>
<td>(F1) DNAgard</td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>10ml purple top (EDTA)</td>
<td>(G1, G2, G3, +1 Buffy Coat) DNA Plasma aliquots Stored for future testing</td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>10ml purple top (EDTA)</td>
<td>(H1, H2, H3, +1 Buffy Coat) Plasma aliquots Stored for future testing</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>4.5ml Blue top (NaCitrate)</td>
<td></td>
<td>(I1, I2, I3) Plasma aliquots Stored for future testing</td>
</tr>
<tr>
<td>S</td>
<td>DNA Mouthwash 50ml</td>
<td><strong>Per Dr. Burke’s Saliva Protocol</strong></td>
<td>S1, S2, S3</td>
</tr>
<tr>
<td>U</td>
<td>Random Spot urine 50ml</td>
<td>(U1) Urine aliquot creatinine, albumin</td>
<td>(U2, U3, U4) Urine aliquot Stored for future testing</td>
</tr>
</tbody>
</table>
H3Africa Kidney Disease Research Network (U54): IRB approval

1. 6 out of 9 centers have IRB approval
2. As of 26/09/2013, 3 out of 9 centers are recruiting
3. By end of October 2013, 7 out of 9 centers recruiting
CURRENT RECRUITMENT

• 138 subjects
TARGET RECRUITMENT

• 228 subjects per month
Pilot Study Recruitment UGMS 05- end 07/2013

- 50 subjects recruited
- Logistics of subject recruitment
- Informed consent document
- Research clinics
- Completeness of CRF
- Logistics of sample transport
- Logistics of result return to subjects
Pilot Study Recruitment UGMS 05- end 07/2013

- Completeness of DNA and other biosample storage
- Quality of DNA
DNA isolation of Mouth rinse and Blood Samples from Korle bu
DNA purity and Concentration

- DNA purity and concentration is done using:
  1. Nanodrop 2000 UV spectrophotometer (Thermo scientific)
     DNA purity Absorbance ratio – A260/280 of 1.7-2.0
  2. Agarose Gel electrophoresis at 1% run in SB buffer at 100V for 40 minutes
  3. Quality Control assays carried out to compare sex of the study participant/donor with recorded information in database
Comments on Gel 1
- For Gel 1 the comb did not work.

Comments on Gel 2
- I used a bigger comb size and increased the sample and LB amount.

30/09/2013 09:41 AM
24-08-2013

amalgemun X7 PCR Master

10X Amalgemun Buffer

60mM MgCl₂

2.5mM dNTPs

2.5% 7K-150

20mM Amalgemun X7 Fak

H₂O

Gel 2  22-08-2113

30/09/2013 09:39 AM

0.2 x 45

0.12 x 45
Pilot Study Recruitment

- Conclusions of pilot study disseminated to other centers
Pilot Study Recruitment

- For all the other centers review after 20 patients recruited
- Special focus on transport of specimens to Ghana
THANK YOU