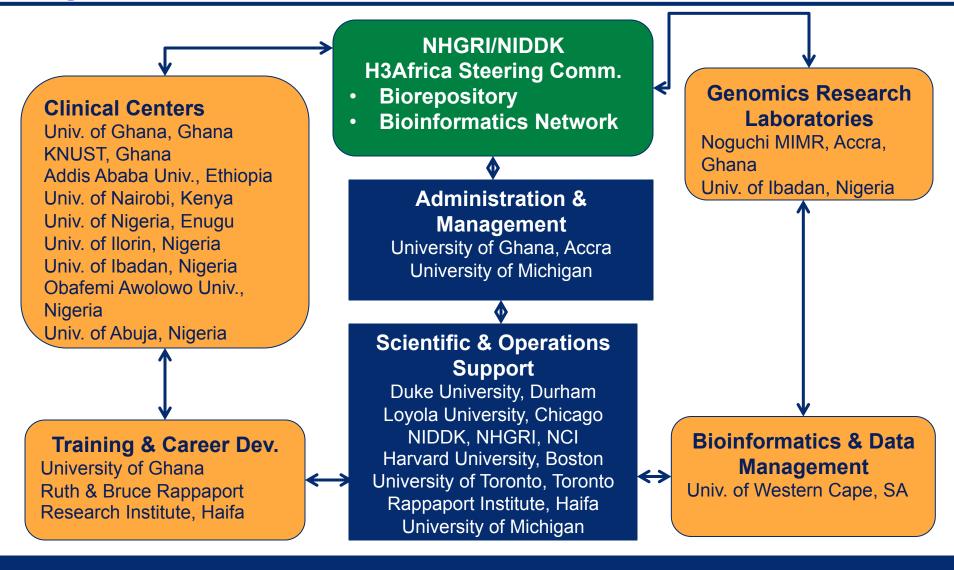
H3Africa Kidney Disease Research Network

A U54 H3A Collaborative Clinical Center Award

The University of Ghana & The Noguchi Memorial Institute for Medical Research, Accra, Ghana

H3A Kidney Disease Research Network: Organizational structure



H3A Kidney Disease Research Network: Research objectives

- 1. Enroll 4000 cases with kidney disease and 4000 controls
- 2. Comprehensive phenotyping of the first ever kidney disease cohort of 8000 cases and controls in four African countries (Ethiopia, Ghana, Kenya, Nigeria)
- 3. Conduct four genetic and translational research projects on chronic kidney disease and glomerular diseases including childhood onset nephrotic syndrome

H3Africa Kidney Disease Research Network: Infrastructure/Capacity Building

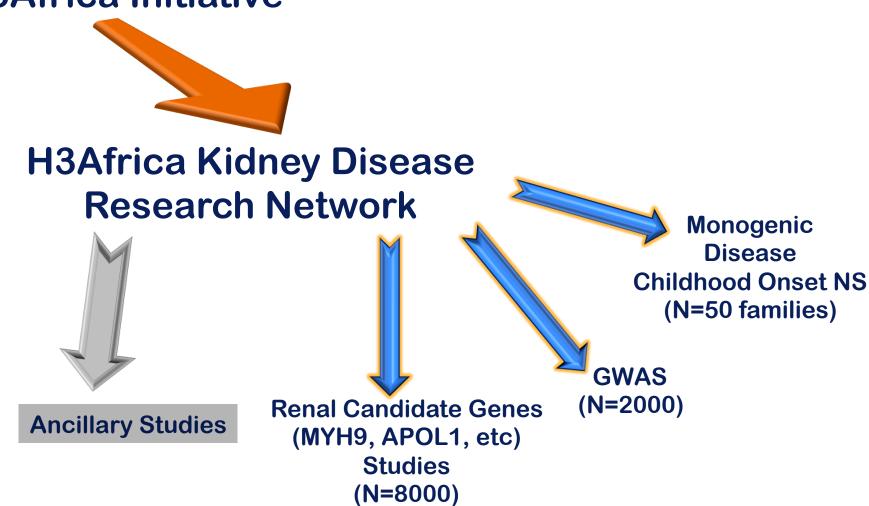
- 1. Two genomic research laboratories in West Africa using sustainable, low capital-intensity laboratory technology platform (Dr. David Burke)
- 2. Develop mechanism for high throughput whole genomic sequencing in collaboration with overseas institutions (Dr. Rob Lyons, Dr. David Burke and Dr. Michael Boehnke)

H3A Kidney Disease Research Network: Training & Career development goals

- Training programs in genetics and genomics science for laboratory technicians, research scientists and research coordinators in Africa (Dr. David Burke/Dr. Bamidele Tayo)
- 2. 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. System biology training through U.S. platform extension to Africa (Dr. Matthias Kretzler)

H3A Kidney Disease Research Network: Research projects

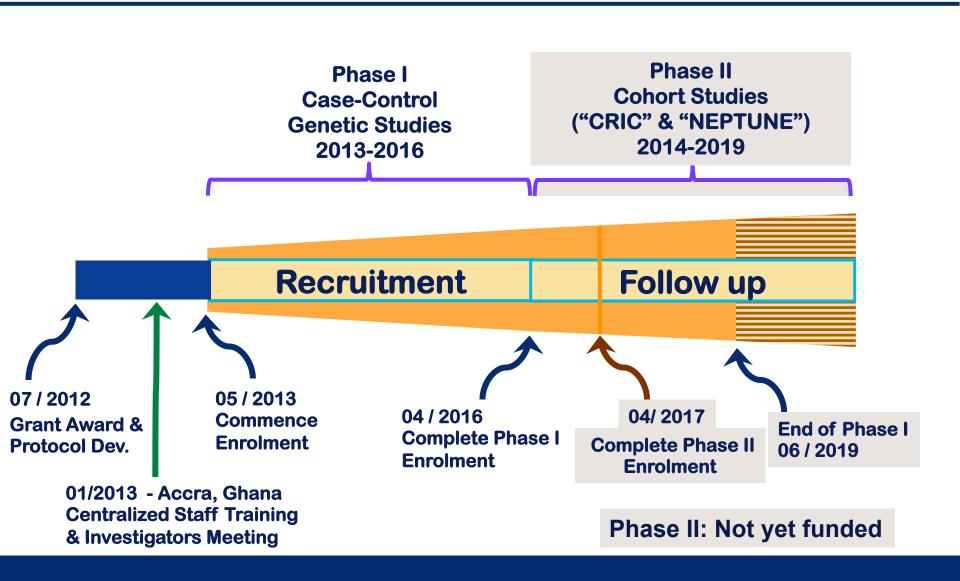
H3Africa Initiative



H3A Kidney Disease Study: Recruitment goals

Recruitment Goals by Clinical Center				
	Number of Participants			
Clinical Center	Kidney	Controls		
	Disease			
Addis Ababa University	750	750		
Kwame Nkrumah University of Science and	500	500		
Technology				
Obafemi Awolowo University, Ile-Ife	500	500		
University of Abuja	250	250		
University of Ghana	750	750		
University of Ibadan	925	925		
University of Ilorin	250	250		
University of Nairobi	750	750		
University of Nigeria, Enugu	500	500		
Total	5,175	5,175		

H3A Kidney Disease Study: Timeline



Case Report Forms (CRFs)

11 Participant CRFs (640 phenotyping variables, 3288 levels)

- 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

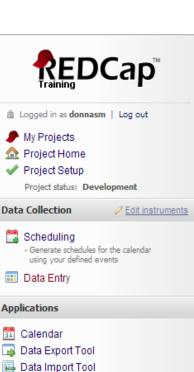
(kg)

4. Weight: (measured in kg)

Confidential H3Africa Page 1 of 5 **BIOSPECIMEN COLLECTION Adult - 57 ML** Participant ID: (Example: Site 04 Participant 0001 Enter: 040001) CRF Date: (dd-mm-yy) CRF Version V1.0.20130805 RC ID: 1. Type of specimen(s): Blood Urine Both ☐ Unable to collect blood or urine Date of birth: (dd-mm-yy) 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-yy)

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)



Data Comparison Tool

Graphical Data View & Stats

File Repository

User Rights

(i) Help & Information

Logging

Data Quality
Report Builder

■ Help & FAQ

Video Tutorials

Suggest a New Feature

If you are experiencing problems, please contact your REDCap administrator.

University of Michigan

Michigan Institute for Clinical & Health Research

H3Africa

■ Data Entry

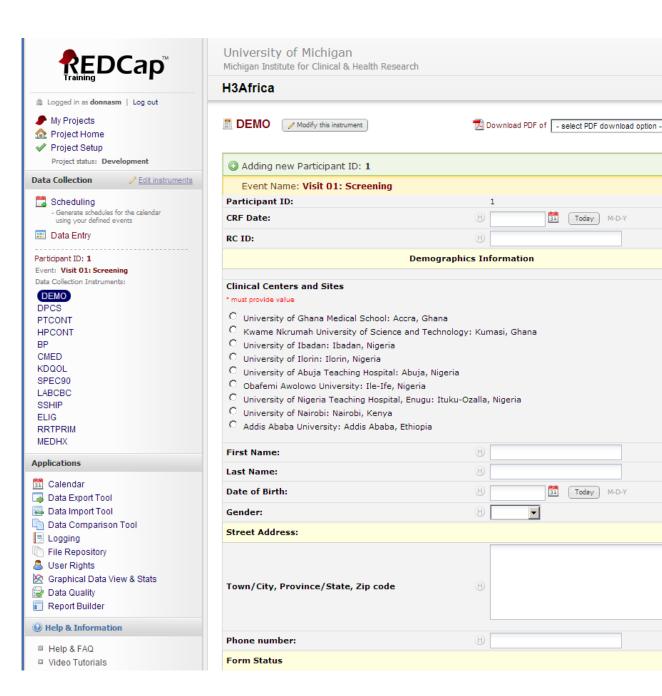
You may view an existing record/response by selecting it from the drop-down lists below. To create a new record/response, type a new value in the text box below and hit Tab or Enter. To quickly find a record without using the drop-downs, the text box will auto-populate with existing record names as you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

(I) NOTICE:

This project is currently in Development status. Real data should NOT be entered until the project has been moved to Production status.



reset value

Expand

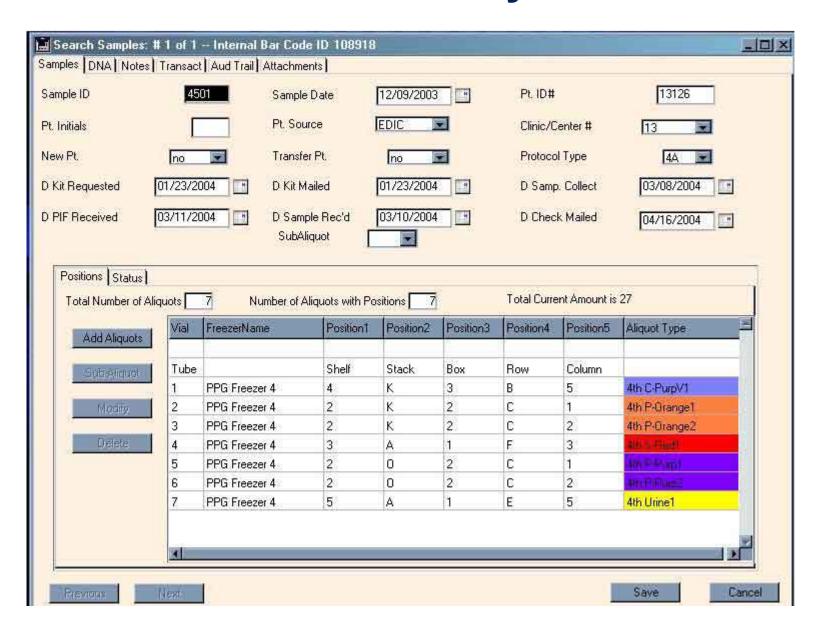
Phenotyping and specimen acquisition resources

- 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

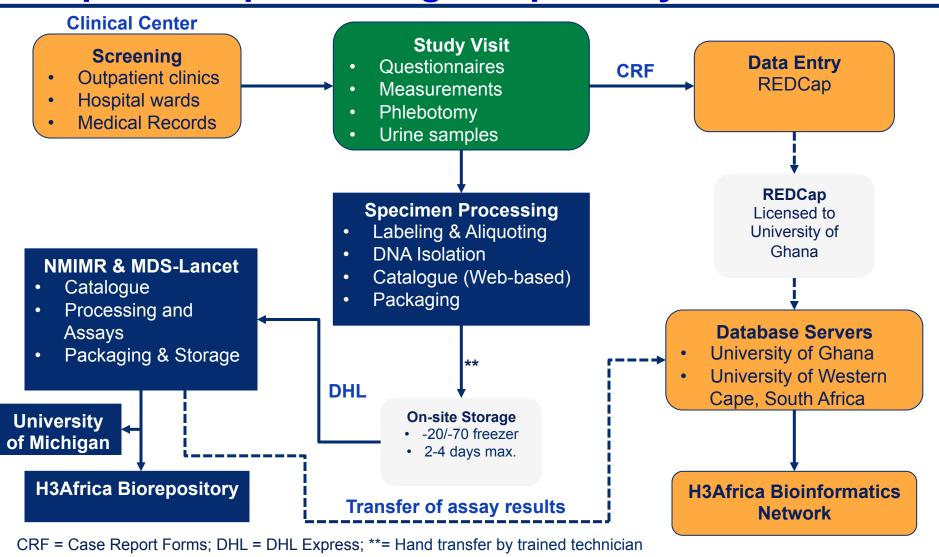
H3A Kidney Disease Study: Biospecimen collection scheme (total blood volume = 57cc/adult)

Specimen	Tube	Overnight ship (cold pack) from CC to MDS Lancet Laboratory	Store in Freeze -80 at MDS Lancet Laboratory
A	10ml SST (Yellow Top)		(A1, A2, A3) Light sensitive aliquots (A4, A5, A6) Serum aliquots Stored for future testing
В	5ml SST Yellow top	(B1) Serum aliquot Serum creatinine. Serum aliquots stored for Hepatitis B & C, HIV antibody	Ctored for fatare testing
С	5ml SST Yellow top		(C1, C2, C3) Serum aliquot Stored for future testing
D	5ml SST Yellow top		(D1) Serum Creatinine
E	3ml Purple (EDTA)	(E1) FBC	
F	6.5ML DNAgard	(F1) DNAgard	
G	10ml purple top (EDTA)	(G1, G2, G3, +1 Buffy Coat) DNA Plasma aliquots Stored for future testing	
Н	10ml purple top (EDTA)	(H1, H2, H3, +1 Buffy Coat) Plasma aliquots. Stored for future testing	
I	4.5ml Blue top (NaCitrate)		(I1, I2, I3) Plasma aliquots Stored for future testing
S	DNA Mouthwash 50ml	**Per Dr. Burke's Saliva Protocol**	S1, S2, S3
U	Random Spot urine 50ml	(U1) Urine aliquot creatinine, albumin	(U2, U3, U4) Urine aliquot stored for future testing

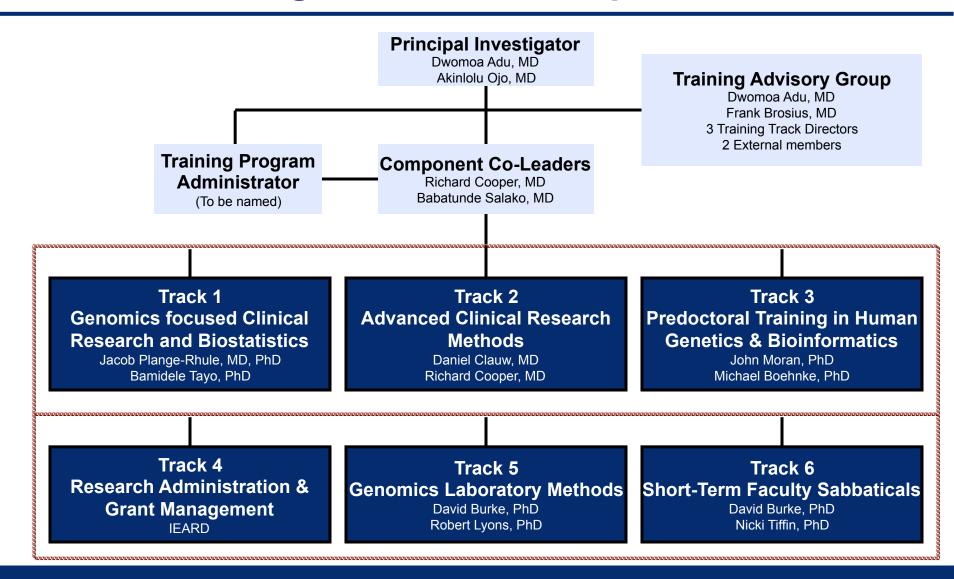
Freezerworks data entry interface



H3A Kidney Disease Research Network: Data & biospecimen processing and pathways



Training & Career Development



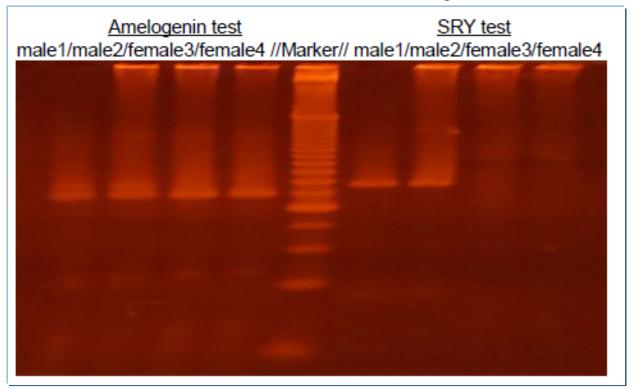
H3Africa Kidney Disease Research Network: Infrastructure/Capacity Building

- 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)

Genomics Research Laboratory at the Noguchi Memorial Institute for Medical Research (NMIMR)

- Assessment of laboratory infrastructure at the NMIMR (Dr. Burke, Dr. Nyarko, Dr. Anita Ghansah, Mr Richard Oppong and Ms. Javada Appenteng)
- Protocols for sample acquisition, shipping, labeling, and processing
- Development of DNA preparation and genetic typing procedures matched to NMIMR infrastructure
- Development of genotyping reagents to provide initial assessments of clinical DNA samples

Genomics Research Laboratory at the NMIMR



Agarose gel SNP genotyping to monitor DNA preparation quality and to assess H3Africa samples for sex. The LDR tests sex-specific genomic sequences in each sample, and size separated on a agarose gel, stained for DNA. Human male (2) and female (2) test samples are shown. The left 4 lanes show the amelogenin test. The **AmelogeninX** PCR band is specific for the X chromosomal variant, and appears, as expected, in both male and female samples. The **AmelogeninY** band is specific for the amelogenin gene Y chromosomal variant. The male samples have both peaks appear, female only one. The right 4 lanes show the SRY sequence test. The male samples have one band appear, females show no PCR product, as expecte

Additional Notes

- Submission of IRB application (7 centers)
- IRB approval (3 centers)
- Recruitment (1 center)

Acknowledgement

- H3A Kidney Disease Research Network Staff & Investigators
- Jeffrey Struewing (NHGRI)
- Jane Peterson (NHGRI)
- Ebony Bookman (NHGRI)
- Chengetai Mahomva (NHGRI)
- Paul Kimmel (NIDDK)
- Marva Moxey-Mims (NIDDK)
- Rebekah Rasooly (NIDDK)
- Mark Guyer (NHGRI)

Observational Study Monitoring Board (OSMB) Members

- David Warnock, MD (Chair), Susan Furth, MD, PhD,
- Jennifer Gassman, PhD,
- Ali Gharavi, MD,
- Maureen Kelley, PhD,

THANK YOU

EXTRA SLIDES FOR DISCUSSIONS

Specific aim 1 (N=50 families)

- Perform mutation analysis in key nephrotic syndrome/FSGS genes (NPHS1, NPHS2, WT1, PLCE1, ACTN4, TRPC6 & INF2) in a cohort of patients with familial NS/FSGS
- Perform genome wide linkage study (GWLS) and whole exome sequencing in a cohort of families in whom mutations in key NS/FSGS have been excluded

Specific aim 2 (N=3000 cases & 3,000 controls)

- Screen for known disease susceptible variants in APOL1 and MYH9 in a cohort of patients with
 - HIV associated nephropathy
 - Sickle cell disease nephropathy and controls without nephropathy and normal controls
 - HIV Nephropathy vs. HIV without nephropathy vs. controls
 - Sickle cell disease nephropathy vs. Sickle
 cell disease without nephropathy vs. controls

H3A Kidney Disease Study Progress & Updates I

- Consent documents finalized and approved by NIH
- 7 out of 9 clinical centers submitted IRB application
- 3 out of 9 clinical centers have received IRB approval
- Revised protocol to be completed in Feb 2013

Specific aims 1-3

Enrollment and high level phenotypic characterization of 4,000 cases and 4,000 controls to enable genetics studies in four cohorts of patients with kidney disease:

- 1. Childhood/Adolescent-onset nephrotic syndrome
- 2. Sickle cell disease and sickle cell trait
- 3. HIV nephropathy
- 4. Chronic kidney disease of due to hypertension, diabetes mellitus and chronic glomerulonephritis

REDCap: Data & Computing Environment Security

- Duplicate servers at University of Ghana & SANBI, Cape Town, SA
- Application and database servers a on virtual machines (VM).
- The VM servers: Red Hat Enterprise Linux Server 5.5 (64-bit, 2.6.18.194.e15-smp kernel), 2 x Dual Core Intel Xeon CPU 3.06GHz with 4GB RAM, running Apache 2.2.3 (application servers) and MySQL 5.0.77 (database servers)
- Physical security for the databases:
 - Professionally managed and equipped tier-2 data center with tightly controlled access.
 - Remote data access employs SSL encryption and 2-tier Level 1 and Level 2 password challenges via LDAP authentication
 - Compliance with HIPAA security and privacy requirements
 - Compliance with the HITECH Act
 - Audit trails on user access to and modification of data
 - Clinical centers BMCE required to meet best practices established in the Federal Information Security Management Act (FISMA)

ENVIRONMENTAL HISTORY

Participant ID:	(Example: Site 04 Participant 0001 Enter: 040001)		
CRF Date:	(dd-mm-yy)		
CRF Version V1.0.20130805			
RC ID:			
During the past two weeks did you work at any ti [INCLUDE UNPAID WORK IN THE FAMILY FARM OF	ime at a job or business, not counting work around the house? R BUSINESS]		
Yes No			
2. Even though you did not work during those two wee	ks, did you have a job or business?		
Yes No			
3. For whom do/did you work last in a full time job or b	usiness lasting two weeks or more?		
☐ Never employed ? ☐ Self-employed [GO TO 5] ☐ Refused			
If worked, please enter name of employer			
4. What kind of industry is/was this?			
manufacturing chemical mining public service, including teaching commercial and retail agricultural and farming self employed professional (doctor, lawyer, account	tant etc)		

H3Africa Kidney Disease Research Network (U54): Training & Career Development Goals

- Genome 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)
- 2. System biology training and U.S. platform extension to Africa (Dr. Matthias Kretzler)

H3Africa Kidney Disease Research Network

Research Projects

Training & Career Development

Research Infrastructure

Project I Single gene mutations I Track 1 Genomics-Focused Clinical Research

Genomics Research Labs

Project II APOL1/MYH9 Track 2
Advanced Clinical Research

Bioinformatics/Data Management

Project III
GWAS of disease loci

Track 3 PhD and MSc

Biorepository

Project IV NEPTUNE-AFRICA Track 4
Laboratory Technicians

Central Biochemical Lab

Track 5
Grant Management

Track 6 Short-term Faculty Sabbaticals

The H3Africa Kidney Disease Study (U54 HG 006939-01)

Dwomoa Adu, MD, FRCP
Principal Investigator (Contact)
University of Ghana, Accra

Akinlolu Ojo, MD, PhD, MBA

Principal Investigator

University of Michigan, Ann Arbor, MI

Specific aim 3 (N=1,000 cases and 1,000 controls)

 Perform GWAS in a cohort of subjects with CKD of varying etiology including hypertension, diabetes mellitus, chronic glomerulonephritis

(Clinical Centers: Nine Centers in Four Countries

Country	Institution	Location
Ethiopia	Addis Ababa University	Addis Ababa
Ghana	University of Ghana	Accra
	Kwame Nkrumah University of Science and Technology	Kumasi
Kenya	University of Nairobi	Nairobi
Nigeria	University of Abuja	Abuja
	Obafemi Awolowo University	lle lfe
	University of Ibadan	Ibadan
	University of Ilorin	llorin
	University of Nigeria	Enugu

Participating Clinical Centers



Study Subgroups

Sample Sizes of the Participants and Controls						
Diagnosis-specific eligibility Age Cases Controls						
Steroid resistant nephrotic syndrome ¹	<18	200	200			
FSGS/MCD & MN	18-70	200	200			
HIV nephropathy	18-70	500	500 ²			
Sickle cell nephropathy	18-70	500	500 ³			
Hypertensive non-diabetics with CKD	18-70	800	800			
CKD due to diabetic nephropathy	18-70	800	8004			
CKD – Unknown etiology	18-70	1,000	1,000			
Total		4,000	4,000			

¹Includes 50 families with index cases and affected family members

²Patients with HIV and no nephropathy

³Patients with sickle cell disease and no nephropathy

⁴Patient with diabetes mellitus and no nephropathy

H3A Kidney Disease Study Research Methods

Framework for the Infrastructure Enhancement for Genomics Research in the H3Africa Kidney Disease Research Network					
Project Period	Year 1	Year 2	Year 3	Year 4	Year 5
Genomics Laboratory Methods					
Single gene mutation analysis & Genome Wide Linkage Studies					
Whole exome sequencing					
SNPs genotyping					
GWAS					—
Site of genomics laboratory studies	Israel/U.S.	Israel/U.S.	Afr	rica, Israel &	U.S.
Site of genomics data analysis	Africa				

H3A Kidney Disease Study Investigators

Country	Institution	Key Personnel	Title	Role
Ethiopia	Addis Ababa University	Y. Menghistu	Consultant Nephrologist/Assistant Professor	Center PI
Ghana	University of Ghana	Dwomoa Adu Charlotte Osafo Alexander Nyarko Michael Mate-Kole Ivy Ekem Vincent Boima Kwame Affram	Consultant Nephrologist Lecturer in Nephrology Director, NMIMR & Professor Consultant Nephrologist/Professor Snr. Lecturer/Consultant Hematologist Physician Specialist/Nephrologist Consultant Nephrologist/Professor	PI
	Kwame Nkrumah University of Science & Technology	Jacob Plange-Rhule Benjamin Eghan Yaw Adu-Boakye Elliot Tannor	Associate Professor Senior Research Fellow Specialist Physician/Int Med. Medical Practitioner	Center PI
Kenya	University of Nairobi	S.O. Mc'Ligeyo James Ochanda Joel W. Ocheng	Consultant Nephrologist/Associate Professor Associate Professor in Biochemistry & Director, Center for Biotechnology & Bioinformatics Research Fellow & Lecturer	Center PI
		Isabella Oyier	Investigator	

H3A Kidney Disease Study Investigators

Country	Institution	Key Personnel	Title	Role
Nigeria	University of Ibadan	Tunde Salako Olukemi Amodu Adebowale Ademola Akinkemi Fedipe	Professor/Consultant Physician Snr. Research Fellow Lecturer/Consultant Physician HOD, Family Medicine	Center PI
	University of Ilorin	Chijioke Adindu Timothy Olarenwaju C. O. Bewaji	Snr. Lecturer/Consultant Physician Consultant Physician Professor, Bioinformatics	
	Obafemi Awolowo University	Fatiu Arogundade	Assoc. Prof/Consultant Physician	
	University of Abuja	Samuel Ajayi Manmak Manven	Consultant Physician/Nephrologist Consultant Physician/Nephrologist	
	University of Nigeria, Enugu	Ifeoma Ulasi Chuba Ijoma	Snr. Lecturer/Consultant Physician Snr. Lecturer/Consultant Physician	
South Africa	University of Western Cape (SANBI)	Nicki Tiffin Junaid Gamiedien	Snr. Lecturer, Bioinformatics Snr. Lecturer, Bioinformatics	

H3A Kidney Disease Study Investigators

Country	Institution	Key Personnel	Title	Role
Israel	Technion – Israel Institute of Technology, Rappaport Research Institute	Karl Skorecki Walter Wasser	Professor & Director Professor	
U.S.	Loyola University	Richard Cooper Bamidele Tayo	Professor/HOD Assistant Professor	Center PI Stat. genetics
	Duke University	Rasheed Gbadegesin		Molecular genetics
	University of Michigan	Akinlolu Ojo Matthias Kretzler Michael Boehnke John Moran David Burke Daniel Clauw Frank Brosius	Professor Professor Professor Professor Professor Professor Professor	Stat. genetics Genetics Genetics TAG TAG
	NHGRI	Adebowale Adeyemo	Deputy Director, CRGGH	
	NIDDK	Jeffrey Kopp		
	Harvard University	Martin Pollak	Professor	
Canada	University of Toronto	Rulan Parekh	Professor	

Success factors for H3A the Kidney Disease Study

- Ability to rapidly to establish kidney disease cohorts for:
 - Relevant major kidney disease phenotypes
 - High risk pediatric cohort
- Access to existing genomic science and bioinformatics infrastructure
- Leading experts in kidney disease on the African continent
- Catchment population of collaborating centers >350 million
- Supportive involvement of U.S. institutions with expertise in genomic science, statistical genetics & kidney disease
- Supportive involvement of African diaspora with relevant multidisciplinary expertise