

# H3ABioNet

## Pan African Bioinformatics Network for H3Africa

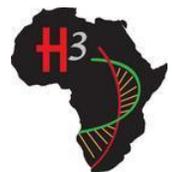
Progress relevant to consortium  
Nov 2014



**H3ABioNet**

Pan African Bioinformatics Network for H3Africa

Nicky Mulder: [Nicola.mulder@uct.ac.za](mailto:Nicola.mulder@uct.ac.za)



# Summary of initial goals

- Short/medium term:
  - Store H3Africa data & enable submission to EGA
  - Build human and computing infrastructure
  - Train in bioinformatics theory and techniques
  - Apply techniques to data, with skills transfer
- Long term:
  - Provide African repository of data (internal use)
  - Build network of bioinformaticians and data analysts
  - Train bioinformatics academics and support staff in H3ABioNet and H3Africa projects



# What's new?

- H3ABioNet and SAB consortium meeting
- Infrastructure progress
- H3Africa archive
- New training activities
- Research projects



# H3ABioNet GA and SAB meeting Morocco



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Pan African Bioinformatics Network for H3Africa



# Developing computing infrastructure

- Rollout of computing equipment to nodes, complete now, except Sudan
- Several nodes now have computing facilities
  - **Use H3ABioNet helpdesk to get info and access**
- Developed documentation for sys admins
  - **Useful for anyone investing in computing equipment**



# System Administrator Assistance

- Developed a workflow to determine the hardware required based on the nodes research
- Developed server installation documentation
- Developed preferred list of bioinformatics applications based on survey
- Developing server security and best practices documentation
- Future development of a server monitoring best practice documentation



# H3Africa Archive

- Submission of H3Africa data is a funder requirement
- Estimated overall storage capacity of 500TB
- Architecture modeled on EGA system, components:
- Landing area
  - datasets are encrypted by submitter
- Vault area
  - Focus on security, data only ever decrypted in Vault
  - All access and operations are logged
  - Analyses are limited to
    - QC validation
    - Checking EGA file format requirements
    - H3A metadata validation
  - Can assist with additional analyses, but only by agreement with PI
- Archive area
  - Purely for storage, no processing
  - encrypted files are mirrored to a separate physical location



# H3Africa archive submission process

## 1) Register project with the Archive

- **Submit:**
  - Submission timeline
  - Blank consent form, ethics clearance numbers
  - Estimated sample count
  - What phenotype data
    - Will be collected by the project
    - Will be submitted for H3A storage
    - Submitted to EGA
- Will be assigned EGA accession numbers for project and samples

## 2) Raw sample and phenotype data are submitted according to timeline

- Datasets are validated by H3ABioNet
- After grace period (9 months), submitted to EGA
- Access to data pre-EGA submission is only via project PI
- Access to data in EGA only via DBAC



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# Submission to EGA

- H3ABioNet will assist with submission of datasets to EGA
- Developing guidelines for the data submission requirements, formats and labelling of data and meta-data for submission to EGA to provide to the H3Africa projects
- Regular monthly meetings will be scheduled with EGA
- H3ABioNet staff to spend time at EBI in Feb



# Data transfer (1)

- Traditional transfer methods such as FTP are not optimal for large datasets
- Globus Online (GridFTP) and Aspera use different protocols, and are more reliable and secure
- E.g. 16GB dataset from EBI to UCT
  - FTP: 22 Mb/s
  - GridFTP: 220 Mb/s
- Recent transfer experiences
  - Genome and exome datasets from 3 different sites in the US
  - 24 full genomes between 2 H3ABioNet nodes (UCT, WITS)
  - Microbiome data from JCVI
  - RNASeq data from Qatar to UCT to Bulgaria
  - 1000 genomes subset (7TB)



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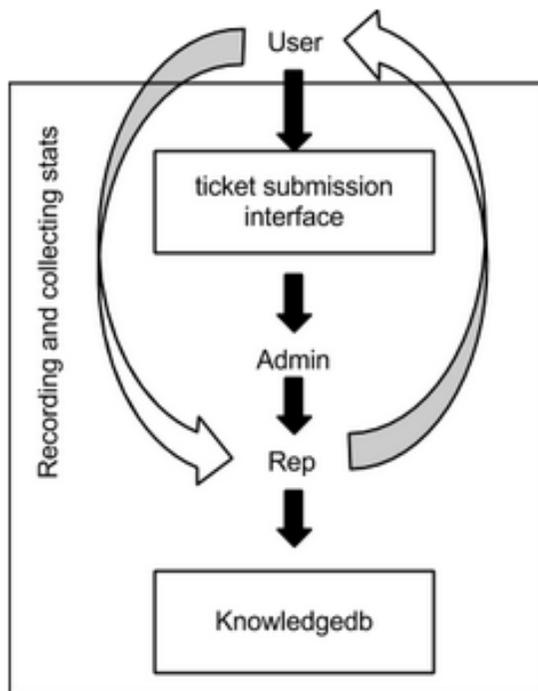
# Data transfer (2)

- Globus Online (GO) Deployment
  - Assisting nodes with deploying Globus Online -will be the default data transfer mechanism for transferring data to the archive
  - **Need contact and location of where data will be coming from**
- Netmap project -Document network topology / bandwidth between H3ABioNet node and non-African sites (JCVI, NCSA, EBI, NCBI)



# H3ABioNet help desk

- <http://www.h3abionet.org/support/help-desk>
- Managed by 15 volunteers with experience and expertise in Bioinformatics and Genomics.
- <http://www.h3abionet.org/support/helpdesk-reps>
- Easy to use web-based system



Network for H3/

### Helpdesk

New Ticket

Submit Print Close Refresh Home

<b>Contact Information</b>	<b>Classification</b>
User Name: <input type="text"/>	Category: Select Category
E-Mail: <input type="text"/>	Status:
Department: Select Department	Priority:
Location: <input type="text"/>	Assigned To:
Phone: <input type="text"/>	Time Spent: (minutes)

---

**TicketInformation**

Title:

Description

B I U

# Developing skills: Node assessment

- Protocols and practice data in place for GWAS,NGS & 16sRNA metagenomics



# Developing skills: Node

- Protocols and practice data in place & 16sRNA metagenomics

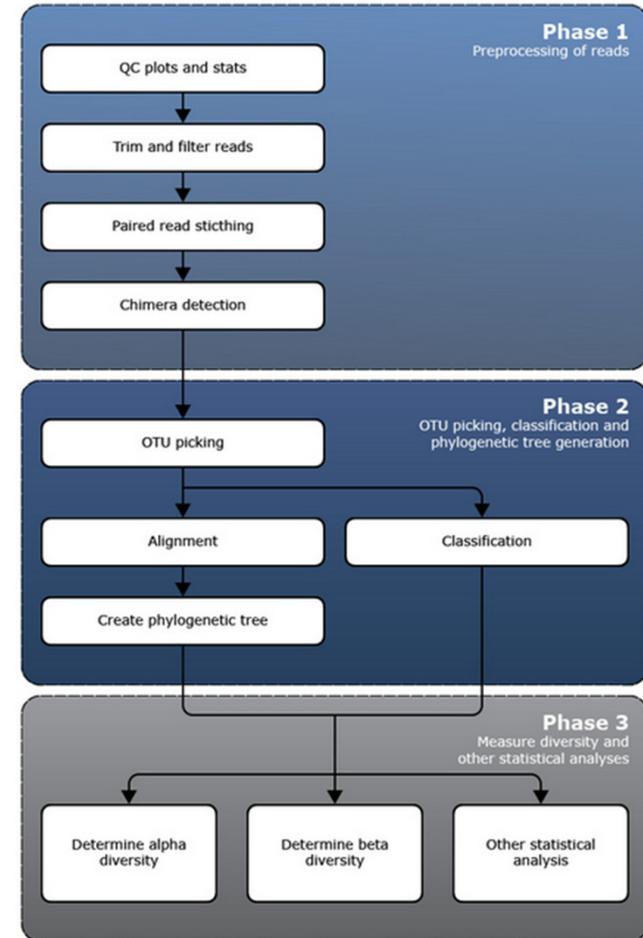
## Standard operating procedure for 16S rRNA diversity analysis

### Introduction

The genes encoding the RNA component of the small subunit of ribosomes, commonly known as the 16S rRNA in bacteria and archaea, are among the most conserved across all kingdoms of life. Nevertheless, they contain regions that are less evolutionarily constrained and whose sequences are indicative of their phylogeny. Amplification of these genomic regions by PCR from an environmental sample and subsequent sequencing of a sufficiently large number of individual amplicons enables the analysis of the diversity of clades in the sample and a rough estimate of their relative abundance. The analytical process is known as "16S rDNA diversity analysis", and is the focus of the present SOP.

The procedure and tools are only recommendations and it is up to the user to evaluate what works best for their needs.

### Schematic workflow of the analysis



#### Definition of terms used

Phase 1: Preprocessing of reads

Phase 2: OTU picking, classification and phylogenetic tree generation



**H3ABioNet**

Pan African Bioinformatics Network for H3Africa

# Developing skills: Node

- Protocols and practice data in place & 16sRNA metagenomics
- 1<sup>st</sup> node completed assessment
  - Wits node



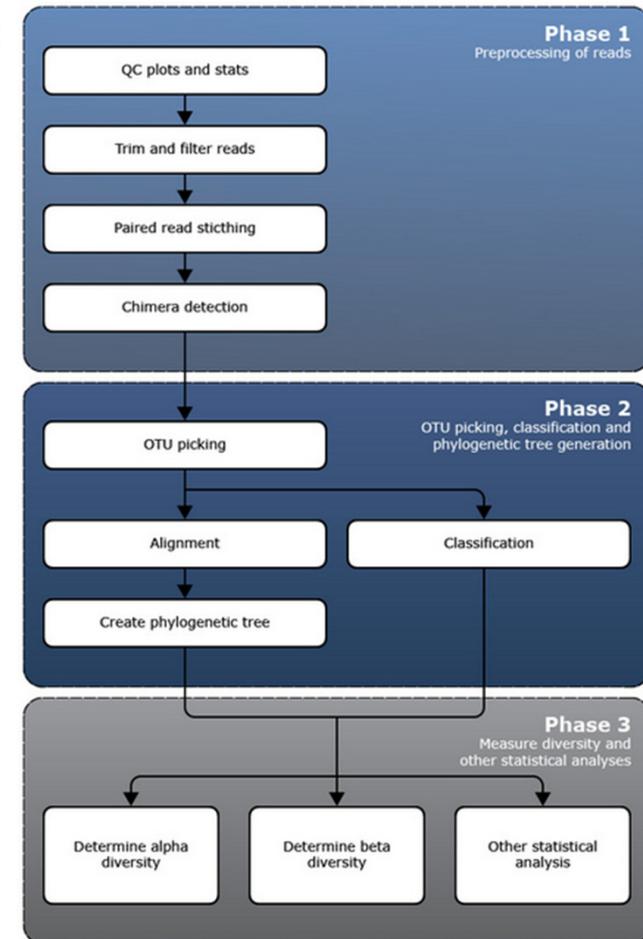
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# H3ABioNet training activities

- Hosted Data Management workshop
- Metagenomics workshop Abuja
- **Trained >230 people directly**
- Placed interns –**internships available\***
- NGS Train-the-trainer program with EBI
- Ongoing evaluation of online courses
- Wordpress sites available for all courses –many have recorded lectures
- Progress on African Bioinformatics Education Committee activities



# H3ABioNet training activities

- Hosted Data Management workshop
- Metagenomics workshop Abuja

Workshop Name	Period / location	Number of people trained
Grants management	May 2013 – South Africa	19
Technical (Sys admin) workshop	June 2013 – South Africa	18
Train the Trainer workshop	July 28 <sup>th</sup> – Kenya	21 (6 participants from H3Africa projects)
eBioKits workshop	August 2013 – Kenya	26 (some local student participants from ICIPE)
NABDA visual analytics workshop	August 2013 – Nigeria	~ 20 participants (10 H3ABioNet, 5 H3Africa)
Curriculum Development workshop	March 2014 – Botswana	25 (6 H3Africa participants)
Introductory Bioinformatics workshop	March 2014 – Ghana	36 participants
GWAS workshop (part funded in conjunction with AWI-GEN)	April 2014 – South Africa	28 participants from various funding streams (H3ABioNet had 5 participants)
Postgraduate workshop	April 2014 – Nigeria	26 (3 H3Africa participants)
Data management workshop	June 2014 - South Africa	33 participants (19 H3Africa)
Intermediate Bioinformatics workshop	July 2014 – Ghana	36 participants
Metagenomics data analysis workshop	July 2014 – Nigeria	21 participants



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# African Bioinformatics Education Committee

- Members within H3ABioNet, H3Africa and others
- Aim to provide:
  - Support for starting new degree programs
  - Relevant documents and processes
  - Curriculum and content development
  - Match making for regional groups
  - Identify lecturer availability/limits
  - Online materials
  - Train-the-trainer



# ABEC websites

## African Bioinformatics Education Committee

The [African Bioinformatics Education Committee \(ABEC\)](#) originated from an H3ABioNet Degree Development Workshop held in Gaborone, Botswana in March 2014 (See: <http://www.h3abionet.org/curriculum-development>). It was established to provide a support vehicle for groups planning to develop new Bioinformatics degree programs.

The role of the committee is to:

- Provide general support for setting up and monitoring bioinformatics degrees
- Provide materials such as teaching methods, course materials, administrative forms, etc.
- Organise a train-the-trainer program to develop a cadre of bioinformatics trainers
- Provide a mechanism for monitoring quality of courses and assessing relevance of projects
- Facilitate cross-talk between programs and institutions
- Identify current trends in bioinformatics education
- Link with GOBLET, ISCB and other education initiatives
- Create a directory of programs and trainers (possibly with assessment)
- Create a directory of possible supervisors and their areas of expertise
- Create a tracking mechanism to see how long it takes for a University to put together their curriculum submission proposal, have their degree programme accepted and factors which enable the successful acceptance of a degree programme by their institute

## Curriculum Development Task Force

The Degree Development Workshop proposed a set of core and elective modules that should be incorporated into a Masters program in bioinformatics by coursework and dissertation available [here](#). The curriculum development task force was established to develop the proposed content for each of the modules. This information is being collected [here](#). This task force will work with the ISCB Education Committee Curriculum Development task force.

For more information please contact: [info@h3abionet.org](mailto:info@h3abionet.org)

## Documents and Resources:

[ABEC Meeting Minutes](#)

[Curriculum Development Task Force Meeting Minutes](#)

[Key Steps for Starting a Degree Program](#)

[Are you starting a new bioinformatics degree programme?](#)

[Directory of online bioinformatics courses](#)

[Additional links](#)



# ABEC websites

## H3ABioNet Curriculum Development Taskforce

H3ABioNet taskforce to develop a curriculum of bioinformatics to be used throughout the continent

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HOME	<b>BIostatISTICS I</b>	DATABASES I	DATABASES II	ETHICS	EVOLUTION AND PHYLOGENETICS
GENOMICS AND COMPARATIVE GENOMICS		HIGH-THROUGHPUT SEQUENCING		INTRODUCTION TO LINUX	
INTRODUCTION TO PROGRAMMING FOR BIOLOGISTS		MACHINE LEARNING	METABOLOMICS	MOLLECULAR BIOLOGY	
POPULATION GENETICS AND GWAS	PROGRAMMING I	PROGRAMMING II	PROTEOMICS	SEQUENCING	
STRUCTURAL BIOINFORMATICS	WG MEETING MINUTES	WRITING & PRESENTATION SKILLS			

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## Biostatistics I

### Module Name: Biostatistics I

**Prepared by:** Jean-Baka Domelevo Entfellner

**Possible Lecturers:** Jean-Baka Domelevo Entfellner, or any bioinformatician with a strong background in mathematics and statistics, ideally from his/her primary education.

**Contact hours:** For consistency reasons, each contact hour is fixed at 45min.  
Theory (23), Practicals (30)

### SPECIFIC OUTCOMES ADDRESSED

1. Generally speaking: develop an understanding of stochastic experiments
2. Understand and be able to build the framework of a statistical test

### BACKGROUND KNOWLEDGE REQUIRED

Basic general-purpose scientific knowledge, basic arithmetic skills, and some familiarity with basic linear algebra.

### BOOKS & OTHER SOURCES USED

1. *Fundamentals of Biostatistics*, 7th edition, by Bernard Rosner (Cengage Learning, 2011)
2. *Biostatistics with R — An introduction to statistics through biological data*, by Babak Shahbaba (Springer, 2012)

### COURSE CONTENT

#### A) Theory lectures

##### I. Probability theory:

1. Atomic and complex events, probabilities as a measure on sets. Probabilistic experiments, concept of expectation.
2. Conditional probabilities, Bayes' law.
3. Enumerative combinatorics: counting permutations, combinations and partitions. Binomial coefficients.
4. Some common discrete probability distributions: Bernoulli, binomial, Poisson. Behaviour of a binomial when the number of trials tends to infinity. Concepts: probability mass, expectation of a discrete distribution.
5. First continuous probability distributions: uniform, exponential
6. Central limit theorem and the normal distributions
7. Other continuous distributions: Student's t and chi-square distributions.

##### II. Statistical hypothesis testing

##### III. Analysis of variance and regression models

##### IV. Multidimensional dataset analysis: Principal Component Analysis

#### B) Practical component

We suggest the use of Rstudio throughout the course, as an integrated development environment to work with R. Being the fundamental statistical software in use across various research areas, it is essential that the students develop mastery over R during this course.

Alternatively, if computing resources are extremely scarce, use an interactive R interpreter to demonstrate the concepts, plus a simple text editor later on, once the students start writing functions.

This section "practical component" follows the same structure as the previous section "Theory lectures": practicals just aim at having the students manipulate the concepts seen in the lectures, right after they were introduced to them.

### ASSESSMENT ACTIVITIES AND THEIR WEIGHTS

# Upcoming training

- Metagenomics course (Dec) - Mauritius
- **Technical workshop I and II (Jan/Feb) - Pretoria**
- **Introduction to Biostats course (March) -Tunisia**
- **GWAS course and mini symposium with AIMS (April) –Cape Town**



# Research and tool development – H3ABioNet

- Several projects within the network to build capacity and skills, as well as tools
- Genesis –working with GWAS output figures
- HUMA –browsing variants and structures



# HUMA

- HUman Mutation Analysis (HUMA) web server
- Database consisting of genes, proteins, diseases, and variants
  - Links disease to mutations in genes and proteins
  - Designed to accommodate new African SNP data
- Provides tools to analyse data -homology modelling pipeline
- Provides social network aspects to allow researchers to work together, sharing jobs and results and using discussion boards
- Provides access to tools and data via a RESTful Web API and intuitive website



# Search for a gene or disease

The screenshot shows the HUMA website interface. The browser address bar displays 'huma.ru.ac.za/#diseases/diabetes'. The website header includes 'HUMA' and navigation links for 'Search', 'Tools', 'Documentation', 'Cite Us', and 'About Us'. A search bar on the left contains the text 'diabetes'. The main content area is titled 'Search for a disease:' and shows a search input field with 'diabetes' and a 'Search' button. Below the search bar, a message states '74 diseases were found that match your search term...'. A table displays the search results, with columns for ID, Name, and Description. The table lists several entries related to diabetes, including MIM\_125700, MIM\_125800, MIM\_125850, MIM\_125851, MIM\_125852, MIM\_125853, MIM\_137920, and MIM\_158500.

ID	Name	Description
MIM_125700	DIABETES INSIPIDUS, NEUROHYPOPHYSEAL	A disease characterized by persistent thirst, polydipsia and polyuria. Affected individuals are apparently normal at birth, but characteristically develop symptoms of vasopressin deficiency during childhood. Note=The disease is caused by mutations affecting the gene represented in this entry.
MIM_125800	DIABETES INSIPIDUS, NEPHROGENIC, AUTOSOMAL	A disorder caused by the inability of the renal collecting ducts to absorb water in response to arginine vasopressin. Characterized by excessive water drinking (polydipsia), excessive urine excretion (polyuria), persistent hypotonic urine, and hypokalemia. Inheritance can be autosomal dominant or recessive. Note=The disease is caused by mutations affecting the gene represented in this entry.
MIM_125850	MATURITY-ONSET DIABETES OF THE YOUNG, TYPE 1	A form of diabetes that is characterized by an autosomal dominant mode of inheritance, onset in childhood or early adulthood (usually before 25 years of age), a primary defect in insulin secretion and frequent insulin-independence at the beginning of the disease. Note=The disease is caused by mutations affecting the gene represented in this entry.
MIM_125851	MATURITY-ONSET DIABETES OF THE YOUNG, TYPE 2	
MIM_125852	DIABETES MELLITUS, INSULIN-DEPENDENT, 2	
MIM_125853	DIABETES MELLITUS, NONINSULIN-DEPENDENT	A multifactorial disorder of glucose homeostasis caused by a lack of sensitivity to the body's own insulin. Affected individuals usually have an obese body habitus and manifestations of a metabolic syndrome characterized by diabetes, insulin resistance, hypertension and hypertriglyceridemia. The disease results in long-term complications that affect the eyes, kidneys, nerves, and blood vessels. Note=Disease susceptibility is associated with variations affecting the gene represented in this entry.
MIM_137920	RENAL CYSTS AND DIABETES SYNDROME	
MIM_158500	MUSCULAR ATROPHY, ATAXIA, RETINITIS	

# Disease results

huma.ru.ac.za/#diseases/MIM\_125851

**Disease Name:** MATURITY-ONSET DIABETES OF THE YOUNG, TYPE 2

**Description:**

**Source:** Office of Rare Diseases

**MIM ID:** 125851

**MedGen ID:**

**Genes** +

**Variants** -

No. of Known SNPs: 75

Show 10 entries Search:

Variant ID	Chromosome	Pos (hg19)	Pos (hg18)	Reference Allele	Alternative Allele	Reference Codon	Pos in Codon	CDS Strand	Protein (Position in Protein)	Reference Amino Acid	Alternative Amino Acid	Associated Diseases
7-44184747-C-A-ATG-3	7	44184747	44151272	C	A	ATG	3	-	C9JQD1(462) P35557-2(462) P35557-3(462) P35557(462)	M	I	MIM_125851
7-44184775-G-A-TCG-2	7	44184775	44151300	G	A	TCG	2	-	C9JQD1(453) P35557-2(453) P35557-3(453) P35557(453)	S	L	MIM_125851
7-44184788-C-T-GCG-1	7	44184788	44151313	C	T	GCG	1	-	C9JQD1(449) P35557-2(449) P35557-3(449) P35557(449)	A	T	MIM_125851
7-44184794-G-C-CGG-1	7	44184794	44151319	G	C	CGG	1	-	C9JQD1(447) P35557-2(447) P35557-3(447)	R	G	MIM_125851

huma.ru.ac.za/#proteins/P35557

H3ABIONet SAB Meeting, Casablanca 2014



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# Disease results

huma.ru.ac.za/#diseases/MIM\_125851

**Disease Name:** MATURITY-ONSET DIABETES OF THE YOUNG, TYPE 2

**Description:**

**Source:** Office of Rare Diseases

**MIM ID:** 125851

effective only when glucose is abundant. The role of GCK is to provide G6P for the synthesis of glycogen. Pancreatic glucokinase plays an important role in modulating insulin secretion. Hepatic glucokinase helps to facilitate the uptake and conversion of glucose by acting as an insulin-sensitive determinant of hepatic glucose usage.

**Sequences**

Canonical Sequence: P35557

**Uniprot Accession:** P35557

**Database:** SwissProt

**No. of Known SNPs:** 3094

**Sequence:**

```
MLDDRARMEAAKKEKVEQLAEFQEEEDLKKVMRQKQKEMDRLRLHEEASVKMLTYVRSPTPEGSE
VDFLSLDLGGTNFVMLVKVGEEGEQNSVKTKKQNSIPEDAMTGTAEMLFDYISECISDFLDKHQMK
HKKLPVFTSFSVHEDIDKILLNWKFKASGEEENNVGLLRDQIKRRGDFMDVVAIVNITVAT
ISCYIEDHCGVGMIGGCNICYEEMONVELVEGDEGRICMTDNGAGDSELDEFLEYDRLVES
SANPGQQLYEKLIIGGKYMVELVLRLLVDENLWHEASEQRTRGAFETRFVSQVEDTGDGRKQVYN
ILSTLGLRPSITDCDIVRRACESVTAHHSASAGVMMNRESRSEDVMTITVGDGGSVYLHPSFK
ERHASVRRTPSCEITFIESEEGSGGALVAVACKKACILGQ
```

Model

**SNPs occurring in this protein:**

Show 10 entries Search: MIM\_125851

Variant ID	Position	Reference Residue	Alternative Residue	Associated Diseases	Select
7-44193051-G-C-ATC-3	19	I	M	MIM_125851	<input checked="" type="checkbox"/>
7-44193034-A-C-CTG-2	25	L	R	MIM_125851	<input checked="" type="checkbox"/>
7-44193001-C-G-CGG-2	36	R	P	MIM_125851	<input checked="" type="checkbox"/>
7-44192977-C-T-GGC-2	44	G	D	MIM_125851	<input checked="" type="checkbox"/>
7-44192962-G-T-ACC-2	49	T	N	MIM_125851	<input checked="" type="checkbox"/>
7-44192933-G-A-CCC-1	59	P	S	MIM_125851	<input checked="" type="checkbox"/>
7-44192019-C-T-GGG-1	72	G	R	MIM_125851	<input checked="" type="checkbox"/>
7-44191980-T-A-AGG-1	85	R	W	MIM_125851	<input checked="" type="checkbox"/>
7-44191911-A-C-TAC-1	108	Y	D	MIM_125851	<input checked="" type="checkbox"/>

# H3Africa consortium projects

- Recruitment 'database'
- **Ontologies for metadata**
- Biobank data integration
- **Custom chip design**
- Trainer/trainee database
- Liaisons



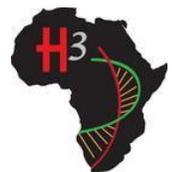
# Ontologies project

- 24 questions from the Phenotype Harmonization working group plus domain specific questions e.g. CVD
- Not always a standard way of reporting these –need ontologies
- Different parts of the EGA data submission will require different ontologies e.g
  - experimental factor ontology -NGS/array platform, clinical measurements
  - disease ontology for phenotypes for diseases
- Mapping 24 phenotypes to ontologies
- Curator appointed to assist with the mapping and curation of the ontologies to the phenotypes and CRFs
- Aim is to integrate these ontologies as metadata for the Data archive so the contents can easily be searched
- Funding to run pilot project on SCD ontologies



# H3Africa custom chip design

- Chip design working group through Genome Analysis WG, in collaboration with Wits, Sanger and many other experts
- Develop a set of markers with optimal coverage of H3Africa populations
- Platform agnostic as far down the pipeline as possible
- Improve negotiating power by working as a consortium
- Working meeting 20-21 Nov Cape Town



# Acknowledgements

Name	Institution	Country
Simani Gaseitsiwe	Botswana Harvard AIDS Institute Partnership	Botswana
Ahmed Mansour Alzohairy	Zagazig University	Egypt
James Brandful	NMIMR	Ghana
Ellis Owusu-Dabo	KNUST	Ghana
Daniel Masiga	ICIPE	Kenya
Dean Everett	Malawi-Liverpool Wellcome Trust Clinical research Programme	Malawi
Seydou Doumbia	University of Bamako	Mali
Yasmina Jaufeerally Fakim	SANBio	Mauritius
Hassan Ghazal	University Mohammed First	Morocco
Azedine Ibrahim	Faculte de Medecine et de Pharmacie de Rabat	Morocco
Ahmed Moussa	Abdelamlek Essaadi University, Tangier	Morocco
Fouzia Radouani	Pasteur Institute Casablanca	Morocco
Fouad Seghrouchni	Institut National d'Hygiène, Rabat	Morocco
Fatima Gaboun	National Institute of Agronomic Research, Rabat	Morocco
Khalid Sadki	Mohammed V University, Rabat	Morocco
Alami Raouf	Centre National de Transfusion Sanguine, Rabat	Morocco
Odile Ouwe Missi	CERMES	Niger
Ezekiel Adebisi	Covenant University Bioinformatics Research	Nigeria
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Judit Kumuthini	CPGR	South Africa
Nicki Tiffin	SANBI, University of the Western Cape	South Africa
Ozlem Tastan Bishop	Rhodes University	South Africa
Scott Hazelhurst	Wits University	South Africa
Fourie Joubert	University of Pretoria	South Africa
Hugh Patterton	University of the Free State	South Africa
Faisal Fadlelmola	Future University	Sudan
Sylvester Lyantagaye	University of Dar es Salaam (UDSM)	Tanzania
Nzovu Ulega	MDH	Tanzania
Julie Makani	MUHAS	Tanzania
Alia Benkahla	Institute Pasteur of Tunis	Tunisia
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Win Hide	Harvard School of Public Health	USA

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