

# Cape Town H3Africa Biorepository Akin Abayomi abayomi@sun.ac.za



Inaugural Meeting of the H3Africa Consortium.





Addis Ababa 8<sup>th</sup> Oct 2012

wellcometrust



National Human Genome Research Institute

## Global Human diversity all represented in Africa Tishkoff S 2009



























# H3A Cape Town BR Team

- PI: Akin Abayomi (NHLS, SU & Cape Haem)
- Co-investigators
  - Ravnit Grewal (NHLS SU)
  - Carmen Swanepoel (NHLS)
  - Alan Christofells (SANBI)
  - Tayo Fakunle (Scripps USA)
  - Fatima Bassa ( TBH SU)
  - Michael Sheldon (Rutgers USA)
  - Jeanne Loring (Scripps USA)



#### Tygerberg : 1,400 bed multi-disciplinary teaching hospital serving population of 5 million





**Project Title:** Development of H3 Africa Biorepositories to facilitate studies on Biodiversity, Disease & Pharmacogenomics of African Populations



Location: National Health Laboratory Services, Tygerberg Hospital, Stellenbosch University, Faculty of Medicine, Cape Town, South Africa.



RUCDR





# Strategic Vision for the CT H3A BR

- Preservation of high quality HBM
- Think futuristically
- Add value to HBM. Renewable cell line & DNA
- Biz and Science of sustainability
- Ethics of Biobanking HBM
- Cost effective BB such as RTS
- Integrate Clinical and Laboratory data (BIMS), [BioNet, BR and Research collaborations]

# Project summary: Phase 1

- Network & assess needs of the H3Africa consortium
- Set up Governance, Operations and SOPs
- Harmonise with sister BR in Abuja, Nigeria
- LIMS [interrogate Open Source vs Commercial]
- Evaluate room temperature storage [RTS]
- Evaluate automation platforms
- Pilot renewable cell lines by iPSC technology
- Conduct pilot studies and proof of principle H3A BR
- Initiate business model analysis

# Phase II

- Integrating accumulating data BIMS
- Advocacy towards appropriate legislation nationally and continentally
- Deeper engagement with stake holders
- Automate
- Scale up to 100,000 samples per year
- Implement business model of sustainability











UNIVERSITY of the WESTERN CAPE

## **Rutgers. Our Technical Partners**

















# National Health Lab Service

- Largest lab organization in Africa
- Services entire population of SA from 360 labs
- Staff Complement of 7000
- Responsible for national training of:
  - Pathologists
  - Scientists
  - Technologists

# Vision in conjunction with Abuja

- To develop full scale Africa biorepositories
- Comparable to any in Europe and America
- Harness deep intra continental collaborations
- Standardize and harmonize
- Engender confidence amongst our African colleagues and governments
- Facilitate BR tech transfer onto the continent

Strategies for Quality and preserving the appropriate and inexhaustible supply of samples cost effectively for Posterity

# Careful freezing of samples

#### **Controlled rate freezing**

- Used routinely for sensitive cells
- Very accurate cooling profile of temperature and time
- Uses liquid nitrogen and laminar airflow



Planer Products

Time in Minutes

#### **Storage Temperature**

"If you don't treat the sample properly, it can limit what you can do,"

#### 'freezing is not freezing',"

A typical freezer is not cold enough to stop degradative enzymes. Most samples can be stored at -80 °C, But certain specimens, such as live cells, need to be kept at temperatures close to -200 °C, at which point enzymes are thought not to be able to function at all Kristin Ardlie, Director of the Biological Samples Platform at the Broad Institute in Cambridge, Massachusetts.



"The published temperature for the glass transition point varies slightly from researcher to researcher but is generally regarded as being -132°C."

#### Room Temperature Storage technology (RTS)

- □ The technology prevents the degradation of biological materials at room temperature (extremophile biology)
- □ Eliminates the need for cold storage and cold shipping.
- Biomolecules, such as DNA, RNA and bacteria can be stabilized at ambient temperatures.



Figure 2 – Structural prediction of SampleMatrix interacting with nucleic acids

Figure 3 – Electron micrograph of protective thermostable barrier.

# RTS research @ Stanford

#### Key Findings and Conclusions:

- An estimated nine to thirteen million samples (representing 20-25% of the total Stanford sample could be moved from freezers to room temperature technology.
- The initial investment in transferring these samples could be recovered within three to five years under abroad implementation program.
- The program could generate an estimated eleven to twenty million dollars in cost reductions as well as prevent seventeen to twenty thousand tons of CO2 from entering the environment.
- In addition to direct benefits, transferred samples would be shielded from degradation due to power disruptions, and thousands of square feet of lab space could be liberated for better use.

#### Room temperature storage @ Stanford

Stanford University could cut usage of electricity by forty million kilowatt-hours (kWh) Reduce it carbon footprint by an estimated twenty thousand metric tons and save \$16 million dollars in operating costs over the next ten years by transferring biological samples from frozen storage to room temperature storage



#### Induced pluripotent stem cells (iPSC's)



iPSC technology has created access to cell line based disease modeling

# Existing infrastructure at Tygerberg

- Pathology Research Facility (Mol & sequencing)
- Cape Town Lymphoma Repository
- Stem Cell Repository
- Cell Culture Facility
- South African German HIV BR project
- Hundreds of thousands of Research Samples in storage in extensive HIV and TB research Projects.
  Fragmented and disorganized.

## H3Africa Cape Town BR



# Reception to the current Haematology tissue sample repository



## Freezers within Facility



# SU Projects with Repository Freezers in Corridors



## Flow cytometry research and training lab



- Research and Training
- 2x Flow cytometers BC
  - Navios -10 colour/3 lasers
  - FC 500-5 colour/2 lasers

#### Stem Cell Harvest Unit



## Stem Cell Graft Manipulation



#### Legislation, Ethics and Oversight

# Existing legislation in South Africa

- Health Act
  - Import export permits thru DOH
- IP Act
- HPCSA regulations on material transfer
- Evolving National MTA

# BR science in South Africa

- DST oversight
  - Human
  - Biodiversity
  - Plant
  - Micobiomes
- Stake Holders
  - DOH, DST, DOEnv,
- NHLS
  - Oversee Human banks
- Academic
  - 5 large tertiary and 2 quaternary institutes
  - Numerous international multi-collaborative projects

#### Proposed Oversight and Governance

- Internal Governance
  - Local stake holders in CT
  - Ethics review and advisory committee
- External Governance
  - To include stem cell oversight
- Community liaisons committee
  - Sense the feeling of the African cultures
- H3A Advisory committee

# Recent Biobanking events in CT

- ARESA seminars on ethics of BB
- Path congress featuring biobanking session
- Biobank vendor meeting
- Staff expansion
  - Addition of 2 senior research post PhD assistants this year




ADVANCING RESEARCH ETHICS TRAINING IN SOUTHERN AFRICA

### **Annual Research Ethics Seminar**

Southern Sun Hotel, Newlands • 30-31 August 2012

#### Day 1: Thursday 30 August 2012

- Ownership of biological samples a conceptual analysis
- The use, storage and export of biological samples ethical complexities
- Human tissue legislation in SA: an Update
- Genetic Research: The ethics of community engagement
- Ethical review and governance of genomic research

## Industry and support services in SA

## Biobank Vendors Workshop Division of hematology 2/10/2012



## Inqaba: NanoDrop



#### Storage systems



Chart MVE Variõ Series Dewar

- Vapor storage
- Uses heat exchanger and LN
- 81000 x 2ml vial storage
- High degree of security
- User defined temperature -50°C to 150°C
- Lower operating costs to mechanical freezer







www.chartbiomed.com

#### **Transport of Frozen Samples**



#### Chart MVE Vapor Shippers

- Vapor shipping of samples
- Hold time 10 days (upright)
- IATA compliant









www.chartbiomed.com

## Transportation of samples through Africa

## MARKEN

Global Life Science Supply Chain Solutions

### MARKEN track record within Africa

- Presently handle approximately 30 shipment a month from various African states (excluding South Africa).
- Type of samples handled within Africa vary from lifespan ambient samples, frozen samples on dry ice and frozen samples on liquid nitrogen.
- An average of 98% of the shipments handled within Africa are delivered on time.

### Hamilton's Integrated Solutions Automation and robotics



## Open Source Laboratory Information Management Systems LIMS BIMS

## Hellit as it is

bika (bi:ka Zulu trad) report, from clan to clan, bring news of weddings, births, festivals and funerals



## **Open Source Benefits vs Commercial**

- No license fees
- Unlimited users
- Superior security
- No vendor lock-in
- Tailor made customisations
- Robust industry proven servers
- Low hardware costs

# Components of the Proposed Pilot with collaborators in the H3A consortium

- We need to engage H3A researchers

   Sample, SOPs, needs, expectations of BRs
- Understand legislation in African countries
- Understand cultural and ethical issues
- Understanding logistics of transportation on the continent
- How we can apply advocacy to national, regional and continental governance structures. Govt, SADC, ECOWAS, AU, NEPAD etc

## Abuja and Cape Town H3A Biorepositories



Alash'le Abimiku Inst of Human Virology Abuja H3 Africa BR



Akin Abayomi Stellenbosch University Cape Town H3 Africa BR

## What might the H3A investigators provide to H3A Biorepositories

- Local policies, laws, regulations governing biospecimen collection, use, transfer
- Shipping companies you have used and your experiences with them
- Types of biospecimens your project has or will obtain
- What QC do you use to check integrity of processed or stored samples and how regular?
- Procedures used in past to collect existing biospecimen resources for new H3A studies

## Emulation and practice



## Thank you. Akin Abayomi abayomi@sun.ac.za



wellcome<sup>trust</sup>





UNIVERSITEIT STELLENBOSCH UNIVERSITY





#### Storage systems



#### Chart Cryosystems

- Liquid storage
- Low liquid nitrogen consumption (normal working duration full days 38 – 104)
- Mid range vial capacity 750 6000
- Can be used with level alarm





www.chartbiomed.com



are monitored and reported

## Solutions for collection and stabilization

| Method                                       | Sample   | Collection    |
|--|--|---------------|
| Stabilization of DNA                         |  |               |
| PAXgene Blood DNA                            | Blood  | Tubes         |
| QIAcard FTA spots                            | Blood, bone marrow, buccal cells, buffy coat, cells, plasma, and tissues | Cards         |
| QIAsafe DNA                                  | Blood, purified DNA  | Tubes, plates |
| Stabilization of RNA                         |  |               |
| PAXgene Blood RNA                            | Blood  | Tubes         |
| PAXgene Bone Marrow RNA                      | Bone Marrow  | Tubes         |
| RNeasy Protect                               | Tissue   | Tubes         |
| RNeasy Protect Animal Blood                  | Animal Blood   | Tubes         |
| RNeasy Protect Bacteria                      | Bacteria   | Tubes         |
| RNeasy Protect Saliva                        | Saliva   | Tubes         |
| RNAlater                                     | Tissue   | Tubes         |
| Stabilization of DNA, RNA, miRNA and protein |  |               |
| AllProtect Tissue                            | Tissue   | Tubes         |
| Stabilization of morphology, DNA and RNA     |  |               |
| PAXgene Tissue                               | Tissue   | Container     |

## NanoDrop Technology

- Stand-alone Systems
- NA Qantification and Purity 260/280
- Microvolume spectrophotometry
- No Expensive consumables
- Simple Procedure
- Robust



## LIMS BIMS

- BIKA
- Linux
- Plone
- Python
- Unbuntu

## Air-links to South Africa



## Medi-Clinic Hospital. Bone Marrow Transplant unit.





## **Experience with Biobanking**

- Lady Meade HIV Reference Unit. University of the West Indies
  - Largest inventory of data linked HIV sample repository in the Caribbean
- SSALC & Tygerberg Lymphoma Study Group
   African Lymphoma Biorepository





## History of Relationship

- University College Hospital, Ibadan, Nigeria.
- 2 pathologists from IHV hosted in Stellenbosch on Clements request
- SSALC
- ASCO and develop ASCO University Tumour Boards
- Stellenbosch outreach activity to Abuja
- Abuja PI Alash'le Abimiku invites Cape Town PI to Annual Gallo Meeting in Baltimore

## QIAGEN

#### Sample and assay technologies



It all starts with a sample...

## **Highest Process Safety**

#### QIAsymphony SP/AS



#### Agilent 2100 Bioanalyzer product options PC and Software Software only, no PC included Desktop PC and Software

Desktop PC and Software Desktop PC and Software Laptop PC and Software Security Pack for 21 CFR part 11



## **RNA** Applications



**RIN: RNA Integrity Number** 

## Strategy of CT biorepository

- RTS
- Cell Lines
- LIMS BIMS
- Science of sustainability
- Stem cell Manipulation
- Storage with quality for posterity
- Cant anticipate needs of the future, so just keep cells or nucleic acid in good state

### **Biobanks – Planning for ideal lab set up**

Ground floor against an external wall •Short SIVL line for LN2 delivery •Reduced losses in line during fill process •Simplifies ventilation •No transporting of LN2 Storage Vessels in lifts

•No pressure drops due to rises in pipework


# **Bika Open Source Platform**

Developed in content management framework Plone that can be used as lab document repository

Plone Used by eBay, Nokia, many governments and universities, NASA, CIA and more

Programmed in Python. The language Preferred by Google, Yahoo, Disney

> Platform independent Ubuntu Linux or FreeBSD preferred PostgreSQL

MySQL or PostgreSQL database



498 Of the fastest 500 super computers run Linux (Forbes) 65% of all web servers (Netcraft.com)

No license fees - Big global communities

# Project roadmap: Collaborating with Cape Town and Abuja BRs

Requirements analysis & functional design

Software development and customisation

Installation

- Configuration & set-up
- Training
- Start-up assistance
- Post implementation user and technical support

## colorika col

# Tygerberg Lymphoma Study Group

• On going Biorespository Project

• Tissue and data stored from 2002 to date

 Monitoring impact of HIV on haematological malignancy

## PI of the ACSR Prof Leona Ayers, Ohio State University.



### **Pathology consultation**

#### Format

- -Follow up African NHL TMAs to ACSR
- -Sub-typing panel antibodies/probes
- -Image-sharing
- Diagnosis







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## Example of Tygerberg Lymphoma Tissue Repository

- HIV+ and HIV-
- Digital record of TMA samples

Key:

+

\_\_\_\_+ ₩+

F+

NC.

negative positive

n% positive

weak positive

focal positive unknown

no core

|    | CD44 | HI∨ | MYC | CD20 | CD10 | BCL6 | BCL2 | Ki-67 | CD38 |   |
|----|------|-----|-----|------|------|------|------|-------|------|---|
| 1  | -    | +   | +   | +    | +    | +    | -    | 95+   | +    |   |
| 2  | -    | +   | +   | +    | +    | +    | -    | 95+   | W+   |   |
| 3  | -    | +   | +   | +    | +    | +    | -    | 90+   | W+   | Ч |
| 4  | -    | +   | +   | +    | +    | ÷    | -    | 90+   | 75W+ |   |
| 5  | -    | +   | +   | +    | +    | +    | -    | 90+   | 75W+ |   |
| 6  | -    | +   | +   | +    | +    | 75+  | 90W+ | 80+   | +    |   |
| 7  | -    | +   | -   | +    | 50+  | +    | NC   | 95+   | +    |   |
| 8  | -    | +   | -   | W+   | +    | 90+  | 90+  | 90+   | W+   |   |
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| 10 | -    | +   | -   | +    | +    | +    | -    | 90+   | +    | Ĕ |
| 11 | -    | +   | -   | W+   | +    | 90+  | 90+  | 85+   | W+   | B |
| 12 | -    | +   | -   | +    | +    | 90+  | 90+  | 85+   | +    | Ы |
| 13 | -    | +   | -   | +    | +    | 85+  | -    | 80+   | +    |   |
| 14 | -    | +   | -   | +    | +    | 50+  | 85W+ | 75+   | +    |   |
| 15 | -    | ?   | +   | +    | +    | 90+  | 85W+ | 95+   | +    |   |
| 16 | -    | ?   | +   | +    | +    | 75W+ | 75W+ | 95+   | +    |   |
| 17 | -    | ?   | +   | +    | W+   | w+   | -    | 95+   | W+   |   |
| 18 | -    | ?   | +   | +    | +    | 90+  | -    | 95+   | +    |   |
| 19 | -    | ?   | +   | +    | +    | 85+  | -    | 95+   | W+   |   |
| 20 | -    | ?   | +   | +    | +    | +    | -    | 95+   | +    | Ы |
| 21 | -    | ?   | +   | +    | +    | -    | +    | 95+   | +    |   |
| 22 | -    | ?   | +   | +    | +    | 80+  | +    | 90+   | +    |   |
| 23 | -    | ?   | +   | +    | +    | +    | -    | 90+   | +    |   |
| 24 | -    | ?   | +   | W+   | +    | -    | +    | 90+   | W+   |   |
| 25 | -    | ?   | +   | W+   | +    | -    | +    | 90+   | W+   |   |
| 26 | -    | ?   | -   | +    | +    | 90+  | -    | 90+   | W+   |   |
| 27 | -    | ?   | -   | +    | -    | 90+  | 95+  | 85+   | -    | 8 |
| 28 | -    | ?   | -   | +    | -    | 90+  | 90+  | 80+   | -    | Ĕ |
| 29 | -    | -   | -   | +    | +    | 85+  | -    | 80+   | +    | B |
| 30 | -    | ?   | -   | +    | -    | 90+  | 90+  | 75+   | -    | Ы |
| 31 | _    | ?   | -   | +    | +    | 50+  | 50+  | 60+   | +    |   |



## Disease is not the same across Africa

- Experience from our SSALC study
  NCI AMC ACSR
- Study of effect of HIV on Haematological cancers across Africa
- Differences in prevalence and subtypes across the Continent

# Population 700m, 54 countries, 3000 ethnic groups and languages.













### WORKFLOW OF PILOT

#### 1. SAMPLE COLLECTION AT H3AFRICA AWARDEE SITE

- Sample type depended on facility infrastructure
  - Unprocessed sample
  - Processed sample –DNA
  - Frozen samples DMSO
  - Need clinical and sample info and protocols/SOP's used
  - Batch

#### 2. SHIPPING VIA COURIER SERVICES

- ID Courier services, eg. Marken or World courier
- Hire shippers depend on Tm needs
- Help with customs and regulatory issues
- IATA regulation
- Check that we are complying with regulations

#### 3. RECEIVAL OF SAMPLES AT TSB BIOREPOSITORY

- Incorporate Info on LIMS
  - Check that sample information and labeling correspond to right sample
  - Pre-analytical QC depended on type of sample received
    - Unprocessed sample Process QC Store
    - Processed QC Store
    - Frozen Processed QC Store





NATIONAL HEALTH

LABORATORY SERVICE

### WORKFLOW OF PILOT



NATIONAL HEALTH

LABORATORY SERVICE

#### 4. STORAGE

- Depending on sample type
- Ambient RTS
- -Ultra low Freezing
- -Cryopreservation
- 5. TIME INTERVALS/CHECK FOR DEGRADATION
  - Work in progress



Faculty of Medicine and Health Sciences Stellenbosch University



## Sub Sahara Africa Lymphoma Consortium (SSALC)

- SSALC facilitated the direct collaboration among African pathologists to characterize (WHO 2008) indigenous HIV/AIDS-Related Lymphoma
- SSALC is a project of the AIDS and Cancer Specimen Resource (ACSR/OHAM/NCI/NIH)





# HRL cases increased from 2002-2009 (6% to 37%)



Lymphoma cases by year, HIV status, Tygerberg Academic Hospital, 2002-2009.

FL □ diffuse large B-cell lymphoma (DLBCL) ■ follicular lymphoma (FL) Burkitt lymphoma (BL) small cell lymphoma plasmablastic lymphoma (PL)

peripheral T-cell lymphoma

primary effusion lymphoma

Hodgkin lymphoma (HL)

HIV+

**PL** 

**BL** 

other non Hodgkin lymphoma

DLBCL

HL

- Iymphoblastic lymphoma
- anaplastic large cell lymphoma
- marginal zone lymphoma
- □ Castleman's disease





## Hamilton: Automation and robotics

- Storage Technologies A long term business
- Product Range One Shop Stop Solutions
- Expertise Hamilton supports entire sample workflows
- Company size Approx. 1'500 employees world wide
- Support Global Network of support engineers







## Significant History Between 2 Cities







## Collectively well endowed Academic Environment in Cape Town

- NHLS Tygerberg Hospital
- FMHS and the SU
- UCT GSH
- UWC
- CPUT
- US Biz School