Malaria Evolution in South Asia
International Center of Excellence for Malaria Research
(MESA-ICEMR)

Use of LabKey Server in a globally distributed research program

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Presentation Outline

MESA-ICEMR Operations & Research

Why LabKey?

LabKey System Accomplishments to-date

Challenges
Malaria Evolution in South Asia ICEMR

- Characterize the diversity of malaria parasites
- UW Department of Chemistry
- NIAID program
  - 10 malaria Centers of Excellence worldwide
- 11 collaborating institutions
  - 5 in US
  - 6 field sites in India
- 33 current employees
  - Target 55-60 by end 2014
MESA-ICEMR Program Operations

Projects
1. Epidemiology
2. Parasite Plasticity
3. Pathogenesis
4. Human Genetics

Cores
1. Administration
2. Data Management & Statistics
3. Shared Technology

<table>
<thead>
<tr>
<th>Field Sites</th>
<th>Hospital Surveillance &amp; Community Surveys</th>
<th>Vector Biology</th>
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</thead>
<tbody>
<tr>
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<td>Clinical site</td>
<td>Laboratory site</td>
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<td>Bambolim/Panaji, Goa</td>
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<td>Wardha, Maharashtra</td>
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<td>Dibrugarh, Assam</td>
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</table>
Basic research performed on malaria parasites collected at new clinical research sites across India

Investigating correlations between:
- Parasite phenotypes
- Parasite genotypes
- Disease severity
- Host immunity
- Geographic origin
- Vector competence
- Transmission

Data collected:
- Demographics
- Clinical presentation, care & treatment
- Diagnostics
- Laboratory assay data
- Sample data

Annual Parasite Incidence (malaria cases/1000 people)

Source: National Vector Borne Disease Control Programme, India, 2008
MESA-ICEMR Lab Activities

**Parasite species:**
RDT, thin smear, thick smear, PCR

**Blood data:**
Hb levels, HCT determination

**Drug resistance phenotypes:**
IC$_{50}$: Chl, Mef, Pyr, Sulf, atov, artm. 1843U89, BMS38891, DSM1.

**Blood data:**
Hb levels, HCT determination

**Complexity of infection:**
Microsatellite analysis, MSP1 sequencing

**Drug resistance genotypes:**
PfCRT, PfMDR, PfDHFR, PfDHPS, PfCytb

**Parasitemia and Gametocytemia:**
Percent, density

**Drug resistance genotypes:**
PfCRT, PfMDR, PfDHFR, PfDHPS, PfCytb

**Culture adaptation:**
HCTs, serum vs albumax, unwashed vs washed

**Resistance selection (ARMD):**
1843U89, BMS388892, DSM1, atov, GSK2645947

**Other activities**
Parasite cloning
EC$_{50}$: 1843U89, BMS38891, DSM1, atov, GSK2645947
Gene Seq: var2csa
Genome seq: select clones
Subject Blood

- RNAlater
- Plasma
- WBCs
- Cultures
- Genomics
- Stored Samples
- FTA Card

Genomics
- Selections
- IC₅₀s
- Stored Samples
- Cloning
- DNA
- DNA
- PCR

Selections
- IC₅₀s
- Stored Clonal Samples
- Genomics
- DNA
- PCR
- PCR

IC₅₀s
- DNA
- Start culture again
- PCR
- Start culture again
- PCR

WGS
- Microsatellite Markers
- CGH
- PCR
- PCR
- Repeat all experiments and sample types under culture

DNA
- Microsatellite Markers
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- Repeat all experiments and sample types under culture

Gene-specific PCR
- Repeat all experiments and sample types under culture
- Repeat all experiments and sample types under culture

Purple text = frozen sample type
Why LabKey? (1)

Global research operations
- Experiments planned, performed, analyzed in different locations
- Unreliable power & connectivity at field sites
- Limited experience using data systems amongst field staff

Basic science in the field
- First time experiments performed on field parasite isolates
- Need to monitor experiment progress in real-time
Why LabKey? (2)

Complex experiments
- 3000-5000 data fields per experiment per sample
- 30-60 day assay duration
- Multiple rounds of assays performed on parasites after growth and challenge from each raw sample

Queries of multiple datasets
- Associations between demographic, clinical presentation, parasite growth, drug sensitivity, host immunity data
MESA-ICEMR Data Management

REDCap
- Subject Demographic Information
- Subject Clinical Information

LabKey
- Lab Diagnostics
- Parasite Growth Experiments
- Drug Sensitivity Experiments
- Integrated Study Database

FreezerPro
- Raw Sample Information
- Parasite Clone & Mutant Sample Information
Subject Demographic/Clinical Information

- **Example data**
  - age
  - gender
  - states of birth/residence/travels
  - hospital diagnoses & lab values
  - malaria treatments

- **Entered into REDCap database**
  - easy for Data Management staff to change as forms evolve
  - designed for this type of data
  - longitudinal and one-time information in different projects

- **Solution:** LabKey set up automatic transfer from REDCap into our server
  - still easy to make changes to demographic/clinical forms
Subject Information in LabKey

- Can combine demographic and clinical data sets
  - longitudinal and one visit data sets
- Easy searches
- Easy charts

Glasgow Coma Score vs. Age
Lab Diagnostics Information

- Data collected by staff
  - Hb
  - HCT
  - Species Identification (RDT, smear, PCR)
  - Parasitemia
  - Gametocytemia

- Want to look for correlations between multiple data sets

- Solution
  - web-based interface in LabKey
  - integration into study data set
Lab Diagnostics Charts in LabKey

- Continuously updated as new data is entered
- Can be combined with subject information
Parasite Growth Experiments

• **Culture Adaptation and Drug Selections**
  – Daily measurements
  – Large number of flasks and data collected
  – Multiple experiments going simultaneously
  – Desire to see real-time data entry
  – Option to add phenotype information after experiment completed

• **Solution**
  – Custom LabKey Assay

30-60 days of growth; 15 data points collected per flask per day
Parasite Growth Experiment Assays

• Day 0 Experiment Definition (one-time)
  – Patient ID
  – Volumes
  – Reagent identities (media, drug treatment, etc.)

• Daily Upload (repeated up to 60 times)
  – Parasitemia
  – Gametocytemia
  – Reagent identities
  – Contamination
  – End of experiment

and other QC data
Parasite Growth Charts

• Custom Visualization
  – plot growth of flasks across time
  – roll-over display of selected data, experimental parameters

• Can compare across all experiments

• Charts created in real-time
Drug Sensitivity Experiments

• Determine EC$_{50}$ values of patient lines to various antimalarials
  – flow cytometer data not easily comprehended
  – plotting and calculations require specialized software
  – want consistent analysis

• **Solution:**
  – LabKey converts existing assay for use
Integrated Study Database

- Combines all datasets into one web interface
- Can create views that show important factors from multiple datasets
- Will use for complicated queries
  - Subject was inpatient with resistance to chloroquine but no mutation associated with chloroquine resistance

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<th>Participant ID</th>
<th>Initial Parasitemia</th>
<th>Initial Gametocytemia</th>
<th>Patient Hemoglobin</th>
<th>5. Age</th>
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Sample Information

- History of parasite is very important
  - essential to determine scientific correlations
  - length of time in culture
  - identity of other tests done

- Use other software to store raw and multiple round sample information

- Solution:
  - include sample ID information in LabKey assay data fields
Challenges

In-country data infrastructure & system development expertise
- NIH RFA
- Data & Statistics Core Leader – RMRC, Dibrugarh
- Rathod Lab, UW

Data storage, ownership & sharing regulations
- Government of India
- US NIH

Balancing shifting priorities with LabKey
- Extent of integration with other softwares
- Development
- Operations
- Support for miscellaneous initiatives (manuscripts, presentations)
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