UNIVERSITY OF WASHINGTON

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
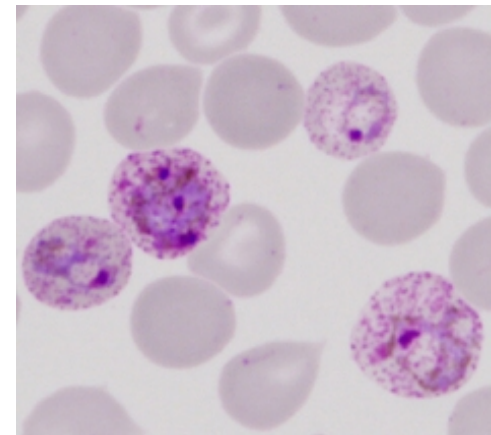
MESA-ICEMR Program Operations

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

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

Field SItes	Hospital Surveillance & Community Surveys		Vector Biology	
	Clinical site	Laboratory site	Mosquito collection	Laboratory site
Bambolim/Panaji, Goa	1	1	1	1
Wardha, Maharashtra	1	1	1	
Ranchi, Jharkhand	1	1	1	
Dibrugarh, Assam	1	2	1	1

MESA-ICEMR Science

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)
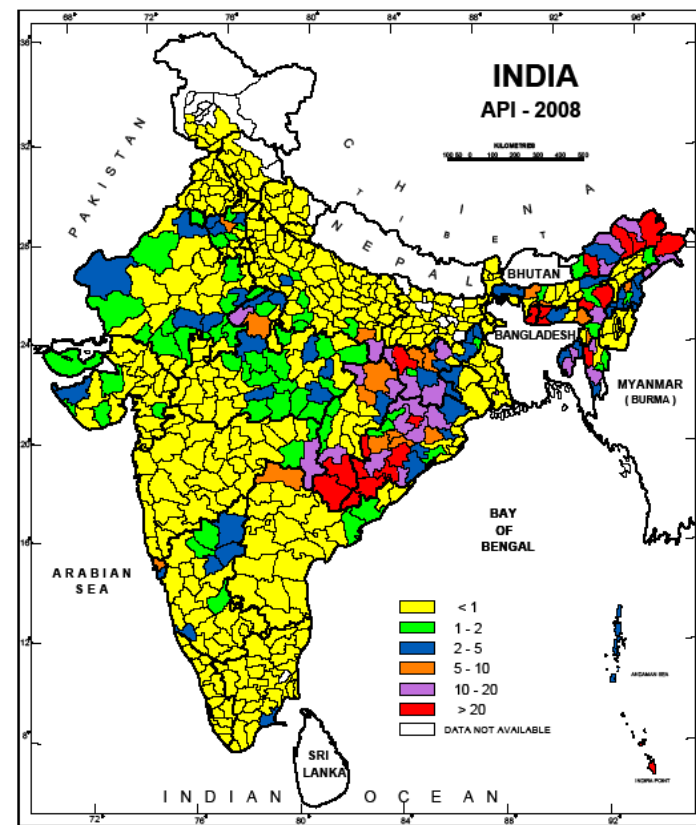
Source: National Vector Borne Disease Control Programme, India, 2008

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.

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

Other activities
Parasite cloning
EC_{50}: 1843U89, BMS38891, DSM1,
    atov, GSK2645947
Gene Seq: var2csa
Genome seq: select clones

Parasitemia and Gametocytemia:
Percent, density

Complexity of infection:
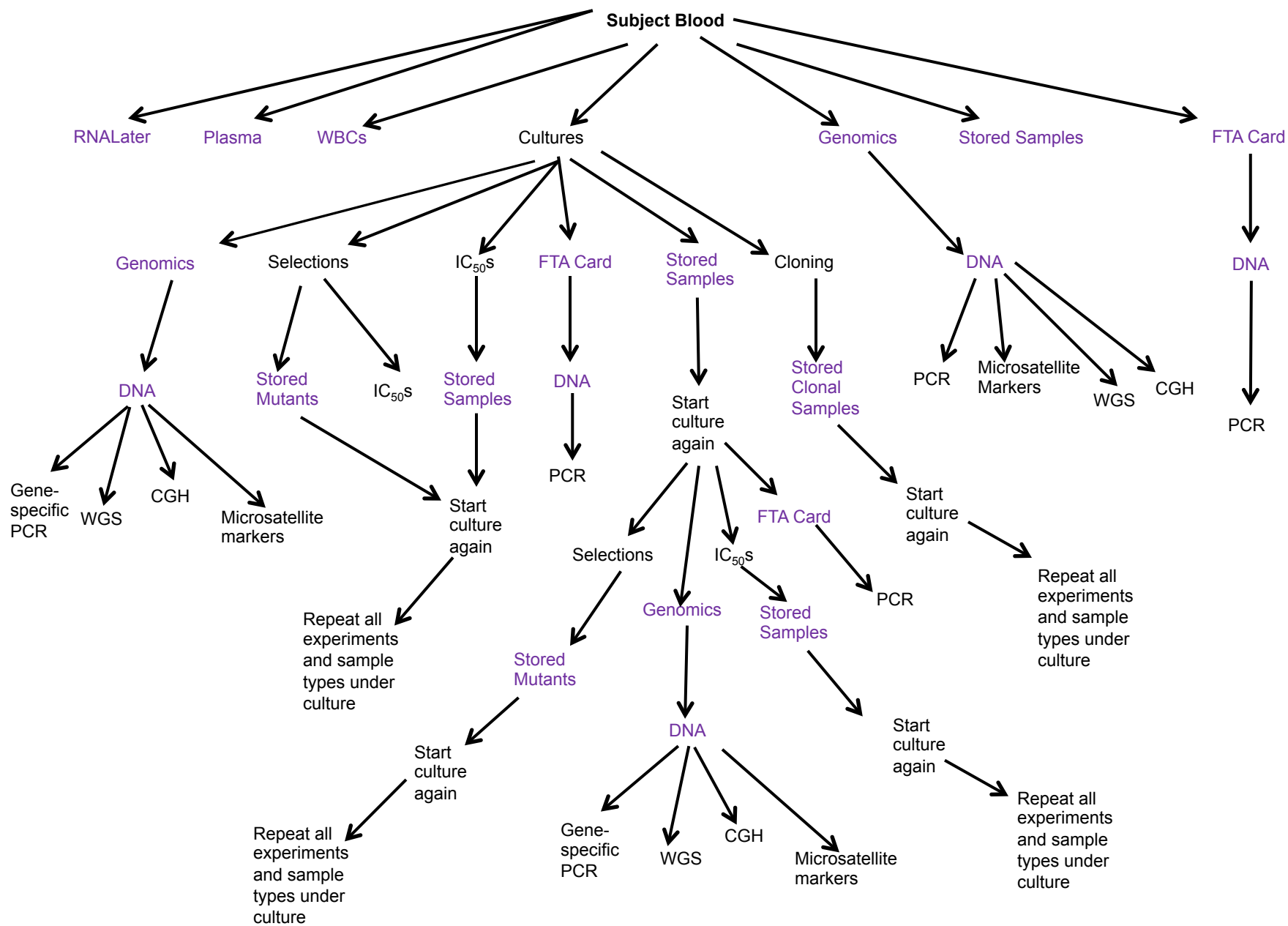Microsatellite analysis, MSP1 sequencing

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

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

Subject Blood

- RNALater
- Plasma
- WBCs
- Cultures
  - Genomics
    - DNA
      - Gene-specific PCR
      - WGS
      - CGH
      - Microsatellite markers
  - Selections
    - Stored Mutants
      - Start culture again
        - Repeat all experiments and sample types under culture
    - IC$_{50}$s
  - IC$_{50}$s
    - Stored Samples
  - FTA Card
    - DNA
      - PCR
  - Stored Samples
    - Start culture again
      - Selections
        - Stored Mutants
          - Start culture again
            - Repeat all experiments and sample types under culture
      - Genomics
        - DNA
          - Gene-specific PCR
          - WGS
          - CGH
          - Microsatellite markers
      - IC$_{50}$s
        - Stored Samples
          - Start culture again
            - Repeat all experiments and sample types under culture
      - FTA Card
        - PCR
  - Cloning
    - Stored Clonal Samples
      - Start culture again
        - Repeat all experiments and sample types under culture
- Genomics
  - DNA
    - PCR
    - Microsatellite Markers
    - WGS
    - CGH
- Stored Samples
- FTA Card
  - DNA
    - PCR

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
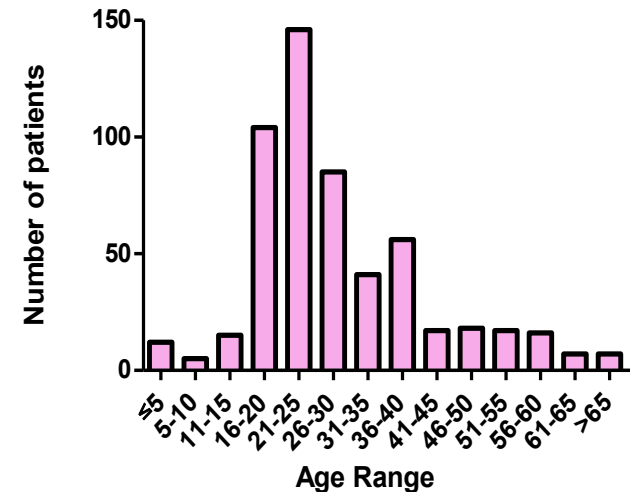
Subject Information in LabKey

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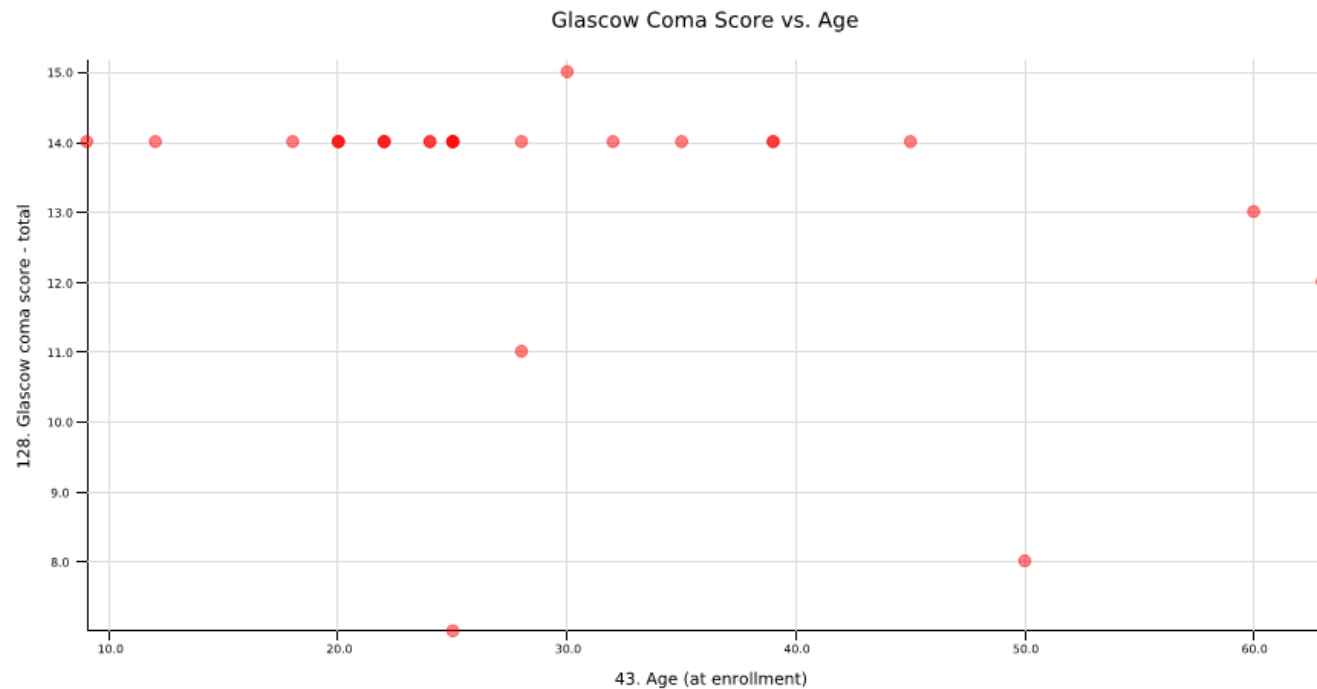
Lab Diagnostics Information

- Data collected by staff
  - Hb
  - HCT
  - Species Identification (RDT, smear, PCR)
  - Parasitemia
  - Gametocytemia
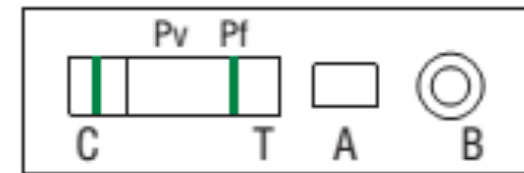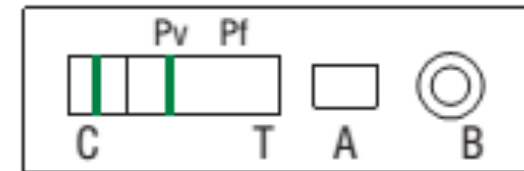
- Want to look for correlations between multiple data sets

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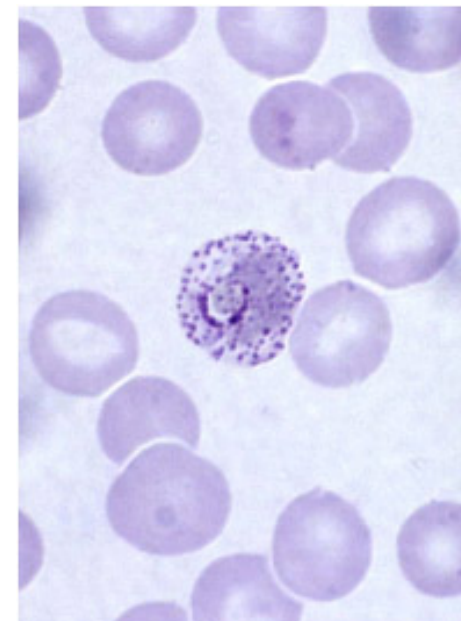
Lab Diagnostics Charts in LabKey

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

Parasitemia vs. Age
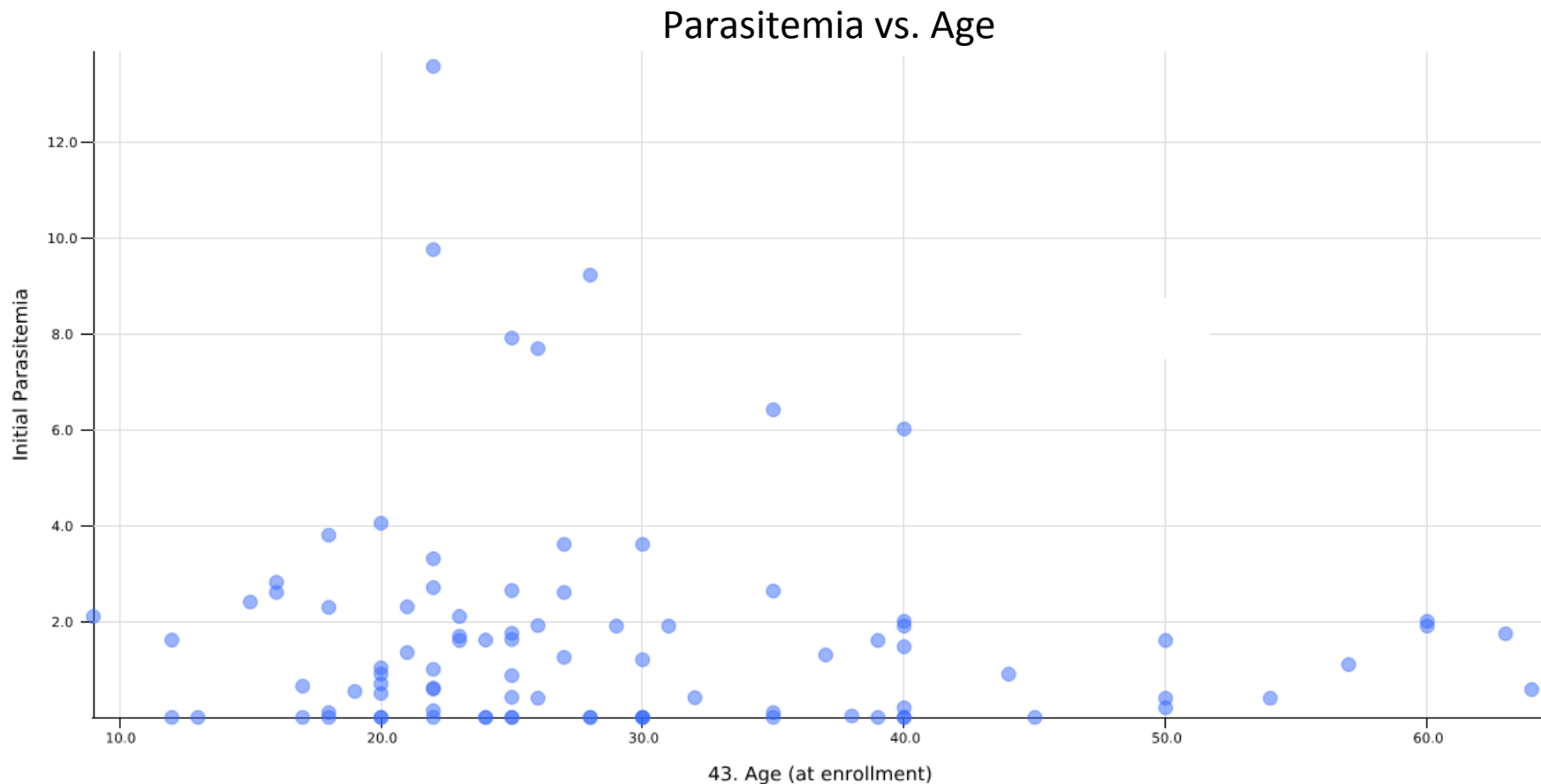
Parasite Growth Experiments

- 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
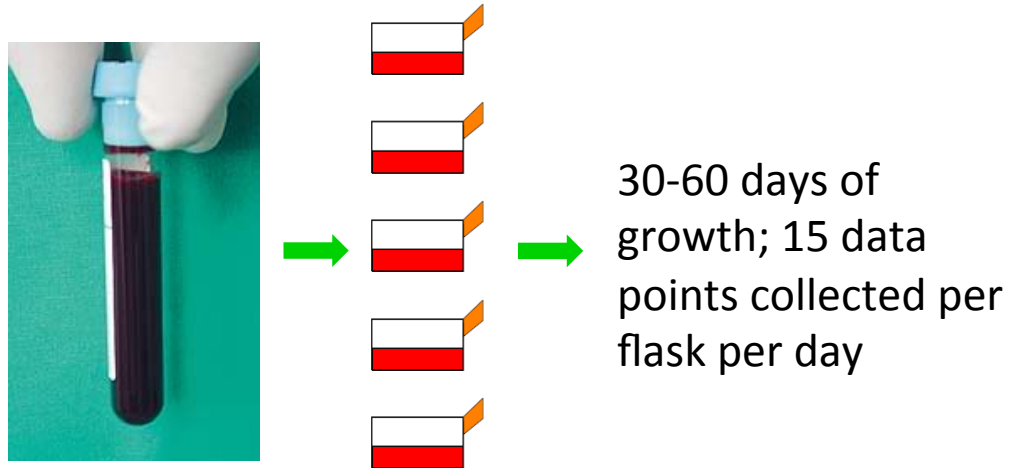
Parasite Growth Experiment Assays

- 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 ⎦ and other QC data
  - End of experiment

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
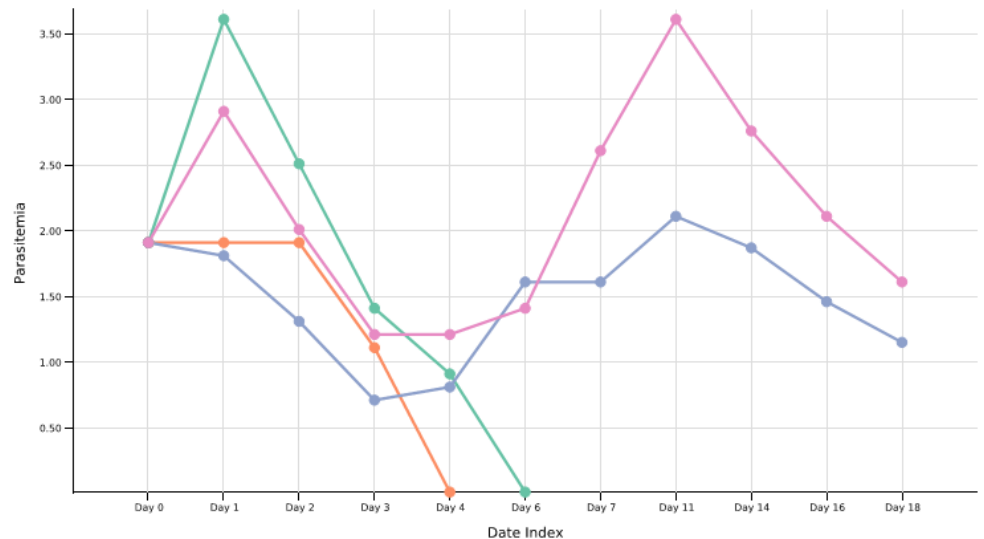
Drug Sensitivity Experiments

- Determine EC_{50} values of patient lines to various anti-malarials
  - flow cytometer data not easily comprehended
  - plotting and calculations require specialized software
  - want consistent analysis

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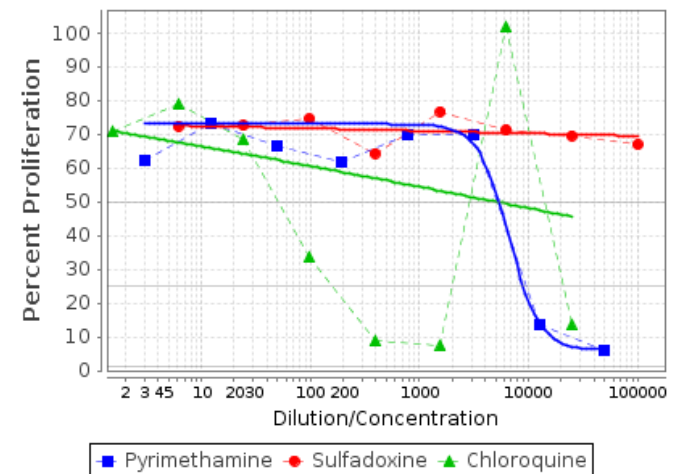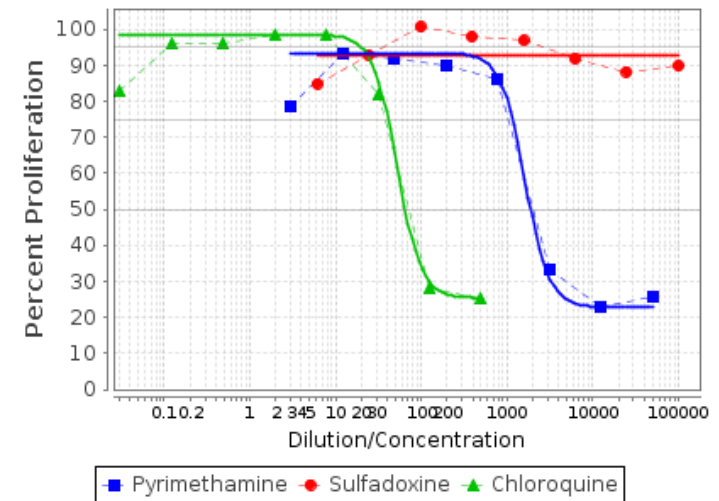
Integrated Study Database

- 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

		Participant ID ▾	Initial Parasitemia	Initial Gametocytemia	Patient Hemoglobin	5. Age	Thick blood	Thin blood
☐	ASSAY ▸	01010001	0.03	88.88	0.0		Pf	Pf
☐	ASSAY ▸	01010002	0.4	99.99	0.0		mixed	mixed
☐	ASSAY ▸	01010003	0.54	0.0	0.0		Pf	Pf
☐	ASSAY ▸	01010004	1.1	0.5	0.0		Pf	Pf
☐	ASSAY ▸	01010005	1.2	0.0	0.0		mixed	mixed
☐	ASSAY ▸	01010009	0.4	0.0	0.0		Pf	Pf
☐	ASSAY ▸	01010015	1.0	0.0	0.0		Pf	Pf
☐	ASSAY ▸	01010016	0.2	0.0	0.0		Pf	Pf
☐	ASSAY ▸	01010021	0.4	0.0	0.0		Pf	Pf
☐	ASSAY ▸	01010022	99.99	0.0	0.0		Pv	Pv
☐	ASSAY ▸	01010024	1.3	0.0	0.0		Pf	Pf

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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