Regional Situation of Resistance to Antimalarials

Kumar V. Udhayakumar, PhD
Malaria Branch
Centers for Disease Control and Prevention
Atlanta, USA

PAHO
Malaria Project Managers Meeting
November 14-16, 2018
Washington, DC

Molecular Markers of Drug Resistance Surveillance Update -Brazil and Haiti

Update on Roraima, Brazil

Haiti

Molecular Surveillance Study Partners in Roraima State, Brazil

Prof. Joseli de Oliveira Ferreira
FIOCRUZ
Mr. Jaime Louzada
Federal University of Roraima

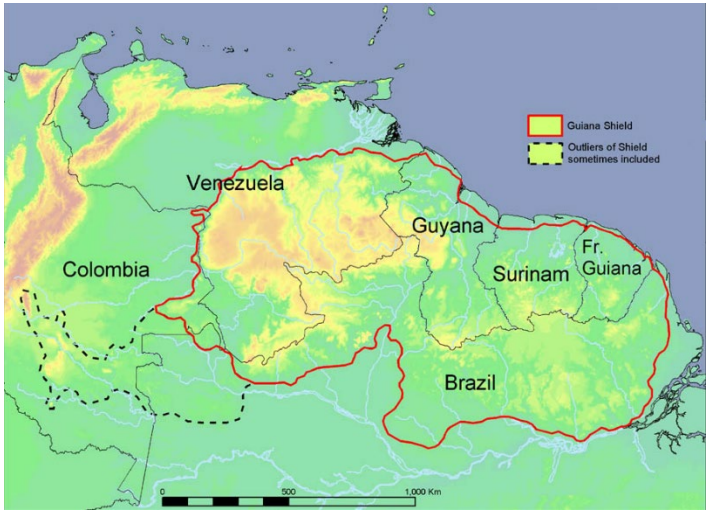
Institute Oswaldo Cruz- Fiocruz, Rio

Federal University of Roraima

UFRR

CDC

Is there any migration of artemisinin resistant K13 markers to Roraima State, Brazil?



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Molecular Surveillance Study Sites

- Three sites in the study:
  - Pacaraima
  - Boa Vista
  - Rorainopolis
- Collect filter paper samples from enrolled patients:
  - Malaria diagnosis
  - Molecular resistance markers
    - *pfK13*, *pfcrt* sequencing
    - *pfmdr1*: gene duplication and SNP
    - Neutral microsatellite analysis

Total number of samples collected 2016-Feb 2018

751 enrolled patients

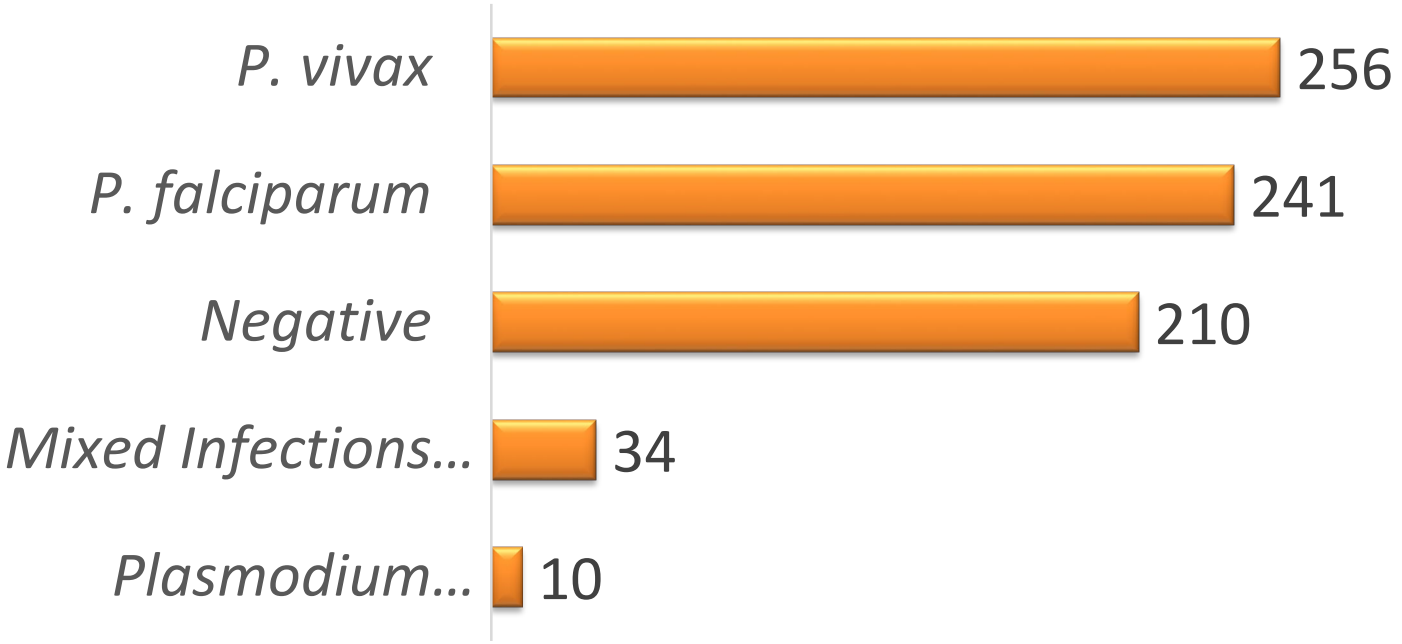
346: Pacaraima	348: Boa Vista	57: Rorainapolis

Dried blood spots collected for molecular diagnosis and characterization of drug resistance markers

275 *P. falciparum* positives (including mixed Pf/Pv)

Kelch 13 SNPs	*Pfmdr1* SNPs	*Pfcrt* SNPs	*Pfmdr1* CNV

Plasmodium Species Detected by PET-PCR in 2016-Feb 2018



Preliminary results: molecular markers of resistance

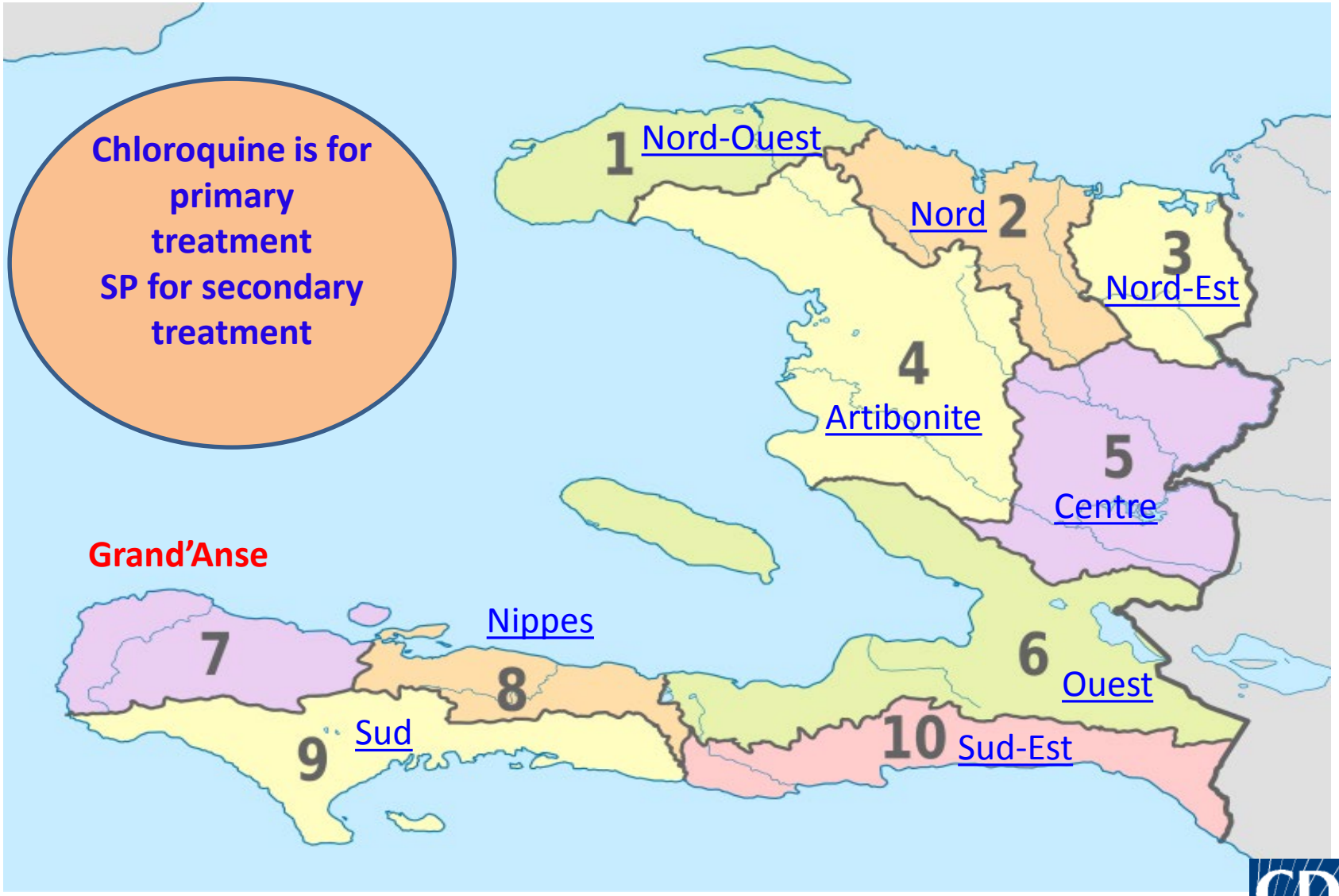
Gene/Codons assayed	Number tested successfully	Mutations observed
PfK13 C580**Y**; R539**T**; Y493**H**; I543**T**	238	No mutations
Pfmdr1 N86**Y**; Y184**F**; S1034**C**; N1042**D**; D1246**Y**	225	184F/1042D/1246Y **(45; 20%)** 184F/1034C/1042D/1246Y **(180; 80%)**
Pfcrt C72**S**; M74**I**; N75**E**; K76**T**	209	**S**VMN**T** =**200; 96%** CVMNK = **4; 2%** **S**VMNK =**3; 1%** CVI**ET** =**2; 1%**
Pfmdr1 Copy number variation (CNV)	246	**6 (2.4%)** with two copies

Preliminary results: molecular markers of resistance

- **We did not observe any artemisinin resistance associated mutations in the *pfk13* propeller domain.**

  – These results suggest that artemisinin resistance mutation (C580Y) found in Guyana has not been detected yet in the Roraima State of Brazil.

Surveillance for Drug Resistance in Haiti



Summary of CQ and SP Resistant Markers in Haiti -2016-17

- **CQ resistant pfcrt mutants (codons 72-76) were 0/741 (Rogier E., et al, unpublished)**
- **Pyrimethamine resistant dhfr triple (51I, 59R, 108N) mutants were 1/548 and 108N single mutants were 33%**
- **Sulphadoxine resistant triple (437G, 540E, 581G) mutants were 0/406 and a single 437G mutant were found**
- **This is consistent with current CQ treatment policy and forms a baseline data for monitoring MDA (using SP) as part of Malaria Zero project**

Training -Peruvian National Institute of Health

Mr. Carlos A Bartra More
Responsible de Laboratorio
Laboratorio de Referencia Supranacional de Malaria, Instituto National de Salud, Peru
June 25th-Aug 3rd, 2018

Sequencing methods:
Artemisinin resistant markers- pfK13
Other resistant markers-pfmdr1

Population based markers:
Microsatellite markers for differentiating recrudescence from reinfection

Training -Planned for Colombia 2019

Ms. Angela Patricia Guerra Vega
National Reference Laboratory
Parasitology Group
National Institute of Health
Bogota, Colombia

March 18-April 27th, 2019

Sequencing methods:
Artemisinin resistant markers- pfK13
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Wikipedia map

Summary, Challenges and Future Directions

- **Molecular markers and tools are complimentary tools for elimination efforts**
- **Valuable in detecting resistant markers, tracking parasite migration, emerging novel strains, HRP2 deletion, evolutionary changes etc**
- **Molecular data bases of population based markers are not available**
- **Long term data collection is critical**
- **Local capacity building is needed; academic, NGO, and MOH partnership is essential**

Acknowledgements

BRAZIL
Jaime Louzda (UFRR)
Joseli de Oliveira Ferreira (FIOCRUZ)
Roraima State Health Department
MOH
FIOTECH
Ana Carolina
CDC Country Office

INS/PERU
Carlos Bartra
Gladys Ramírez
PAHO

COLOMBIA
Angela Patricia Vega, INS, MOH
PAHO

GUYANA
Horace Cox, NMCP
MOH

FRENCH GUAYANA
Lise Musset
Institut Pasteur

SURINAME
Malti Adhin
Stephen Vreden
PAHO

PAHO
Maria Paz Ade
Roberto Montoya
Prabhjot Singh

WHO
Pascal Ringwald
Charlotte Rasmussen

CDC MALARIA BRANCH
Naomi Lucchi
Eric Rogier
Stella Chenet
Camelia Herman
Curtis S. Huber
Ira F. Goldman
Luciana M. Flannery
Samaly Santos
Rispha Abdallah
Alexandre Macedo de Oliveira
Karen Hamre
Michelle Chang
Cecilia Nelson
Pauline Abdallah

Funding

CDC Antimicrobial WG

USAID FROM THE AMERICAN PEOPLE

CDC

Acknowledgements

Haiti

Dr. Lemoine
Dr. Boncy
All staff involved
Study subjects

Haiti National Public Health Lab Staff
Haiti Ministry of Health
Other partners

MALARIA ZERO
THE ALLIANCE FOR A MALARIA-FREE HAITI

BILL & MELINDA GATES foundation

TEMPLE UNIVERSITY

Tulane University

CDC

Acknowledgments -CDC Malaria Lab Team

Gracias