Technical consultation on the role of parasite & mosquito genetics in malaria surveillance to optimize response by national programmes

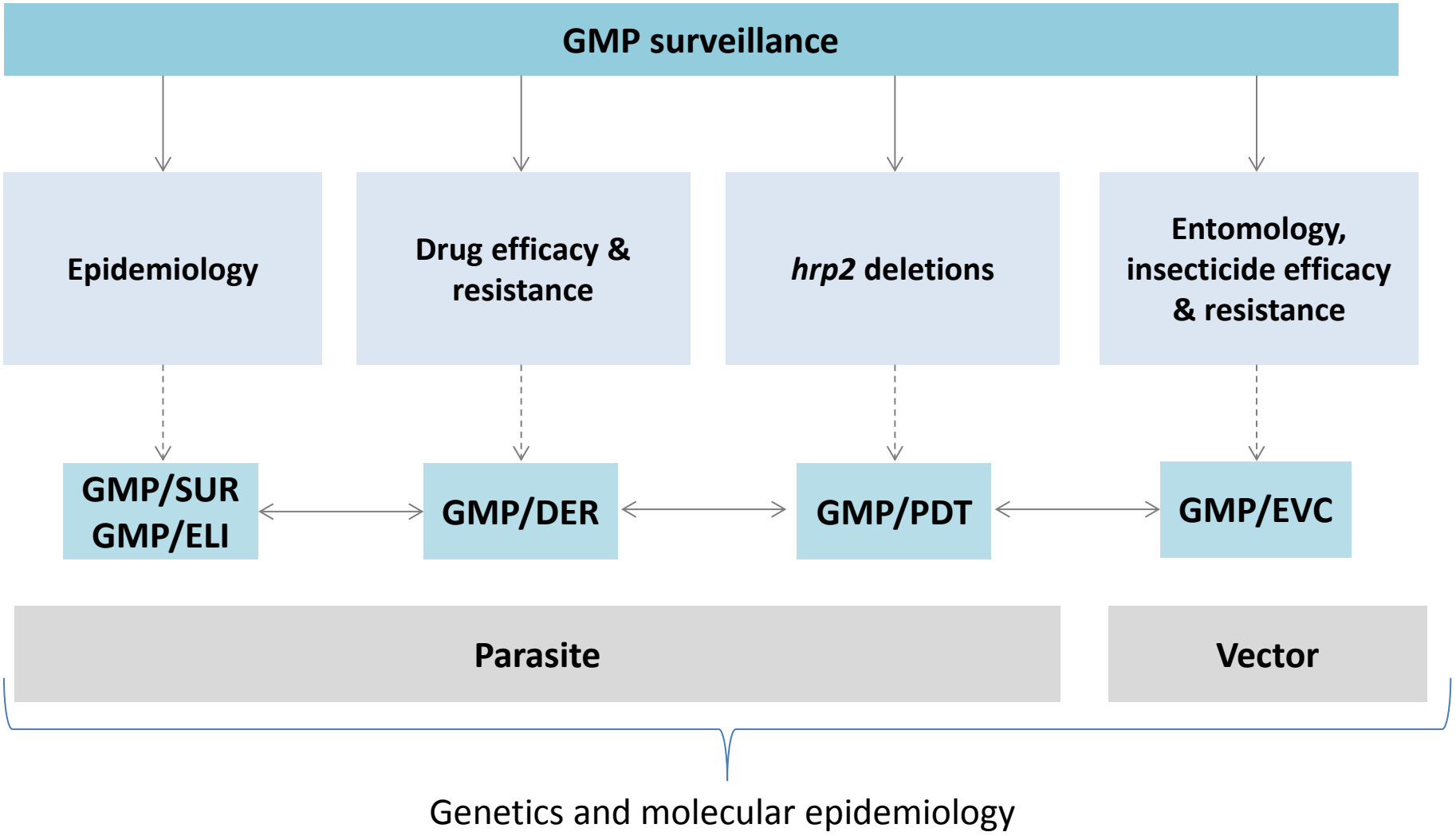
Malaria Policy Advisory Committee
17-19 October 2018

Abdisalan Noor on behalf of SUR, ELI, DER, EVC and PDT units

Global **Malaria** Programme

World Health Organization

Malaria surveillance in GMP



Malaria surveillance in GMP

Malaria Threats Map

Tracking biological challenges to malaria control and elimination

VECTOR INSECTICIDE RESISTANCE

Resistance of malaria mosquitoes to insecticides used in core prevention tools of treated bed nets and indoor residual sprays threatens vector control effectiveness

Go to Threat Map

Read more

PARASITE *pfhrp2/3* GENE DELETIONS

Gene deletions among some malaria parasites cause false negative diagnostic test results, complicating case management and control

Go to Threat Map

Read more

PARASITE DRUG RESISTANCE

Resistance of malaria parasites to artemisinin – the core compound of the best available antimalarial medicines – threatens antimalarial drug efficacy

Go to Threat Map

Read more

Parasite and anopheline genomics

The *Plasmodium falciparum* Genome Project

C. Fletcher

Orlando, FL, USA
December 1997

control malaria, including diagnostics, vaccines and drugs. Building on the malaria

Progress – Nuts and Bolts

MalariaGEN
GENOMIC EPIDEMIOLOGY NETWORK

RESEARCH ARTICLE SUMMARY

MOSQUITO GENOMICS

Highly evolvable malaria vectors: The genomes of 16 *Anopheles* mosquitoes

Daniel E. Neafsey,*† Robert M. Waterhouse,* *et al.*

INTRODUCTION: Control of mosquito vectors has historically proven to be an effective means of eliminating malaria. Human malaria is transmitted only by mosquitoes in the genus *Anopheles*, but not all species within the genus, or even all members of each vector species, are efficient malaria vectors. Variation in vectorial capacity for human malaria among *Anopheles* mosquito species is determined by many factors, including behavior, immunity, and life history.

comparisons to individual genes or sets of genomic markers with no genome-wide data to investigate attributes associated with vectorial capacity across the genus.

RESULTS: We sequenced and assembled the genomes and transcriptomes of 16 anopheline lines from Africa, Asia, Europe, and Latin America, spanning ~100 million years of evolution and chosen to represent a range of

IVCC
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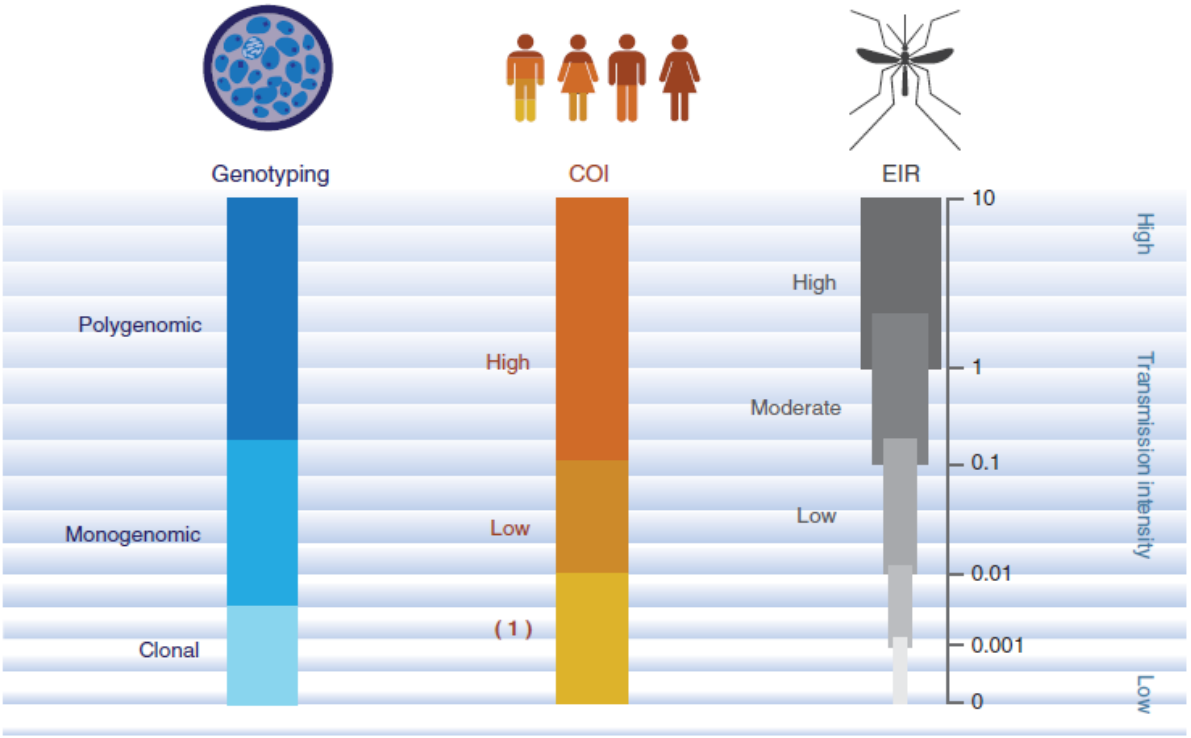
Special Issue: Vectors

Review

Identification, Validation, and Application of Molecular Diagnostics for Insecticide Resistance in Malaria Vectors

Martin J. Donnelly,[1,2,*] Alison T. Isaacs,[1] and David Weetman[1]

Malaria genomics



Neafsey & Volkman (2017)

As the transmission intensity decreases from high to low levels, changes in mosquito (entomological inoculation rate [EIR]; human complexity of infection [COI]), and parasite (genotyping) indicators are anticipated to change. With relatively high transmission (e.g., EIR > 1), there are high COI levels and a predominance of polygenomic infections as assessed through genotyping methods.

As transmission decreases to more moderate (e.g., EIR from 0.1 to 1) or lower levels (e.g., EIR from 0.01 to 0.1), decreases in COI are detected and increases in the proportion of individuals harboring monogenomic infections.

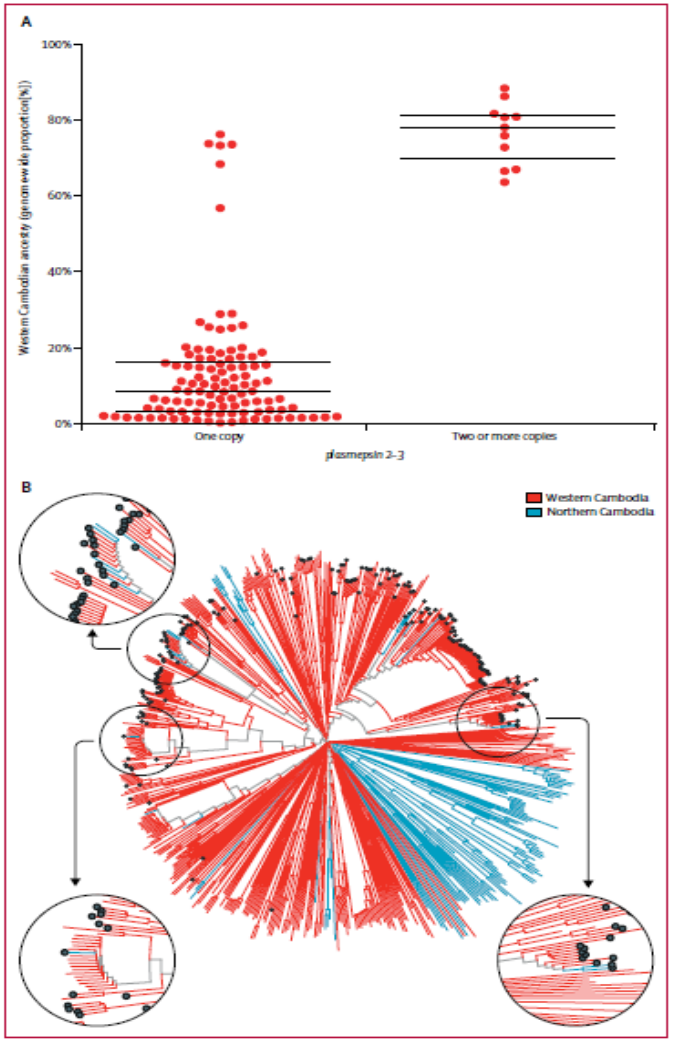
Eventually as transmission intensity is very low(e.g., EIR from 0 to 0.01) evidence of COI = 1 and clonal parasite populations among monogenomic infections are detected using genotyping methods.

Potential use cases

Area	Use	Genetics
Resistance	1. Drug resistance markers	Parasite
	2. Insecticide resistance markers	Mosquito
	3. Drug resistance gene flows	Parasite
Transmission intensity	4. Vector speciation	
	5. Vectorial capacity	Mosquito
	6. Complexity of infections	Parasite
Elimination	7. Identification of foci	Parasite
	8. Identification of imported cases	Parasite
	9. Transmission chains	Parasite

Resistance gene flow

Amato R, Pearson RD, Almagro-Garcia J, Amaratunga C, Lim P, Suon S, Sreng S, Drury E, Stalker J, Miotto O, Fairhurst RM, Kwiatkowski DP (2018). **Origins of the current outbreak of multidrug-resistant malaria in southeast Asia: a retrospective genetic study**. *Lancet Infect Dis*. 2018 Mar;18(3):337-345



Spread of dihydroartemisinin–piperaquine resistance to north Cambodia

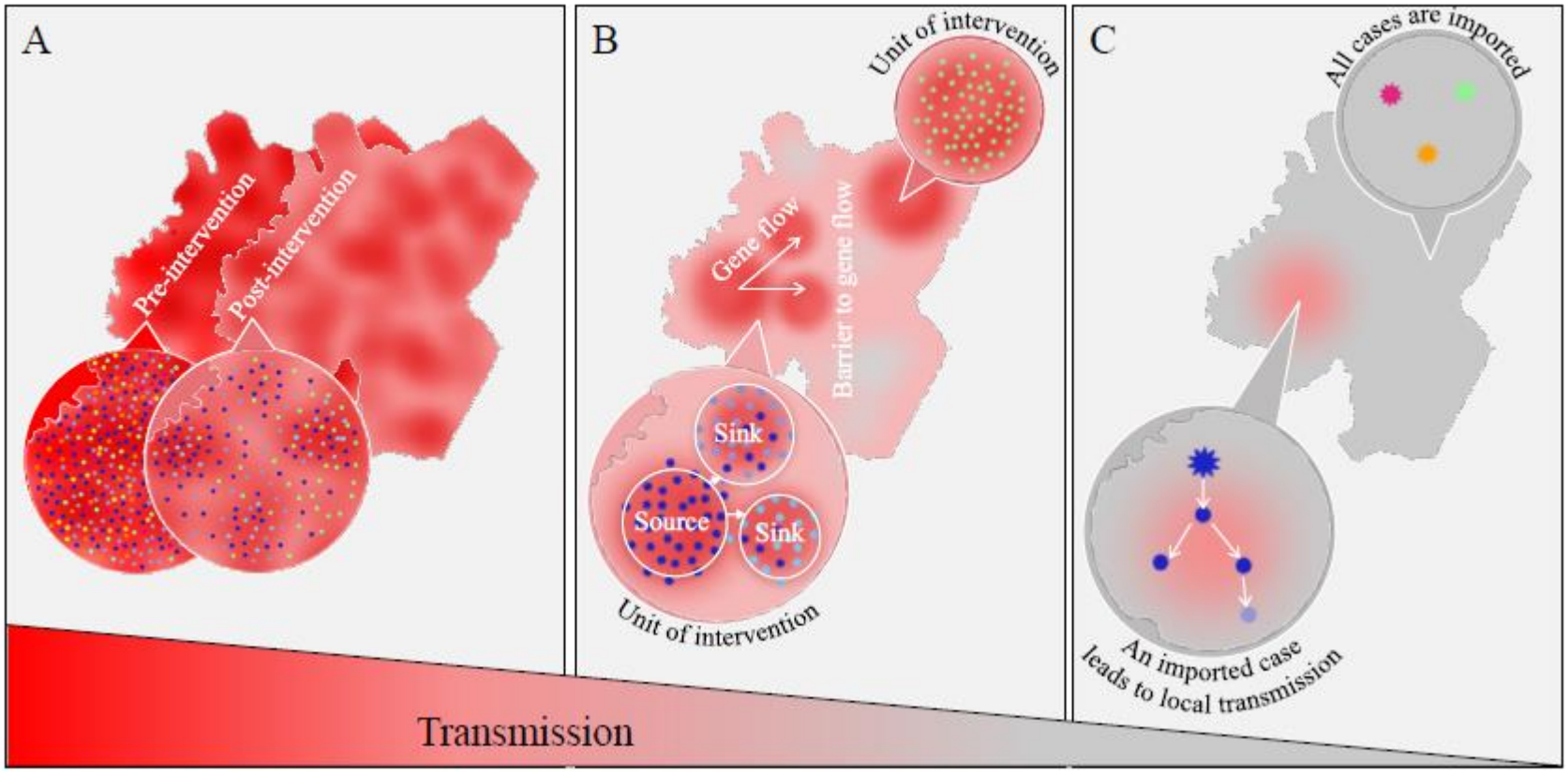
(A) Each point represents a sample from northern Cambodia.

(B) Genome-wide neighbour-joining tree of all samples from northern and western Cambodia in the dataset, with those carrying *plasmepsin 2-3* amplifications identified by black dots at the tip. The circular subpanels show a magnified view of parts of the tree containing samples from northern Cambodia carrying *plasmepsin 2–3*

Mapping transmission intensity

Mapping malaria by combining parasite genomic and epidemiologic data

Amy Wesolowski[1], Aimee R. Taylor[2,3,4], Hsiao-Han Chang[2,3], Robert Verity[5], Sofonias Tessema[6], Jeffrey Bailey[7,8], T. Alex Perkins[9], Daniel Neafsey[4,10], Bryan Greenhouse[6,11], Caroline O. Buckee[2,3]



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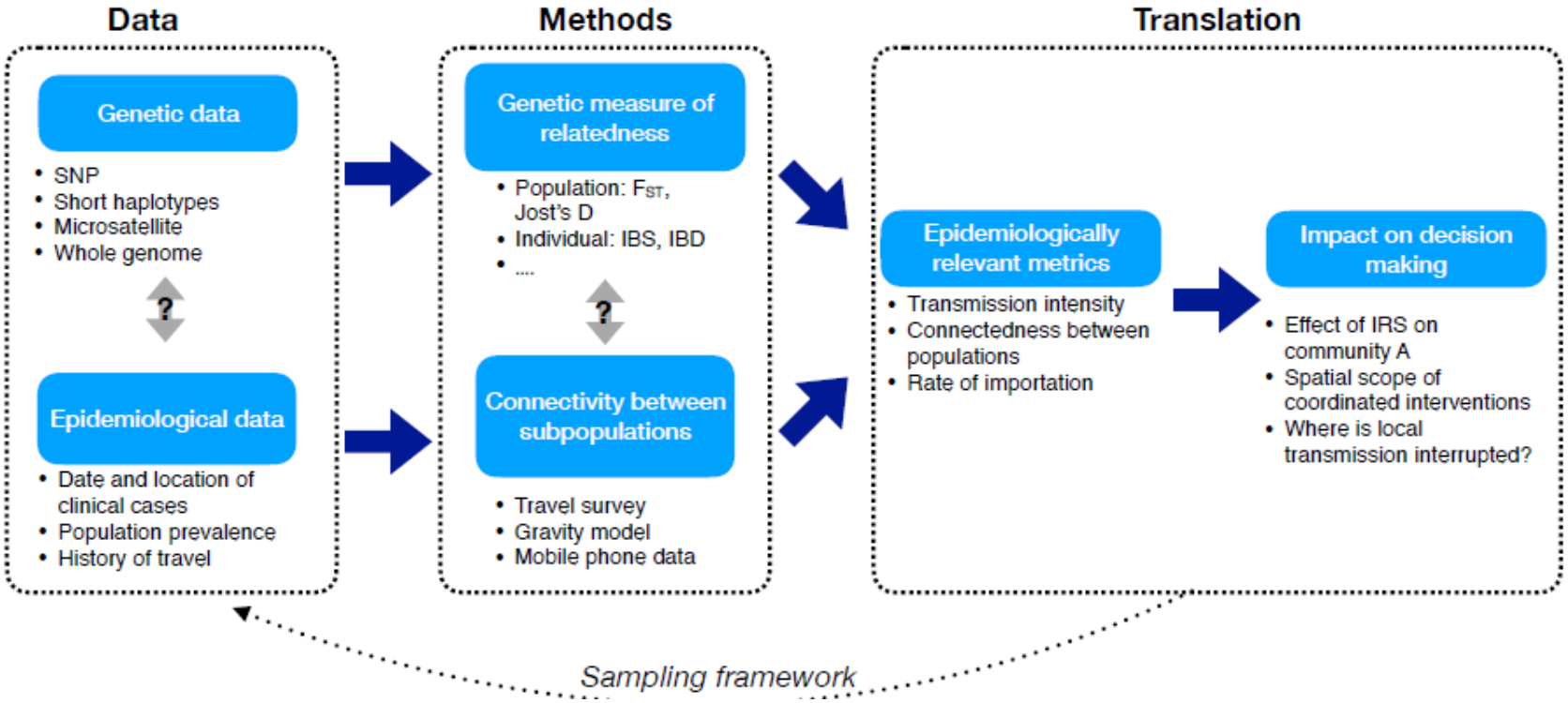
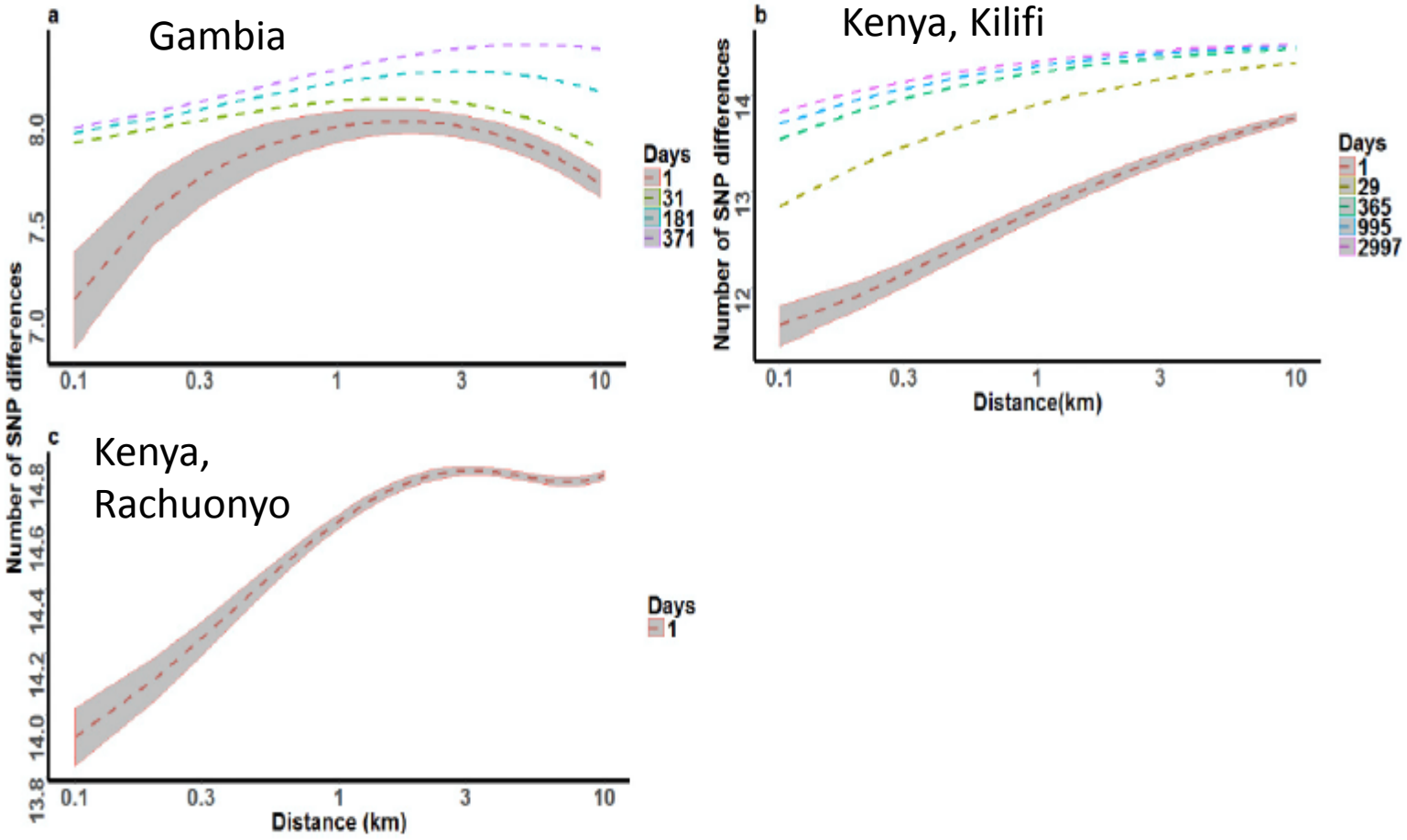


Micro-geographic structures of parasite populations

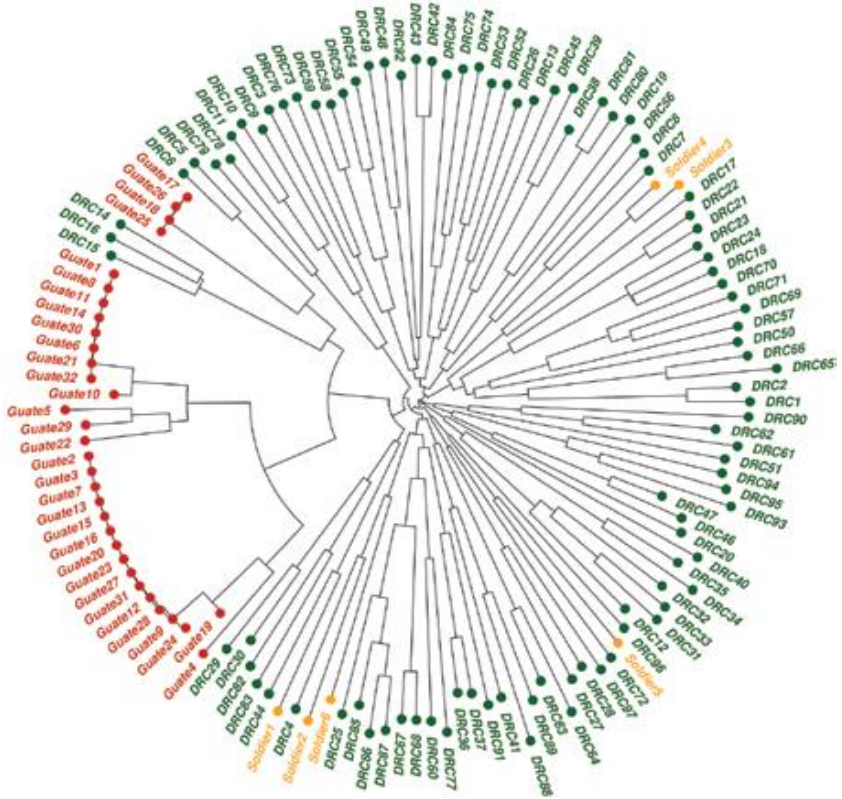
Irene Omedo, et al (2017). **Micro-epidemiological structuring of *Plasmodium falciparum* parasite populations in regions with varying transmission intensities in Africa.** *Wellcome Open Research* 2017, 2:10



Parasite genetics to identify malaria importation

Genetic Evidence of Importation of Drug-Resistant *Plasmodium falciparum* to Guatemala from the Democratic Republic of the Congo

Jaymin C. Patel, Steve M. Taylor, Patricia C. Juliao, Christian M. Parobek, Mark Janko, Luis Demetrio Gonzalez, Lucia Ortiz, Norma Padilla, Antoinette K. Tshefu, Michael Emch, Venkatachalam Udhayakumar, Kim Lindblade, and Steven R. Meshnick



Neighbour-joining tree of *Plasmodiium falciparum* populations.

Prefixes of genomes indicate parasite origins: Green text indicates parasite populations from the Democratic Republic of the Congo (DRC); orange indicates parasite populations detected in soldiers who were returning from the DRC to Guatemala; red indicates parasite populations from Guatemala.

Vectorial capacity

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RESULTS: We sequenced and assembled the genomes and transcriptomes of 16 anopheline from Africa, Asia, Europe, and Latin America, spanning ~100 million years of evolution and chosen to represent a range of

'Variation in vectorial capacity for human malaria among Anopheles mosquito species is determined by many factors, including behavior, immunity, and life history.'

'This variation in vectorial capacity suggests an underlying genetic/genomic plasticity that results in variation of key traits determining vectorial capacity within the genus.'

Oppenheim *et al. BMC Genomics* (2017) 18:205
DOI 10.1186/s12864-017-3590-0

BMC Genomics

RESEARCH ARTICLE Open Access

Genome content analysis yields new insights into the relationship between the human malaria parasite *Plasmodium falciparum* and its anopheline vectors

Sara J. Oppenheim[1*], Jeffrey A. Rosenfeld[1,2] and Rob DeSalle[1]

hrp2 & 3 deletions

SCIENTIFIC REPORTS

OPEN

SUBJECT AREAS:
EVOLUTION
GENETICS
MICROBIAL GENETICS
PARASITOLOGY

Received

Multiple genetic origins of histidine-rich protein 2 gene deletion in *Plasmodium falciparum* parasites from Peru

Sheila Akinyi[1], Tonya Hayden[1], Dionicia Gamboa[2,3], Katherine Torres[2], Jorge Bendezu[2], Joseph F. Abdallah[1], Sean M. Griffing[1], Wilmer Marquiño Quezada[4], Nancy Arrospide[4], Alexandre Macedo De Oliveira[1], Carmen Lucas[5], Alan J. Magill[5], David J. Bacon[5], John W. Barnwell[1] & Venkatachalam Udhayakumar[1]

RESEARCH

Major Threat to Malaria Control Programs by *Plasmodium falciparum* Lacking Histidine-Rich Protein 2, Eritrea

Araia Berhane, Karen Anderson, Selam Mihreteab, Karryn Gresty, Eric Rogier, Salih Mohamed, Filmon Hagos, Ghirmay Embaye, Anderson Chinorumba, Assefash Zehaie, Simone Dowd, Norman C. Waters, Michelle L. Gatton, Venkatachalam Udhayakumar, Qin Cheng, Jane Cunningham

Challenges

- Insufficient discourse between genomics researchers and policy making processes
- Few joint genetics and epidemiological analyses to ease translation of results to policy/operations
- Complex and diverse methods and limited national capacity, insufficient representative samples
- Unresolved ethical, regulatory issues in the collection, sharing and use of genetic materials
- Lack of clear guidance on priority policy relevant research questions

Opportunities

- Increasing number of demonstration studies
- Growing acceptance that genomics can play a role in policy and programme decisions
- Increasing investments in genomics epidemiology research
- Improving sampling and analysis methods and expanding regional capacity
- More clarity on the ethics of use of genetic materials

Potential use cases for technical consultation

Drug resistance gene flow

Transmission intensity

Parasite gene flow

Local transmission chains

Identify foci of transmission

Identify imported cases

***Hrp2 & 3* deletions**

Vectorial capacity

Insecticide resistance

Objectives of proposed technical consultation

1. Review existing evidence across the use cases
2. Refine the use cases to prioritize studies
3. Identify key research questions relevant to policy and operational national programme activities in each use case
4. Discuss the role of WHO in the legal, regulatory and ethics space to set standards for study designs and access to data
5. Explore possibility of a global WHO data portal

Implementation

Nov 2018 – Feb 2019	March 2019	April 2019
Reviews of existing literature on use cases	TC jointly convened by SUR, ELI, DER. EVC and PDT	Report submitted to MPAC