

The RBM Partnership



Sixteenth Board Meeting Information Session

Geneva, 13 May 2009

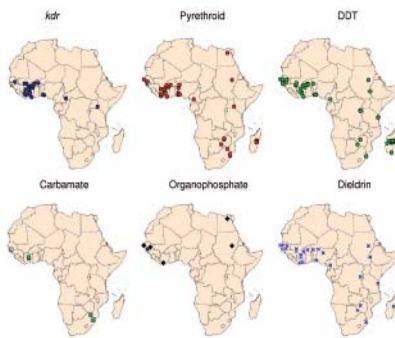


Insecticide Resistance

Janet Hemingway



- **Indoor Residual spraying of Insecticides or use of Insecticide Impregnated bednets are the mainstay of malaria control**



- **Growing observation of insecticide resistance in Vector Mosquitoes.**

- **Only 4 Classes of Insecticide approved for Malaria vector control, Only 1 for nets.**
- **Resistance is known for all these insecticides**

Major biochemical mechanisms of resistance

	Metabolic			Target-site	
	Esterases	Monooxygenases	GSH S-Transferases	kdr	MACE
Pyrethroids	●	●		●	
DDT		●	●	●	
Carbamates	●				●
Organophosphates	●	●	●		●



The Overloaded Bicycle!

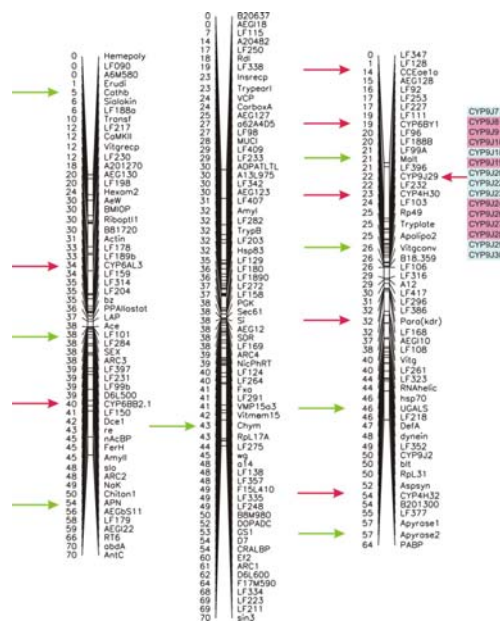
ACTIVITIES

- Collect mosquitoes, use some to do WHO bioassays. Freeze these and other mosquitoes collected
- Establish a cold chain back to a lab and do biochemical and PCR assays on mosquitoes
- Collect clinic malaria data
- Measure number of nets distributed or insecticide used

OUTPUTS

- Lots of frozen *Culex*!
- Some identified *Anopheles* mosquitoes
- A good idea of what resistance you have (but lots of hassle working out cold chain logistics).
- No idea of malaria transmission levels (clinic data in most localities is a poor indicator of malaria transmission, particularly if diagnosis is by clinical diagnosis of fever).
- A rough idea of how many people might have had access to either ITN or IRS interventions
- No evidence on whether the interventions have had impact
- No information if malaria obviously increases why this has happened

QTL mapping of genome regions controlling permethrin resistance in the mosquito *Aedes aegypti*

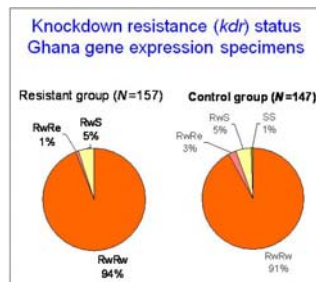


Survival rates of *A. gambiae* s.l. in Uganda to permethrin, deltamethrin, DDT, bendiocarb and malathion

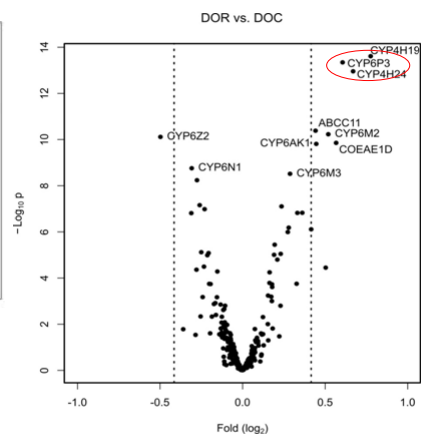
	Site	Insecticide	N	Survivors (%)	95% confidence interval
Phenotype	Busolwe	0.1% bendiocarb	78	0	0 – 4.7
		4% DDT	102	30.4	22.3 - 39.9
Candidate		5% malathion	81	0	0 - 4.5
		0.75% permethrin	77	2.6	0 - 9
Validate	Osukuru	0.1% bendiocarb	203	0	0 - 1.9
		4% DDT	216	76.4	70.3 - 81.6
Technology		0.05% deltamethrin	154	12.3	8 - 18.5
		5% malathion	213	0	0 - 1.8
Field test		0.75% permethrin	196	34.7	28.4 - 41.6

Identification and functional validation of *Cyp6M2*

Phenotype
↓
Candidate
↓
Validate
↓
Technology
↓
Field test



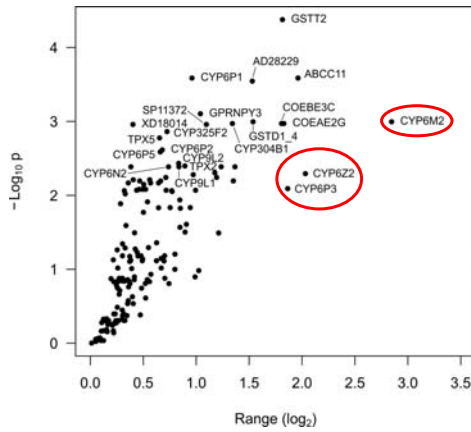
Kdr almost fixed in Odumasy so variability in phenotype must be attributable to a non-target site mechanism



Over-expressed in the control group (green)
Over-expressed in the resistant group (red)

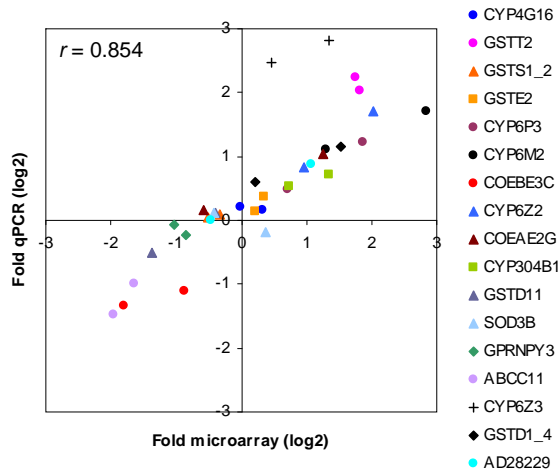
CYP6P3 also found over expressed in a pyrethroid resistant population from Cameroon All specimens showed molecular M-form and lack of *kdr* alleles

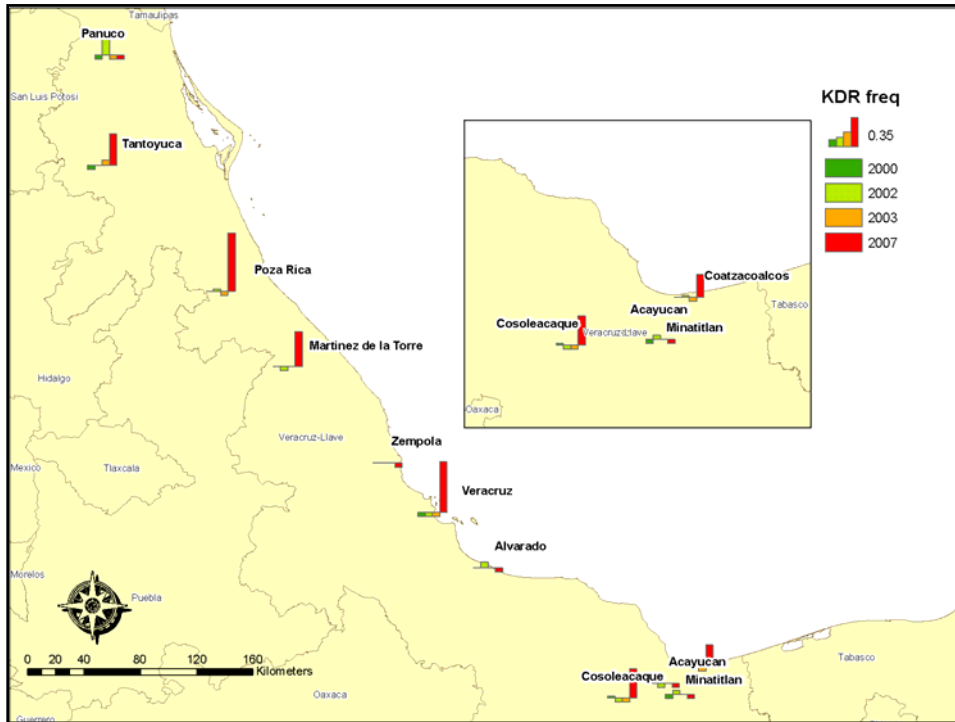
Phenotype
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 Technology
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 Field test



Cameroon microarray data have been validated by quantitative RT-PCR

Phenotype
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 Field test





TaqMan Plasmodium assay

Assay tested with artificially infected mosquitoes (Bob Sinden) and field collected mosquitoes stored in Ethanol, Isopropanol, on Silica

- More sensitive than nested gold standard
- Not inhibited by three storage conditions
- Cheaper than nested PCR (US\$ ~0.5)
- Much higher throughput than PCR
- Now main diagnostic used at MRC, Durban

