

INSECTICIDE RESISTANCE IN MOSQUITOES

MARK PAINE

Basic Research → New Tools



- Genomics
- Biochemistry
- Bioinformatics
- Toxicology

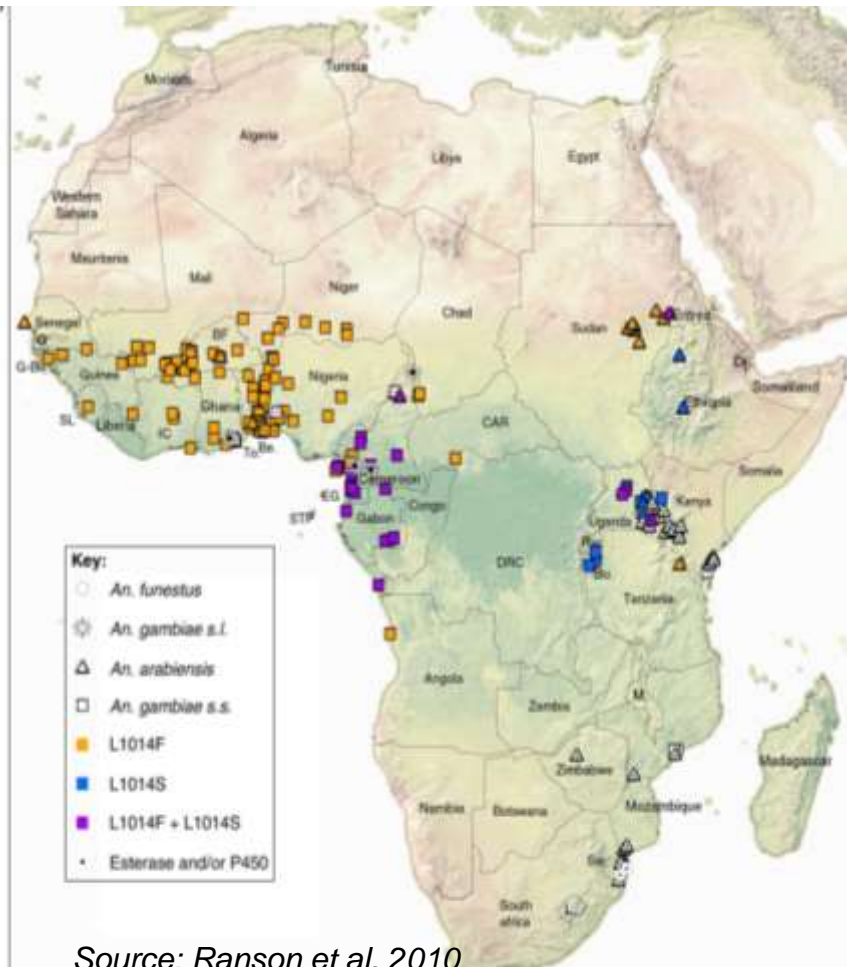


- Resistance monitoring
- Pilot studies of new tools
- Ecology/Behaviour

- Diagnostics for insecticide resistance monitoring
- Insecticide quantification kits
- Insecticide resistance management tools

Developing new tools –First identify resistance candidates

Pyrethroid Resistance



Source: Ranson et al. 2010

© The Liverpool School of Tropical Medicine

Pipeline for identification of resistance candidates

Phenotype



Candidate



Validate

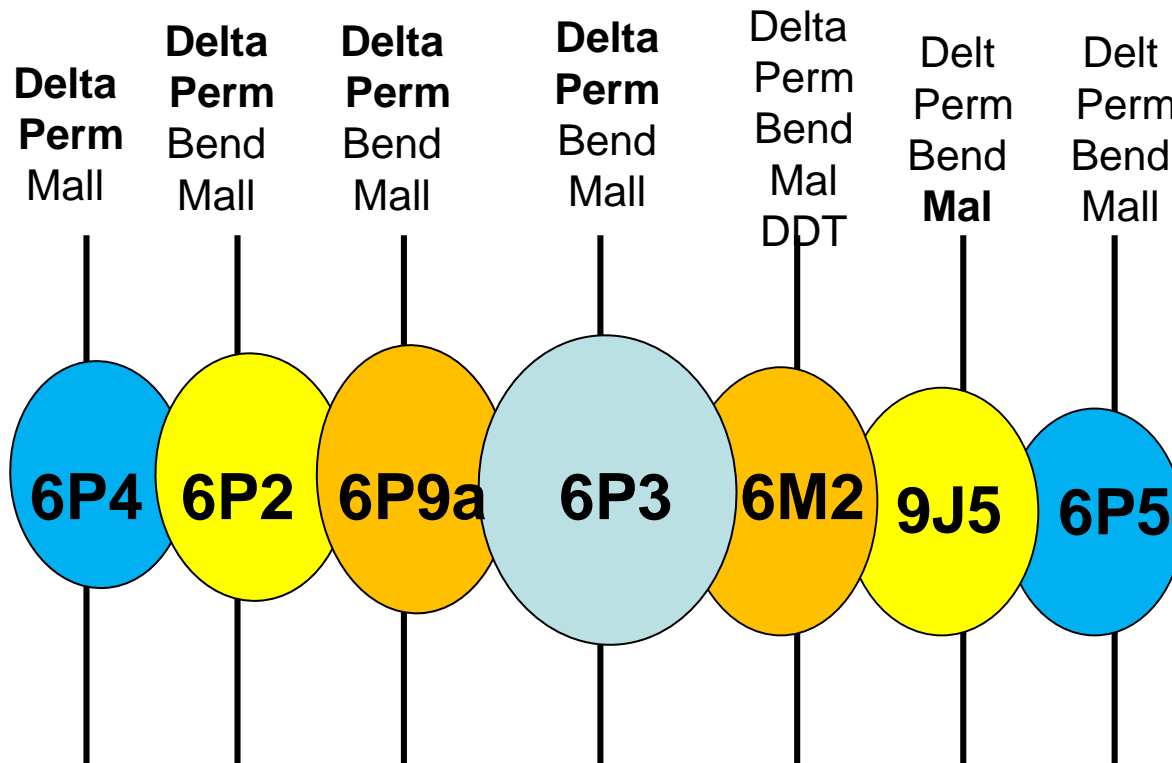


Technology



Field test

✓ Core Metabolic resistance genes are being identified in African mosquitoes



Warning
Overexpression of these enzymes may cause resistance to new insecticides

targets for diagnostics and insecticide development

(With apologies to FP Guengerich)

Tools: Enzymes to assess resistance liabilities



6P3
6P9a
6M2

High Throughput Screens



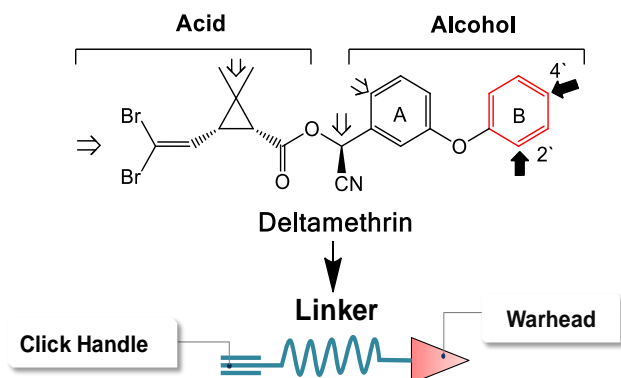
Insecticide Design



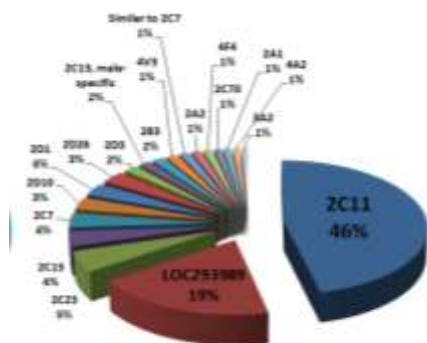
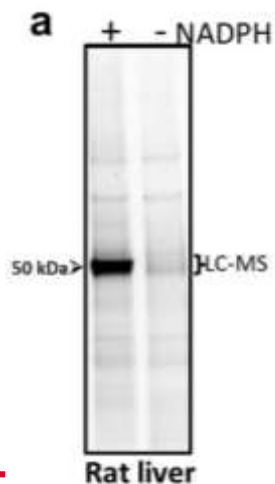
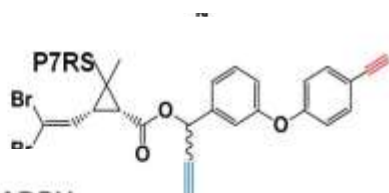
Inhibitor	CYP6M2 IC50 μM	CYP6P3 IC50 μM	CYP6P9a
A	100	20	0.5
B	17	170	3
C	7651	323	85.07
D	No inhibition	500	285
E	No inhibition	No inhibition	No inhibition
F	0.6	4	Not tested yet
G	12	10	7
H	No inhibition	No inhibition	No inhibition
I	6.32	3.05	no inhibition

Scaled Production (Cypex)
Available LSTM/LITE

Tools: Pyrethroid Activity Based Probes (PyABP) for pre-emptive screening of metabolic resistance



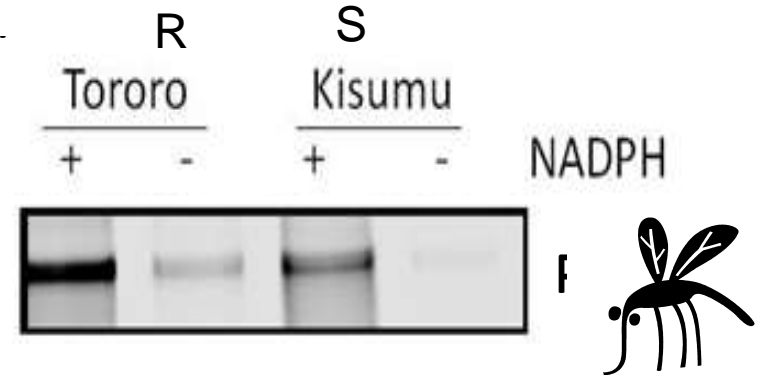
Tag Free Click Chemistry ABP Probes Design



PYRETHROME

New Paradigm?

- Selective Identification of detoxifying enzymes
- Applicable to all organisms
- Identify resistance genes BEFORE they become a problem in susceptible insects



Vector Control is failing due to a lack of QA tools; demand for tools to monitor insecticide use

Bioassays



Insectaries needed

Not Practical

HPLC/GC



\$25 - 50/ test

Too Expensive

Immunoassays



Cross-reacts with analogues

Not Specific

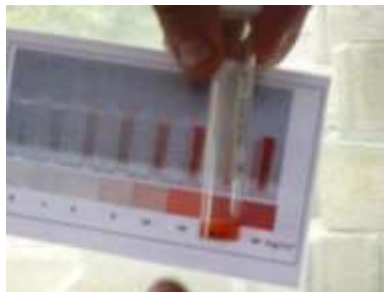
Protective levels of insecticide are not being reached

Tools: Insecticide Quantification Kits (IQK)



Houses
 - palm
 - wood
 - bamboo

Spray quality Vanuatu



IQK

Pooled	House	Individual Pads and Wall Position								
		High			Middle			Low		
3	1	3	3	5	3	20	3	3	3	3
10	2	10	10	20	3	5	5	20	5	10
30	3	30	30	20	30	30	30	30	20	30
30	4	20	10	20	20	30	30	30	20	20
20	5	20	20	20	5	5	20	20	10	20
20	6	20	20	20	20	20	5	20	40	20
20	7	30	10	20	20	20	20	30	10	10
30	8	30	20	20	20	20	20	20	30	30
30	9	30	20	30	20	30	20	20	40	30
30	10	20	20	10	20	30	30	40	40	30
20	11	40	10	50	20	30	10	20	10	20
20	12	10	5	20	30	20	20	10	20	20
30	13	10	1	30	20	20	10	20	20	3
20	14	10	20	20	10	40	30	20	5	3
20	15	3	20	5	10	0	10	0	3	0
20	16	30	30	10	40	30	20	20	1	5
10	17	20	5	3	3	20	20	20	20	10
30	18	30	20	20	20	30	10	20	40	20
20	19	10	10	10	5	30	30	30	10	10
20	20	5	10	10	10	10	20	10	5	40
20	21	20	5	5	20	30	10	20	40	20
20	22	10	20	10	20	20	30	30	20	20
30	23	10	30	40	20	30	20	40	30	20
30	24	20	10	20	30	5	10	30	20	40
30	25	20	30	40	30	30	20	30	30	40
30	26	30	30	30	20	20	30	20	20	10
30	27	10	20	10	10	20	40	30	30	30
30	28	20	20	20	30	20	30	40	40	20
40	29	30	40	30	40	40	30	40	40	30
40	30	40	30	40	40	30	30	20	40	30

- Innovative QA technologies for IRS
- Rapid results
- Low cost
- Easy to use
- Proven in the field

IQK™ – Full suite of tests



IQK Product Variants	Surfaces	Nets	Status
Pyrethroid IQK <i>(for class II pyrethroids)</i>	✓		●
Pyrethroid IQK <i>(for class II pyrethroids)</i>		✓	●
Carbamate IQK	✓		●
DDT IQK	✓		●
Organophosphate IQK	✓		●



WHY DO WE NEED INSECTICIDE QUANTIFICATION KITS

