Rapid Insecticide Resistance Assessment Using Biomarkers

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Definitions & Assumptions

Insecticide resistance:
• “a genetic adaptation enabling arthropod pests to survive exposure to otherwise lethal amounts of insecticide”
• Encyclopedia of Biodiversity

Knockdown resistance (kdr):
• common- any mutation of the voltage gated sodium channel
• specific- a mutation that reduces the sensitivity of the VGSC to a xenobiotic
• primarily pyrethroids

Acetylcholinesterase resistance (AchE):
• mutations to the acetylcholinesterase gene that reduce sensitivity to a xenobiotic
• primarily organophosphates

Biomarker:
• “almost any measurement reflecting an interaction between a biological system and a potential hazard, which may be chemical, physical, or biological. The measured response may be functional and physiological, biochemical at the cellular level, or a molecular interaction”
• WHO 1993
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Requirements for a useful prognostic biomarker

Must correlate strongly with the presence or intensity of the measured outcome

Must be penetrant

- Resistant organisms must possess the biomarker
- Susceptible organisms must not possess the biomarker

Must be easy to measure

Can be any measurable parameter

- Chemical- cholesterol
- Clinical measurement- blood pressure
- Sugars- HbA1c
- Protein- antigens
- Nucleic acid- BRCA1 or genotype

Understand and define the limitations
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Caution:
A biomarker does not necessarily indicate causation
Why use genetic biomarkers for IR assessment in mosquitoes?

- **Use dead organisms from trap collections**
- **Cover large geographic areas**
  - City-wide, statewide or country-wide
  - 3 years versus 3 weeks
- **Rapid**
  - 384 samples in 2.5 hrs
  - ~1200 samples per day
- **Cost effective**
  - Low labor input
  - Reduced shipping
  - Reduced import issues - CDC/USDA/CBP
- **Allows time series studies that are difficult**
- **Provides operationally useful information**
Does \textit{kdr} genotype predict insecticide-resistance phenotype in mosquitoes?

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15 years ago
A qualified yes, but with caveats:

- Depends on the species
- Depends on the target
- Depends on the geographic location

None have been rigorously validated to human biomarker standards
*Kdr* genotypes have distinct toxicologic profiles and operational performance.
Using the *kdr* genotype as a surrogate for resistance to pyrethroids

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\[ \rho = 0.9 \]
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Geographic limitation
- Does not detect novel *kdr* mutations

Limited to *Aedes aegypti*
- Must have proper controls to be valid
Hardee County 2024

2023 dengue outbreak

No known history of IR testing

*Aedes aegypti* has been expanding
24-hour turnaround from sample receipt to result

Result:
- IICC frequency above FL average
- All locations are similar
Almost 70% is the 60x resistant genotype
Almost 20% is the 20x resistant genotype
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This population is likely 40-50 resistant to permethrin
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Hardee County 2024

Operational impact

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This population is likely 40-50 resistant to permethrin

Performance of a pyrethroid field spray is likely low

Synergized formulation is likely ineffective
What to do?

Rely on strong IVM practices

The IVM cycle

- Surveillance
- Habitat control
- Efficacy evaluation
- Larval control
- Education & engagement
- Adult control

Hardee County 2024
Operational response

Organophosphates remain very effective
Hardee County 2024
Operational response

What to do?

Rely on strong IVM practices

Organophosphates remain very effective
Thank you!
Questions?

Just reach out...

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Mosquito & Fly Research Unit