Importance of Vector Control

- Mosquito-borne disease responsible for several million deaths worldwide
- Hundreds of million of cases of illnesses
- Vectors of pathogens that cause human and veterinary illnesses
- Example of viruses and diseases spread by mosquitoes
  - Zika virus (ZIKV)
  - La Crosse virus (LACV)
  - West Nile virus (WNV)
  - Dengue virus (DENV)
  - *Plasmodium falciparum, P. vivax, P. ovale* (species that cause malaria)
Current Vector Control Strategies

- Integrated Mosquito Management –AMCA
  - Surveillance, mapping & rational setting of action thresholds
  - Physical control through manipulation of mosquito habitat
  - Larval source reduction and adult mosquito control
  - Monitoring for insecticide efficacy and resistance
Vector Control Strategies cont..

• WHO recommends Integrated Vector Management (IVM):
  • Advocacy, social mobilization, regulatory control for public health and empowerment of communities.
  • Collaboration within the health sector and with other sectors through the optimal use of resources, planning, monitoring and decision-making.
  • Integration of non-chemical and chemical vector control methods, and integration with other disease control measures.
  • Evidence-based decision making guided by operational research and entomological and epidemiological surveillance and evaluation.
  • Development of adequate human resources, training and career structures at national and local level to promote capacity building and manage IVM programs.
Current Trends in Arboviruses

- Global re-emergence of arboviruses
  - ZIKV - 2016 Florida, Texas
  - CHIKV - 2014 Florida
  - WNV - 1999 New York
  - DENV - 2009 Florida (5% of Population)
  - DENV - 2005 Texas
  - YFV (Yellow Fever virus) - 2016 South America

- Emergence has become rapid and geographically extensive
Arbovirus Trends cont..

- Viral Co-infections
- Arboviruses found co-circulating in same geographic areas
- Clinical manifestations may be similar
  - Difficulty in telling difference between infections
  - Only 1 virus’ symptoms may be recognized
- Human cases of co-infection reported
  - January 2014, New Caledonia, 2 patients tested positive for ZIKV/DENV
  - 2016, Haiti, 1 patient tested positive for ZIKV/DENV
Could One Virus be Used to Suppress Another?

- Mosquito specific viruses
- Birnaviruses found in mosquitoes
- Birnaviridae family
  - CYV - *Culex Y virus* – isolated from *Culex pipiens*
  - ESV – Espirito Santo virus – isolated from biological sample in Espirito Santo Brazil
Espírito Santo Virus (ESV)

• Entomobirnavirus
• ESV, collected from Espírito Santo, Brazil
• Newly observed virus found in C6/36 mosquito (Aedes albopictus) cells
• Currently under study to learn about viral interactions within mosquito
Preliminary and Future testing

• ESV shown to grow in C6/36 insect cells infected with DENV-2
• ESV was not shown to infect mammalian cells
• Studies underway observing effects and differences between co infection of DENV-2 with different levels of virulence
  • C6/36 Ae. albopictus cell line
  • Impacts on different mosquito species
    • Aedes aegypti
    • Aedes albopictus
Immunofluorescence Assay of ESV/DENV Co-infection in C6/36 cells

- A. uninfected C6/36 cells
- B. C6/36 cells infected with dengue virus added to cells after 48 hours
  - Brighter fluorescence due to recognition of dengue virus
  - Appearance of cell structures e.g. endoplasmic reticulum
- C. C6/36 cells co-infected with ESV and dengue virus
  - Less pronounced fluorescence
  - ESV appears to suppress dengue
### Preliminary ESV Co-infection in adult Mosquitoes

- Infected with ESV as larvae
- Adult mosquitoes fed DENV-2 blood meal
- Tested at 14 dpi

<table>
<thead>
<tr>
<th>ESV</th>
<th>Aedes aegypti Anna Marie Island, FL</th>
<th>Aedes albopictus Lab Colony, LA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection Rate (%)</td>
<td>57%</td>
<td>75%</td>
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<tr>
<td>Virus Titer (PFUeq/mL)</td>
<td>2.1 ± 0.7</td>
<td>5.8 ± 0.3</td>
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<td>Dissemination Rate (%)</td>
<td>0</td>
<td>33</td>
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<tr>
<th>Non-ESV</th>
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<tr>
<td>Infection Rate</td>
<td>80%</td>
<td>87%</td>
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<tr>
<td>Virus Titer (PFUeq/mL)</td>
<td>1.5 ± 0.4</td>
<td>6.0 ± 0.7</td>
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<tr>
<td>Dissemination Rate (%)</td>
<td>0</td>
<td>67</td>
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Indications of Preliminary Studies

- More in depth studies needed to understand relationship between ESV and DENV
- Effects of different viral concentrations on each virus
- Effects of virus co-infections on mosquitoes of different mosquito species
- Possibilities of inducing antagonistic effects in viruses
- Ability to promote one virus over another
Future Implications

• Using mosquitoes infected with ‘harmless’ viruses to help with current vector control strategies

• *Wolbachia* infected mosquitoes
  • Studies using *Wolbachia* infected mosquitoes to induce pathogen interference and inhibit growth of pathogens such as Malaria

• Insect specific Flavivirus e.g. Palm Creek virus (PCV)
  • Palm Creek virus (Palm Creek Australia) initial studies showed prior infection of mosquito cells, suppressed replication of medically significant West Nile and Murray virus encephalitis

• Oxitec mosquitoes

• Genetically engineered mosquitoes to help with vector control
Questions?

ESV Mosquitoes
Gen. E. Tic
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