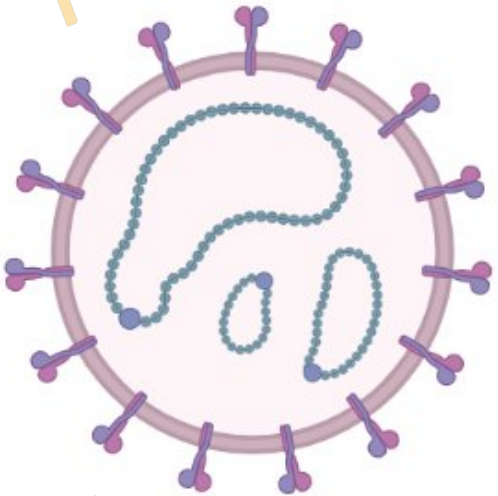
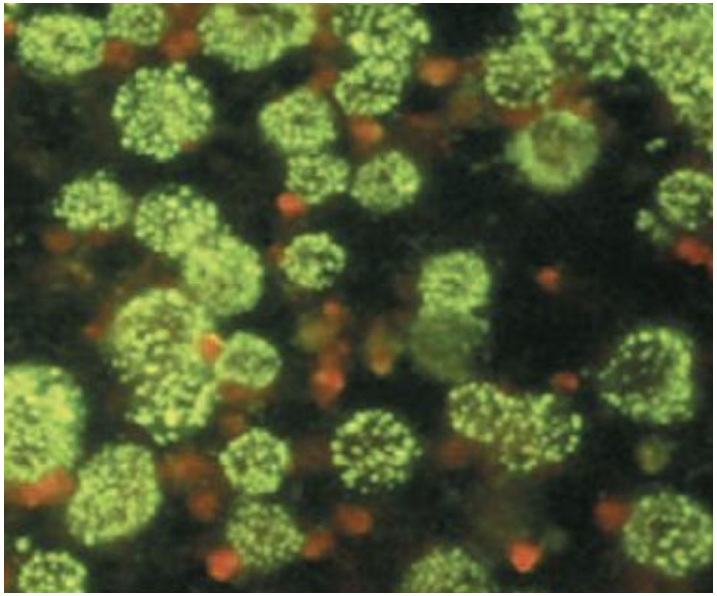


Biotechnology-based biocontrol of the invasive longhorned tick (*Haemaphysalis longicornis*)

SFTSV: a threat to public health



- **Severe Fever and Thrombocytopenia Virus** (SFTSV) is transmitted by Asian longhorned tick (*H. longicornis*)
  - 30%-40% mortality rate
  - Elderly and immunocompromised populations are susceptible
- Over 10,000 cases reported in Asia since 2011

SFTSV transmission

H. longicornis

Humans

Domesticated animals

H. Longicornis invasive in North America

Discovery of *Haemaphysalis longicornis* (Ixodida: Ixodidae) Parasitizing a Sheep in New Jersey, United States

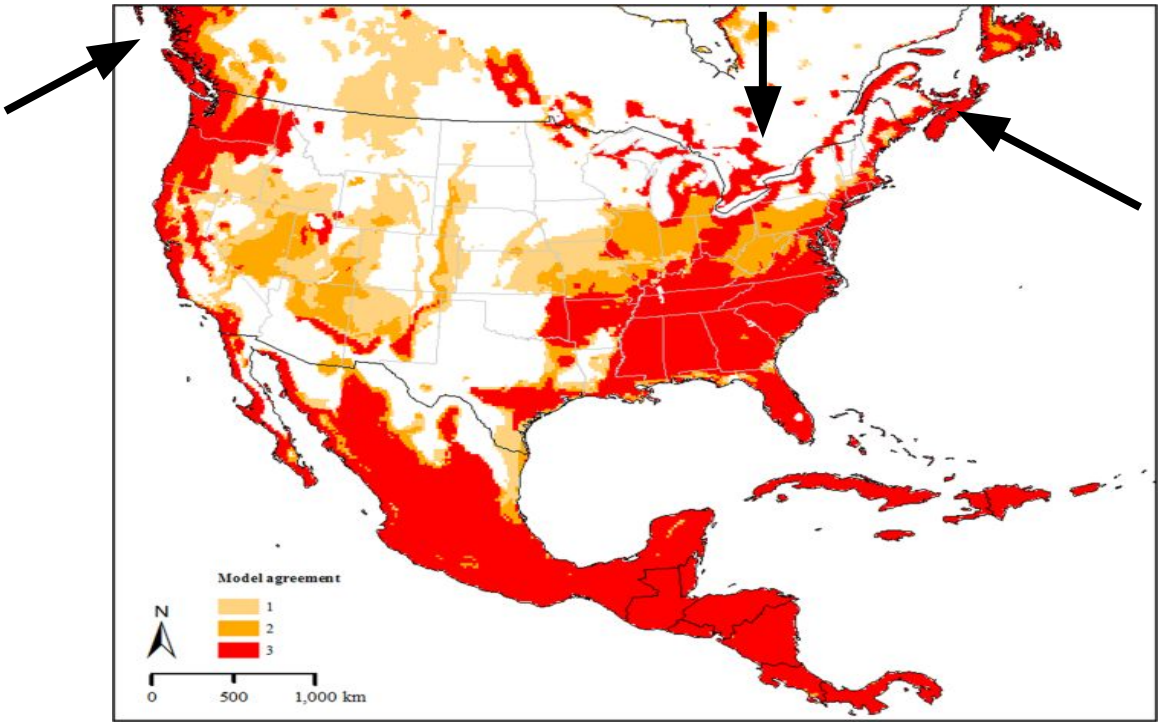
Tadhgh Rainey, James L Occi, Richard G Robbins, Andrea Egizi ✉

Journal of Medical Entomology, Volume 55, Issue 3, May 2018, Pages 757–759,
https://doi.org/10.1093/jme/tjy006
Published: 19 February 2018 **Article history** ▾

H. longicornis has spread to more than **8 states** in the US

(Beard et al. 2018)

Predicted Spatial Distribution Of *H. longicornis*

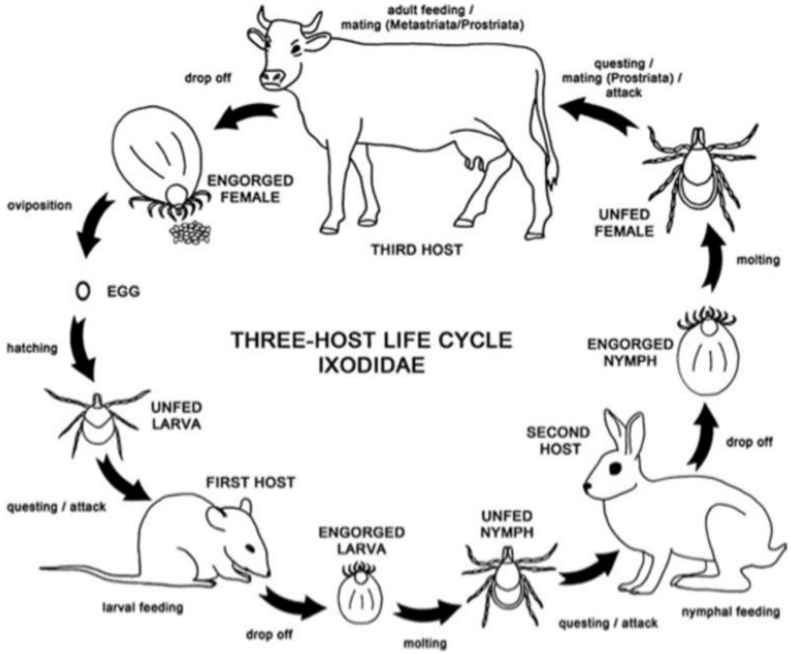


World Health Organization has classified SFTSV as a **prioritized pathogen**

(Ragnavan et al. 2019)

Reproduction of the Asian longhorned tick

- Is a **three host tick**
- Undergoes **two types** of reproduction
  - **Sexual** (mating between a male and female)
  - **Parthenogenic** (asexual reproduction of the female)



(Apanaskevich and Oliver, 2014)

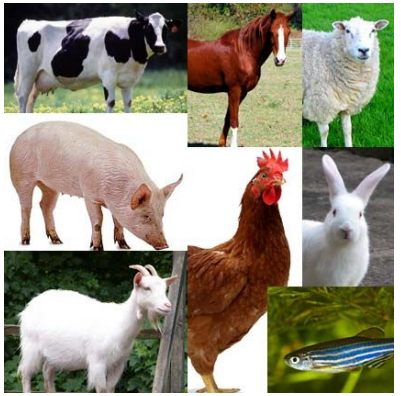
Economic losses

Livestock death

Decreased productivity

Lower working efficiency

Expenditure incurred for control



https://images.app.goo.gl/2dSrk5Pzzw2QZXxE8

- 80 % exposed to ticks-loss of $7.3/head/year
- 65% body weight reduction
- Cost of tick control $275.7 million/year

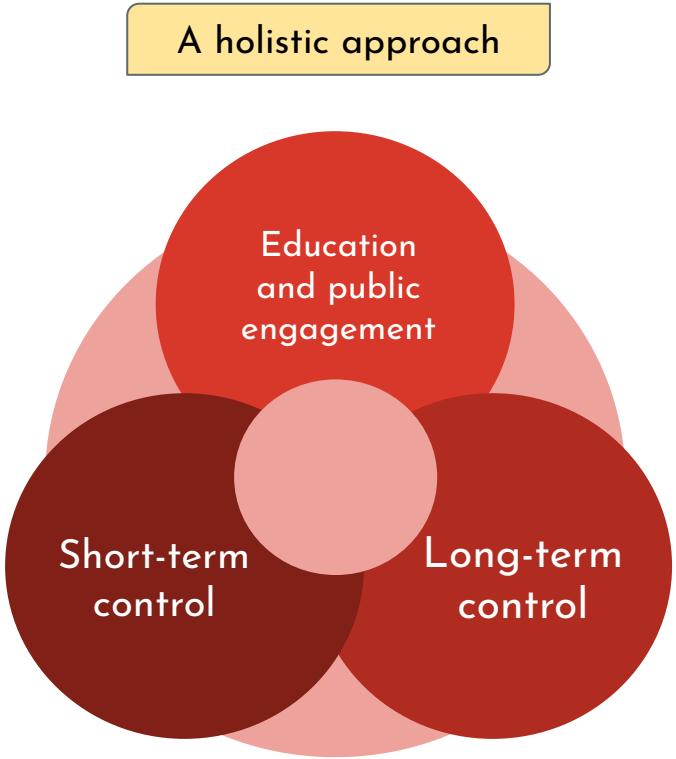
https://www.psi.org/publication/what-is-a-daly/

DALY= 10.55 per 100,000 population of netherland for lyme disease

DALY= 167.8 per 100,000 population of Slovenia for Tick borne encephalitis disease

How do we solve the problem?

- **Education**
- **Short-term strategies**
  - Surveillance
  - Pesticides
- **Long-term strategy**
  - Baculovirus-mediated control



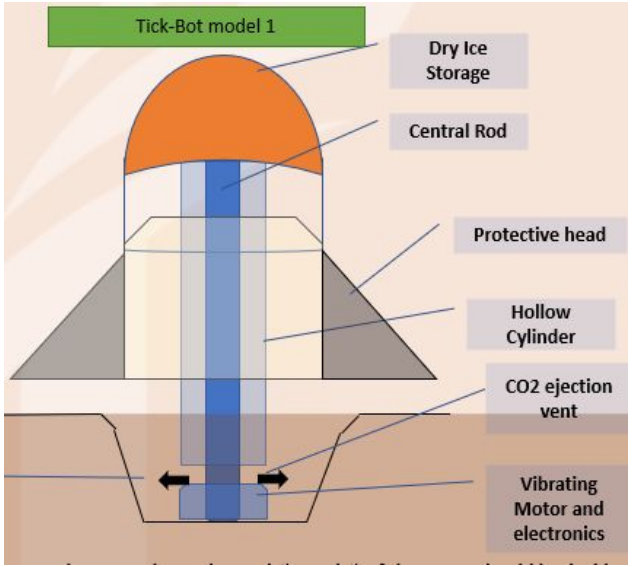
Education

- **Educate** the public
  - Personal Protective Equipment (PPE)
    - protective clothing, gloves, tick repellants, etc.
  - Self and peer checking for ticks
  - Proper yard mowing
  - High-risk areas
- **Information** dispersal
  - News segments
  - Advertisements

Short-term strategies

Surveillance

CO_2-baited traps



Chemical pesticides

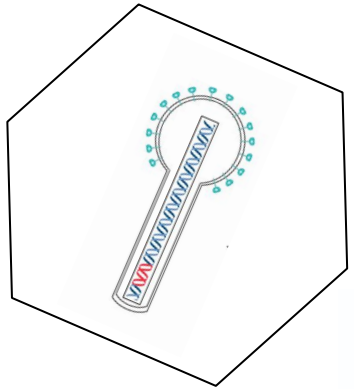
Lambda-cyhalothrin and Carbamate are EPA and Health-Canada approved for use against ticks

Source: http://tremorproject.onmason.com/2020/01/25/31/

Long-term control of Arthropod-borne Diseases

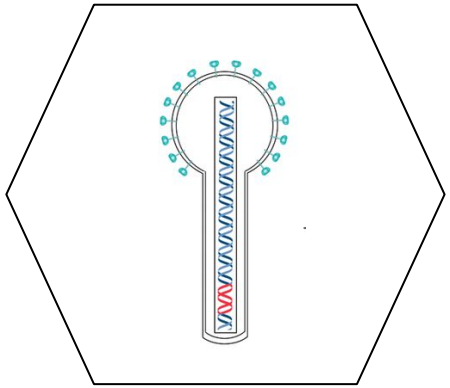
Biotechnology-based solutions

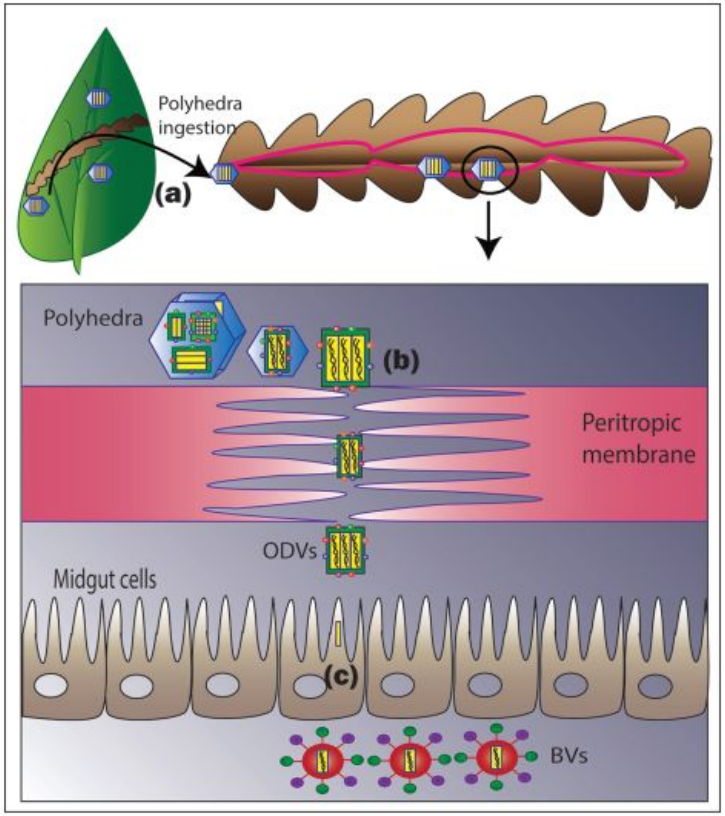
- Vaccines?
- Gene Drive ?
- Wolbachia ?
- **Baculoviruses** ✅
  - Insect Specific
  - Spread by many modes of action
  - Low environmental impact



Tick control via *in vivo* genome editing

Baculoviruses as delivery systems



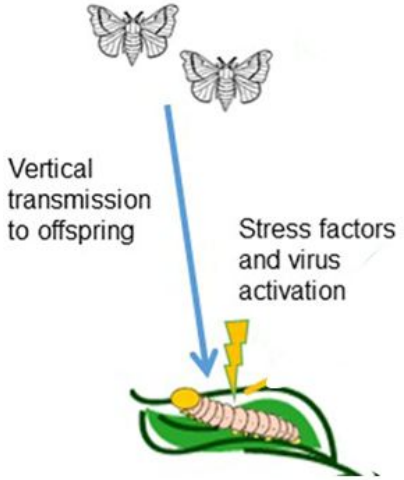


Baculoviruses transmission

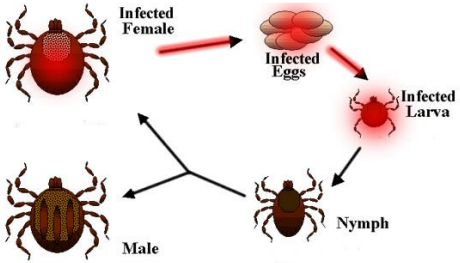
- Ingestion
- Spiracles
- Parasitism

- Mixed-model transmission.
- Insect population fluctuations.
- Secondary infection mechanisms (transovarial and transovum) and covert infection.
- Latency

Vertical



https://www.britannica.com/science/caterpillar



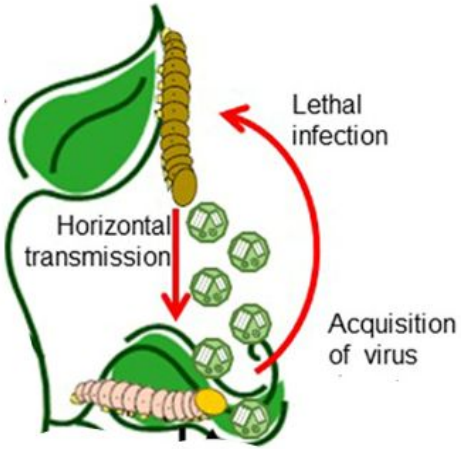
Transovarial transmission

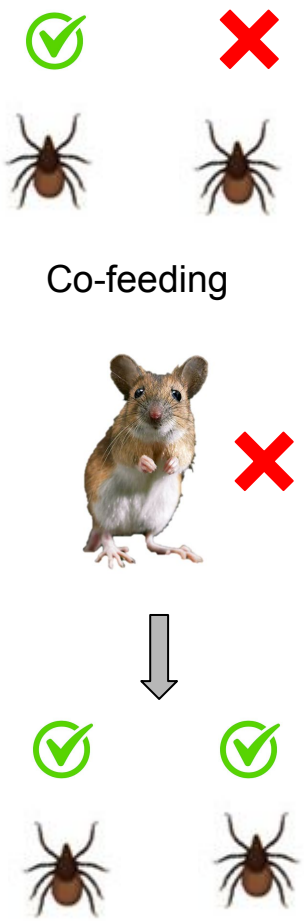
Williams et al. (2017)

Baculovirus Transmission

Ticks:

- Non-viraemic

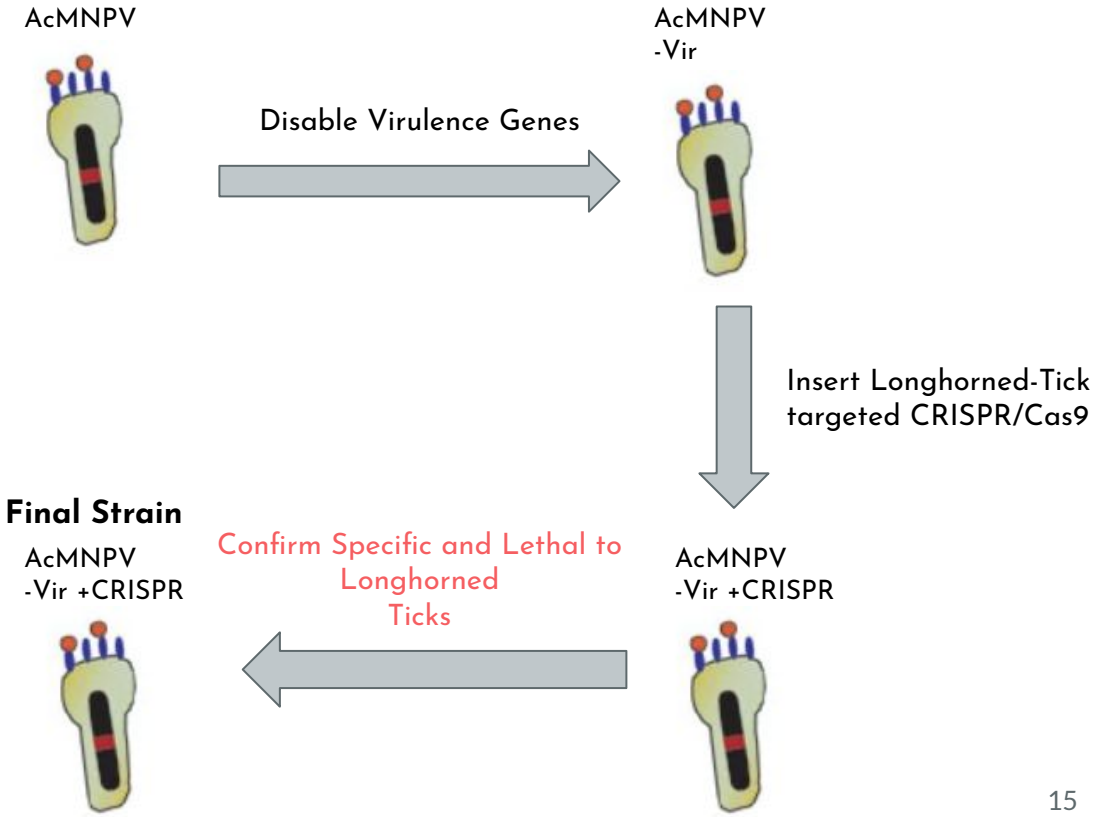




Horizontal

Generating a Longhorned-Tick Specific Baculovirus

- AcMNPV
- Disable Virulence
- Insert Cas9 Gene
- Confirm Lethal and Specific



Gene target candidates for ticks

Reproduction related genes-VgR, Follistatin related, Voraxin

https://animals.howstuffworks.com/arachnids/tick2.htm

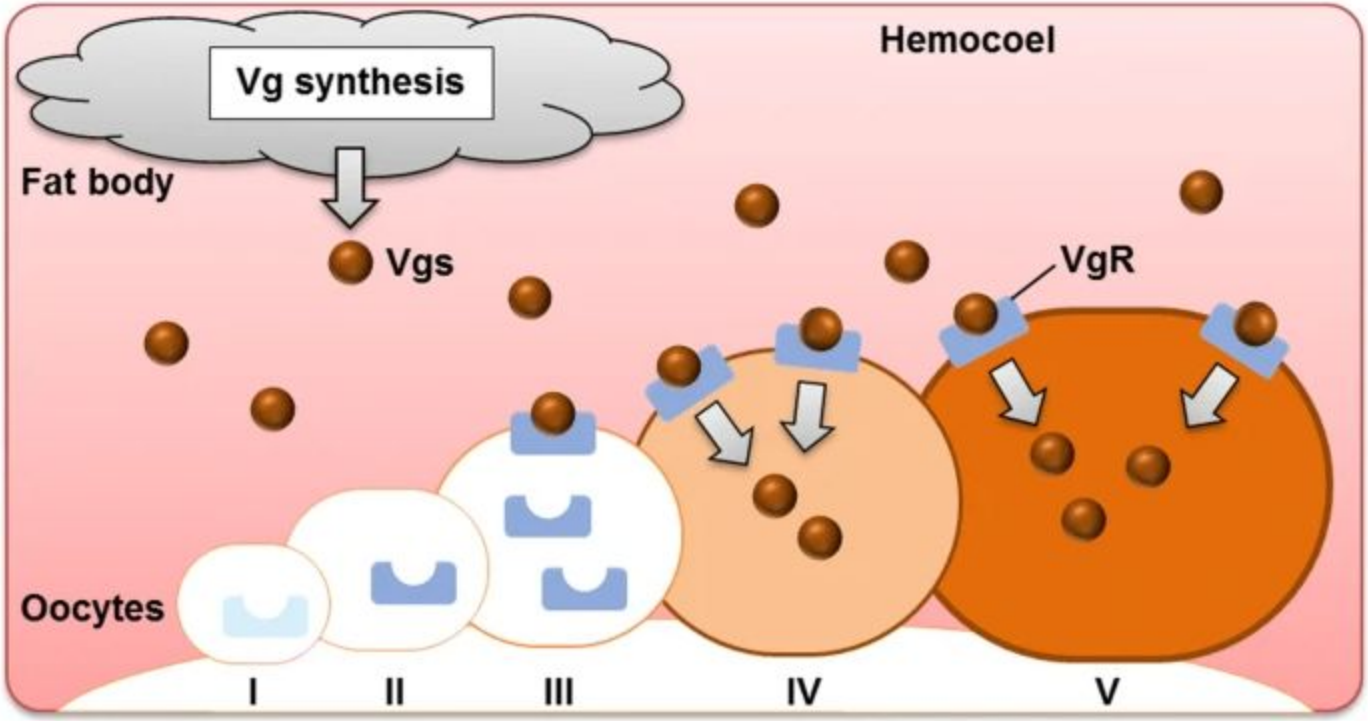
Genes related to feeding

https://images.app.goo.gl/wSpMQz5Ys8Vnx6DQ7

Genes related to structural and metabolic functions

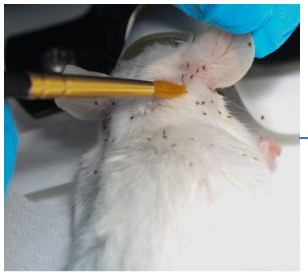
https://images.app.goo.gl/HyeLZG2SSUSqFXrd7

VgR as a gene target

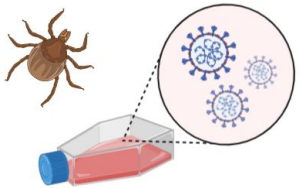


Umemiya-Shirafuji et al., 2019

Industrial Production of the Modified Baculovirus



Mass Rearing



Dip nymphal ticks in a viral cultural solution

Harvest Viral Load

- Spray high-risk areas
- Apply topically to livestock

Risk Assessment

Non-human	Humans	Other viruses
• No observable negative effects to birds, aquatic animals, and pollination bees	• No evidence of eye/skin irritation, chromosomal defects, or carcinogenicity • Slight oral toxicity observed at concentrations 1000x field rate	• Low risk of recombination to other viral species (heterologous recombination)

Regulatory framework for pesticides based on GM microorganisms

CANADA

•1993: Framework for the regulation of biotechnology.
•*Health Canada Pest Management Regulatory Agency (PMRA)* à **Pest Control Products Act (PCPA).**

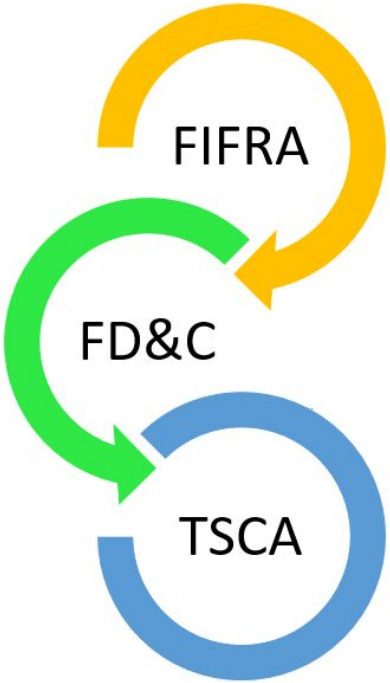
→ •"… including a product, and organism or substance derived through biotechnology…" (Pest Control Products Act, 2002).

The U.S

Environmental Protection Agency (EPA)
Food and Drug Administration (FDA)
U.S. Department of Agriculture (USDA)

→ *Autographa californica* multiple nucleopolyhedrovirus (AcMNPV) → No plant pathogen à Regulated by EPA

Regulatory framework for pesticides based on GM microorganisms

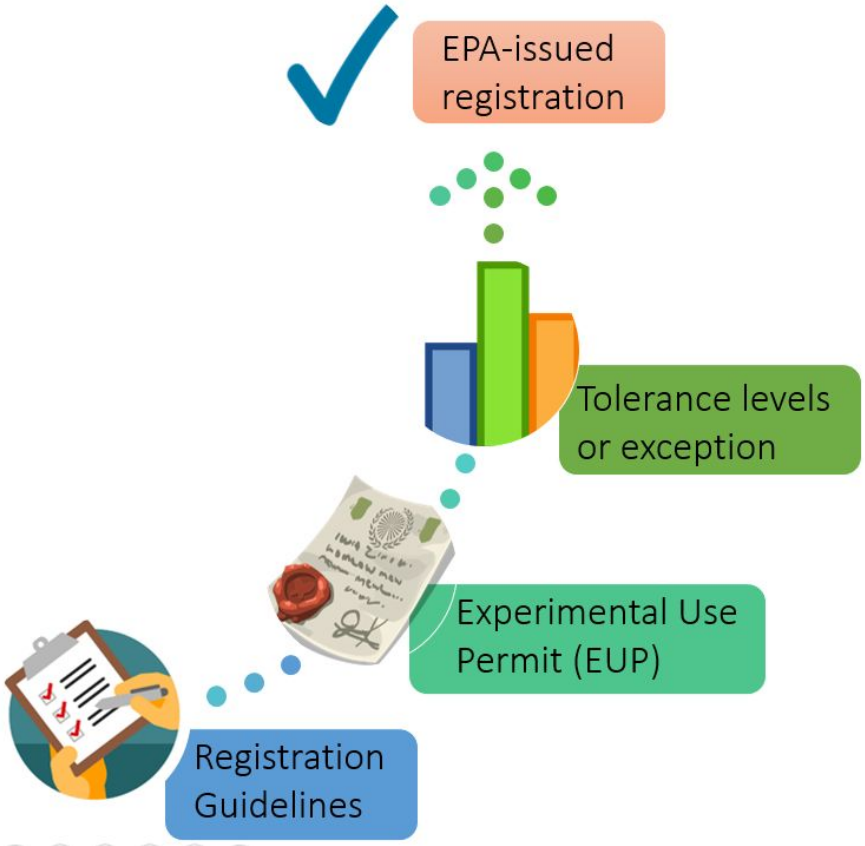


Federal Insecticide, Fungicide, and Rodenticide Act
- General regulation

Federal Food, Drug, and Cosmetic Act
- Residual levels of pesticides in food: Section 408

Toxic Substances Control Act
- Biotechnology products that are *new* organisms

Regulatory framework for pesticides based on GM microorganisms



- Supporting information, scientific reports.
- Techniques, vectors, manipulation, transformation, DNA sequences, description of the new traits or characteristics.

Engineered Baculovirus release

Velvetbean caterpillar
Soybean pest
Baculovirus released in Brazil

Cotton bollworm
Cotton pest
Baculovirus released in China

Rhinoceros beetle
Coconut palm pest
Baculovirus released in Samoa

Case Study: *Cydia pomonella* (codling moth)

- Pest to fruits
- Codling moth has developed resistance to leading chemical insecticides
  - Some studies indicate slight resistance to virus
- Baculovirus commercially available in North America and Europe since 2000

Previously released engineered baculoviruses

Pros	Cons
• High specificity to organism of interest • Effective long-term • Limited reapplication necessary	• Efficacy can be influenced by climate • Slow progress • Possible effect on surrounding ecosystem

“Accidental” Baculovirus-mediated biocontrol

- Spruce sawfly (*Diprion hercyniae*) introduced from Europe as an invasive species in Canada in early 1900s
- Baculovirus effective against spruce sawfly was accidentally brought into Canada in the 1930s
- No pest control has been required since

Public Perception: Integrated Pest Management

- Developed by the IPM Institute of North America
- Combines scientific and cultural information to facilitate decision-making process for pest management and pesticide use
- Works with public and governmental agencies, as well as private organizations and industry to value different opinions

Conclusions

- Asian longhorned tick is vector of **SFTSV**
  - Short and long-term strategies are necessary to **control spread**
- **Baculovirus** is a feasible long-term control strategy
  - Previous examples are **effective**
  - **Do not pose known risk** to humans or environment
  - **Clear regulatory framework** in Canada and U.S.
- **Public engagement** is vital for approval and adoption of this technology

Thank you!

Questions?