



Vestaron Peptide-Based Insecticides

Benefits of Bioinsecticides with the Performance of Synthetics

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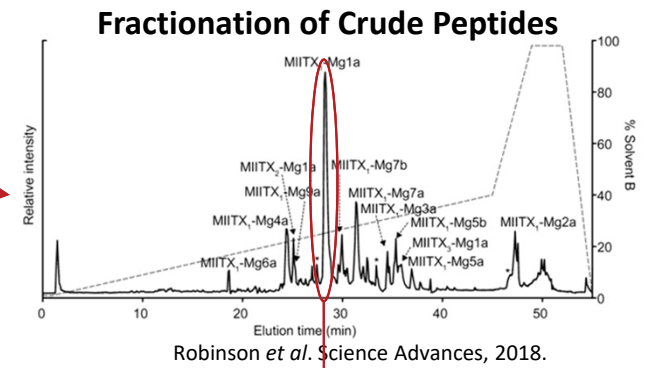
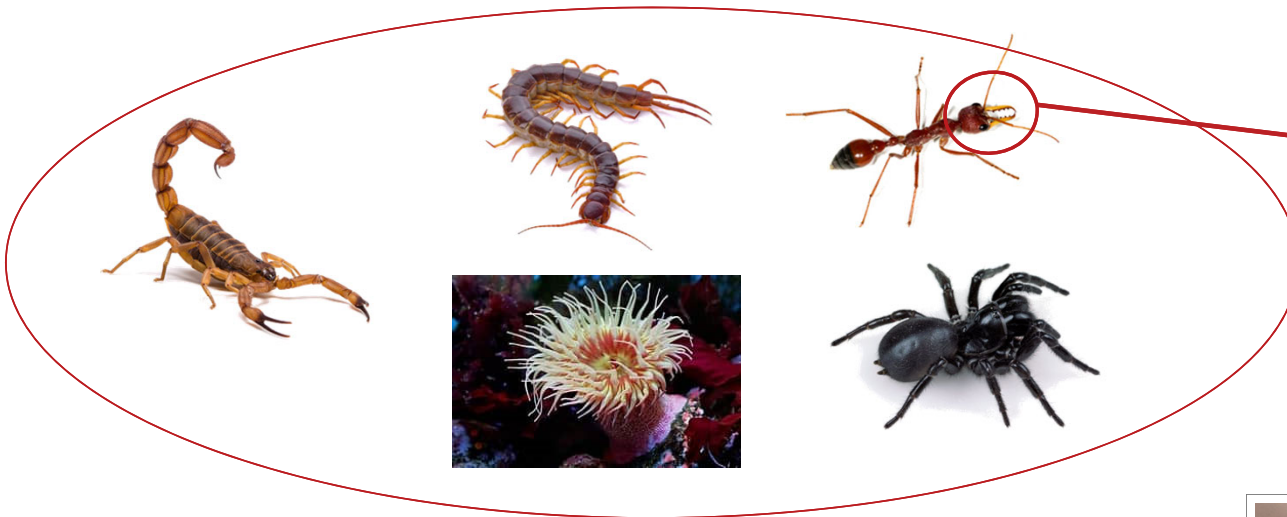
Vestaron appreciates involvement in previous and current IR-4 research projects

Selection of recent projects involving Vestaron products:

- IS00397-22
- IS00405-22
- IS00357-20
- IS00357-21



Where to start? **Nature: predators with bioactive venom**



Naturally occurring peptide



A peptide is selected for **engineering** into a new custom peptide for use as a **pesticide**

Animal venoms contain hundreds of different proteins/peptides

- ~~Digestive enzymes~~
- ~~Antimicrobial peptides~~
- ~~Defense peptides~~
- Insect-selective peptides

Through **proprietary production** techniques, Vestaron builds peptides to intensify potency, increase selectivity, and improve formulation and handling characteristics

- Isolate the active peptide
- **Optimize the peptide for potency and selectivity**
- Use a GMO-engineered yeast to produce the peptide with fermentation
- Filter out the yeast cells and concentrate the peptide
- Formulate and package
- Apply as any other product



Fermentation



Filtration & concentration



Spray drying
and
formulation



Package and
distribute

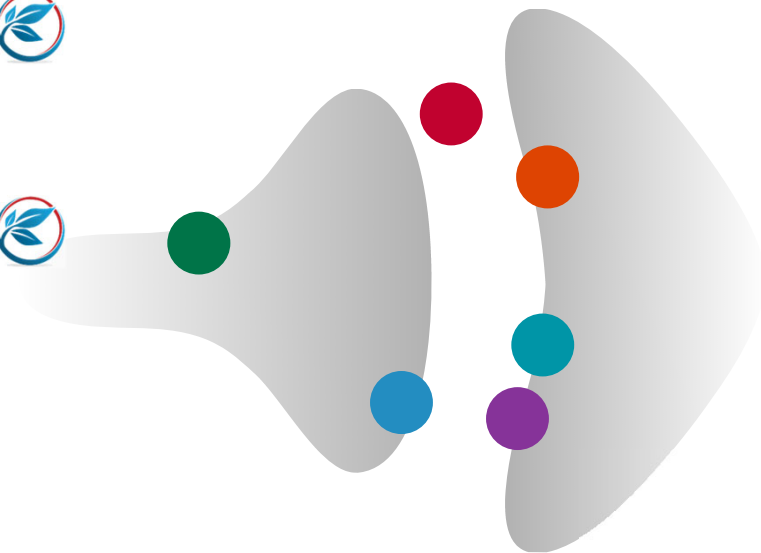


RECEPTOR TYPE	TRADITIONAL PESTICIDE CLASSES	GLOBAL SALES 2020 (\$18bn)
Nicotinic Acetylcholine Receptor	Neonicotinoids, Spinosyns	26%
Acetylcholinesterase	Carbamates, Organophosphates	17%
Voltage Gated Sodium Channel	Pyrethroids, DDT, Oxadiazines	13%
Ryanodine Receptor	Diamides	13%
Glutamate-Gated Receptor	Avermectins, Milbemycins	7%
Gaba-Gated Receptor	Cyclodienes, Fiproles	4%

VESTARON PRESENCE



Nerve or Muscle Receptor



Vestaron's pipeline offers the opportunity to "reset the resistance clock", addressing proven, multi-billion dollar receptor targets with safe and environmentally-friendly peptides

Commercial
 In-Development

SPEAR[®]-LEP



Specialty crops

SPEAR[®]-RC



Row crops

SPEAR[®]-T



Soft-bodied insects
Field and greenhouse

LEPROTEC[®]

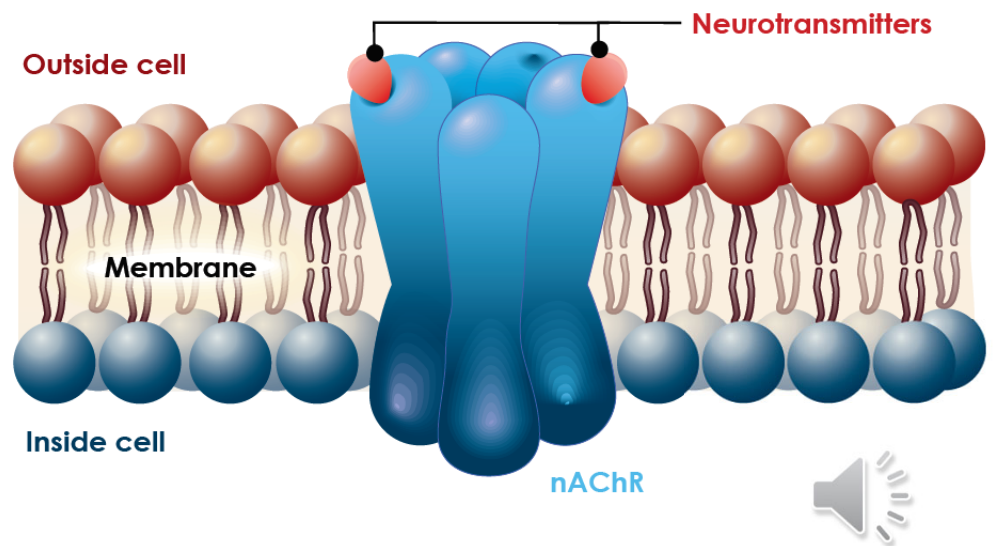


Liquid Btk facilitator

Attributes

Target site specificity

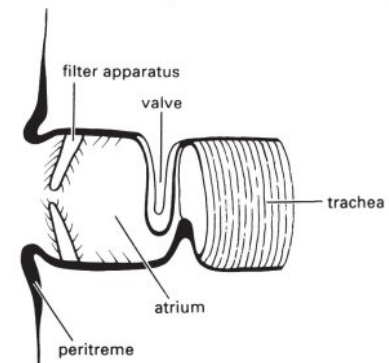
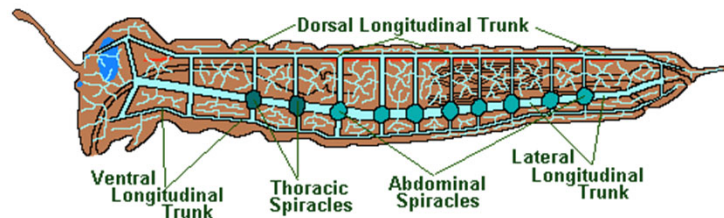
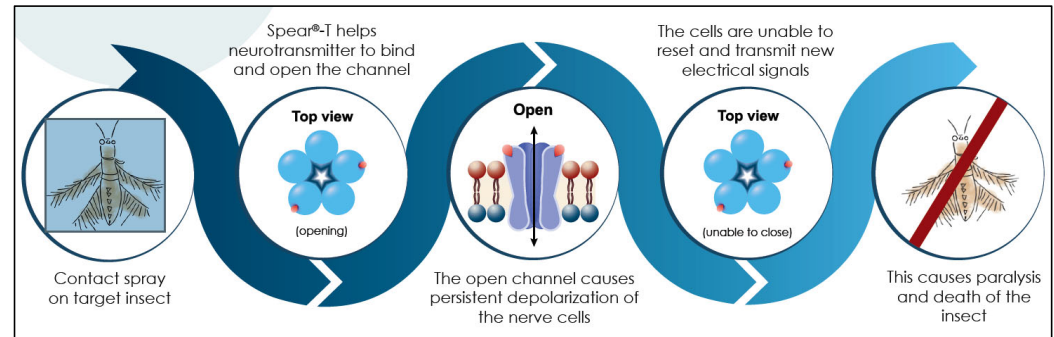
- Nicotinic Acetylcholine Receptor Allosteric Modulators - Site II
- **Binding site different from spinosyns and neonicotinoids**
- Awarded new IRAC Group 32 in Nov 2018
- The 14th neuromuscular IRAC group
- **Unique binding site allows Spear to control insects resistant to diamides, Spinosins, and neonicotinoids**



Contact – Through spiracles: Through spray covered is necessary

Soft Body Insects:

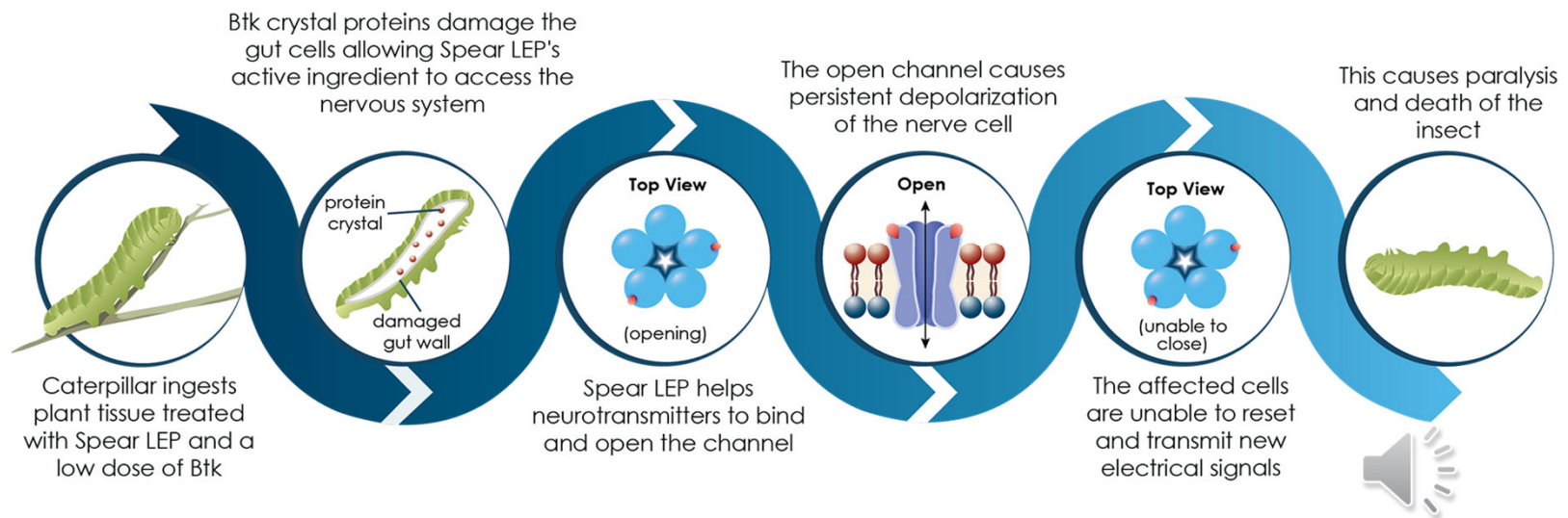
- Aphids,
- Whitefly,
- Thrips,
- Others (see Label)



Ingestion – combined with a sublethal dose of an active Bt for entry through the insect gut

Lepidopteran Insects:

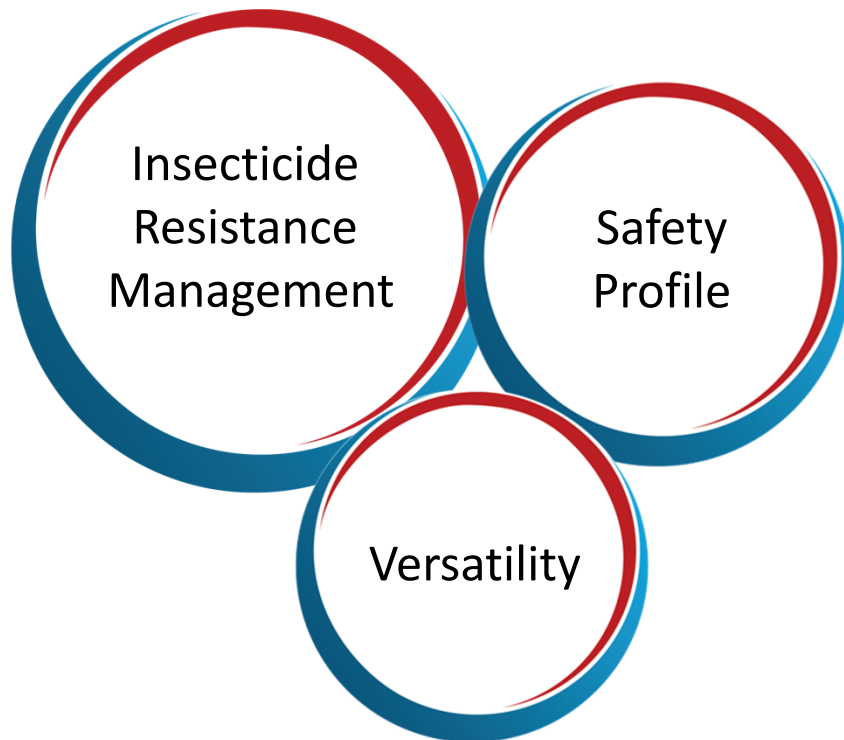
- Codling moth
- Loopers
- Leafrollers
- Diamond back moth
- Fruitworms
- Armyworms
- others (see Label)



Study	Result
Honey Bee Oral Toxicity (<i>Apis mellifera</i>)	LD ₅₀ (48-hour) > 100 µg ai/bee
Honey Bee Contact Toxicity (<i>Apis mellifera</i>)	LD ₅₀ (48 hour) > 25 µg ai/bee
Honey Bee Larval Toxicity (<i>Apis mellifera</i>)	LD ₅₀ (72 hour) > 68.60 µg ai/bee
Honey Bee Adult Chronic Dietary Toxicity (<i>Apis mellifera</i>)	LC ₅₀ > 5000 µg/kg, LDD ₅₀ > 132 µg ai/bee
Bumble Bee Acute Oral Toxicity (<i>Bombus impatiens</i>)	LD ₅₀ (48 hour) > 100 µg ai/bee
Solitary Bee Contact Toxicity (<i>Osmia bicornis</i>)	LD ₅₀ (48 hour) > 31.3 µg ai/bee

Spear® peptide shows no indication of acute or chronic toxicity in bees up to the highest dose levels tested





- **Safety Profile**
 - Biologically based
 - Worker, vertebrate, pollinator, residue safety
 - Little to no impact on natural enemies, no harmful residues
 - Low risk of plant phytotoxicity
- **Insecticide resistance management**
 - New IRAC group 32
 - No cross-resistance and no current resistance
 - Incorporation into rotations with other modes of action
- **Versatility**
 - 0-d PHI, 4-hr REI, MRL-exempt
 - 2-yr shelf life at room temp
 - Substitution for conventional products
 - Pre-harvest application for residue management
 - Tool for all external feeding lepidopteran species





BASIN[®]

FLEX

VESTARON[®]
THE POWER OF PEPTIDES™



Introducing Basin Flex

- Basin Flex is the 2nd generation peptide insecticide from Vestaron
- It exhibits excellent control of lepidopteran pests, with no off-target effects
- There is strong evidence supporting Basin Flex possesses yet another novel MoA. Currently under review by IRAC.

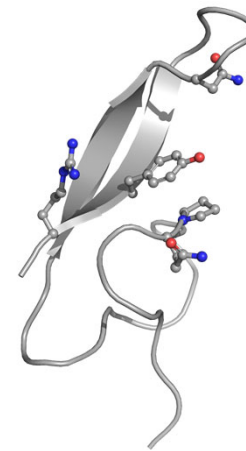
BASIN[®]
FLEX



EPDEICRARMNTNKEFTYKSNV**C**NN**C**GDQVAACEAE**C**FRNDVYT**C**HEAQKG

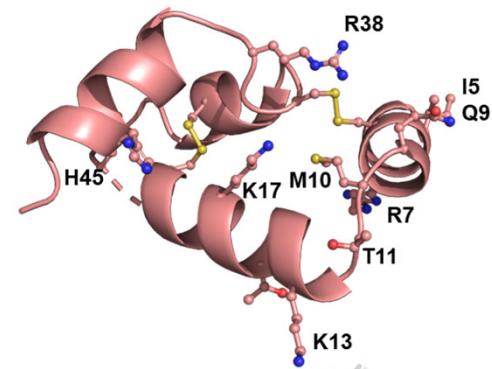
- The structure is a 3-disulfide stabilized helical bundle
- Isolated and characterized from Hobo Spider (family Agelenidae).
- Potent, broad-spectrum insecticide, particularly strong activity on lepidopteran and coleopteran pests.
- Can be manufactured at high titers in Vestaron's production platform.

ω/κ -HXTX-Hv1a



SPEAR-LEP

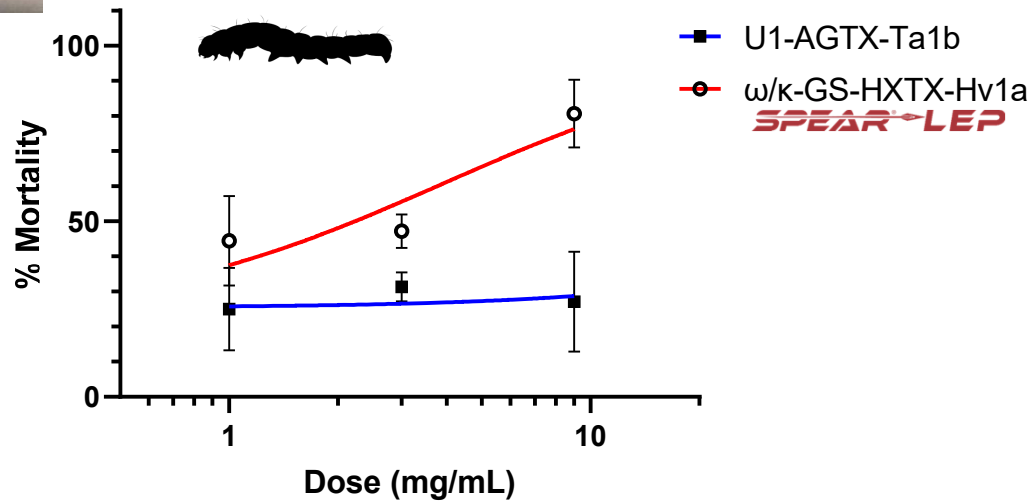
U1-AGTX-Ta1b



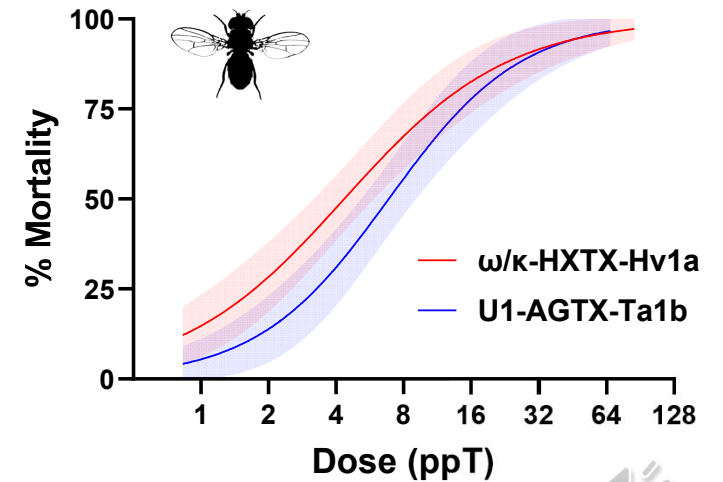
BASIN FLEX



CEW Leaf Disk Feeding Assay



Drosophila melanogaster Oral Activity



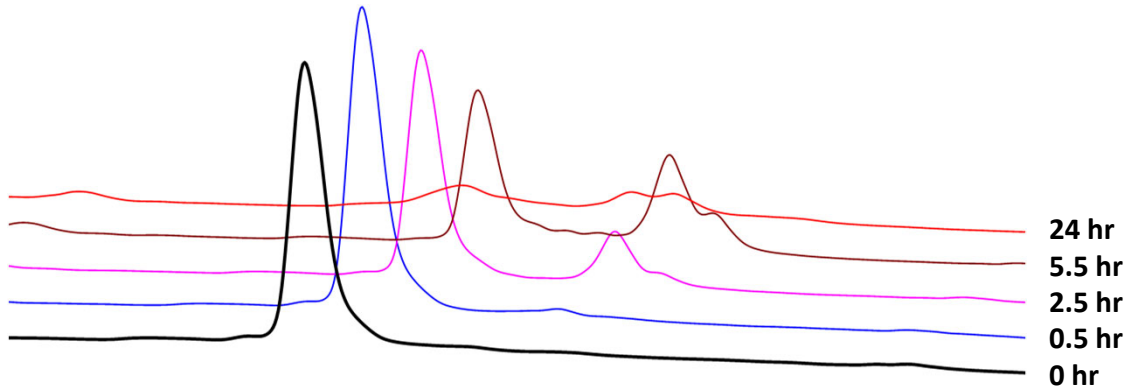
Ta1b lacks bioavailability in Lepidopterans (corn earworm) but not Dipterans (Fruit Fly)

Basin is Degraded by Trypsin-Like Proteases in the Insect Gut

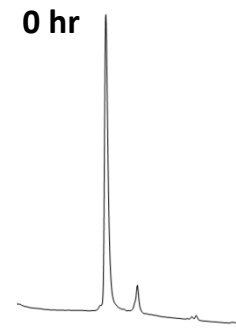


M. sexta (Tobacco hornworm)

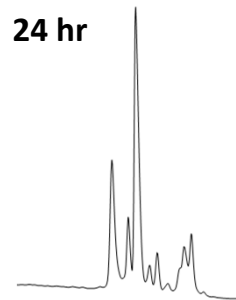
Tobacco Hornworm Gut Extract Digestion



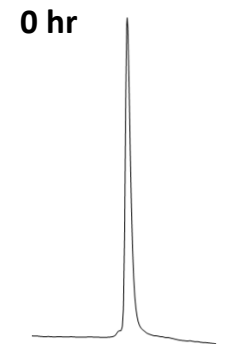
Bovine Trypsin



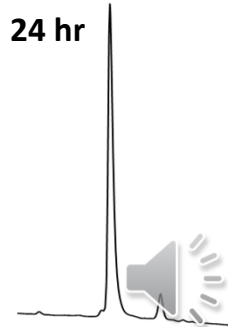
24 hr



Bovine Chymotrypsin

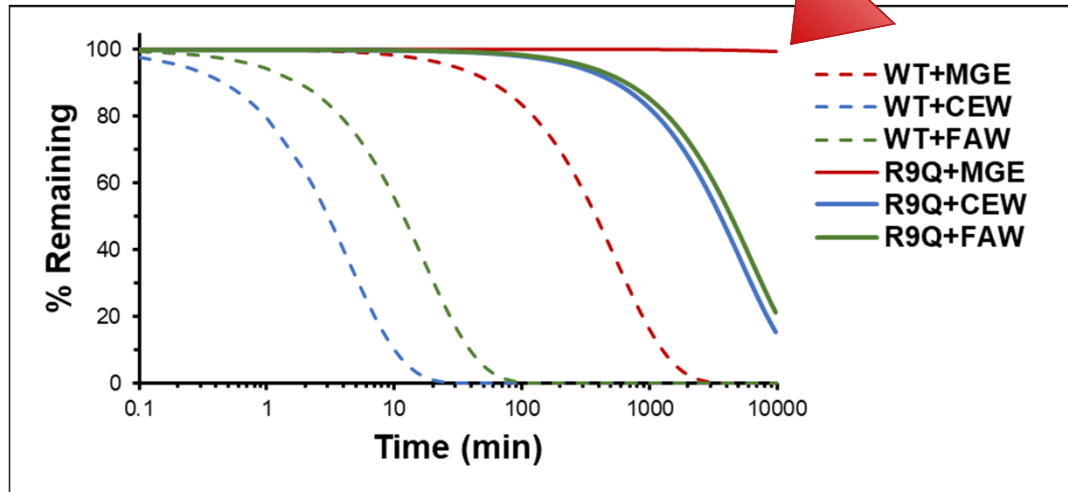


24 hr

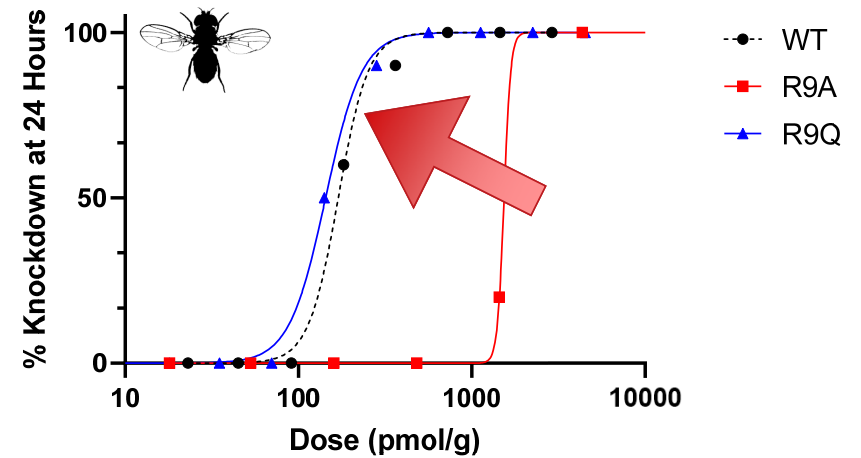


Basin is degraded by insect gut proteases, likely due to trypsin-like enzymes

In vitro Gut Extract Stability



Housefly Injections



Tobacco Hornworm (MGE)

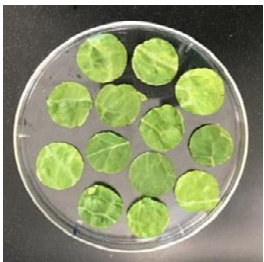


Fall Armyworm (FAW)

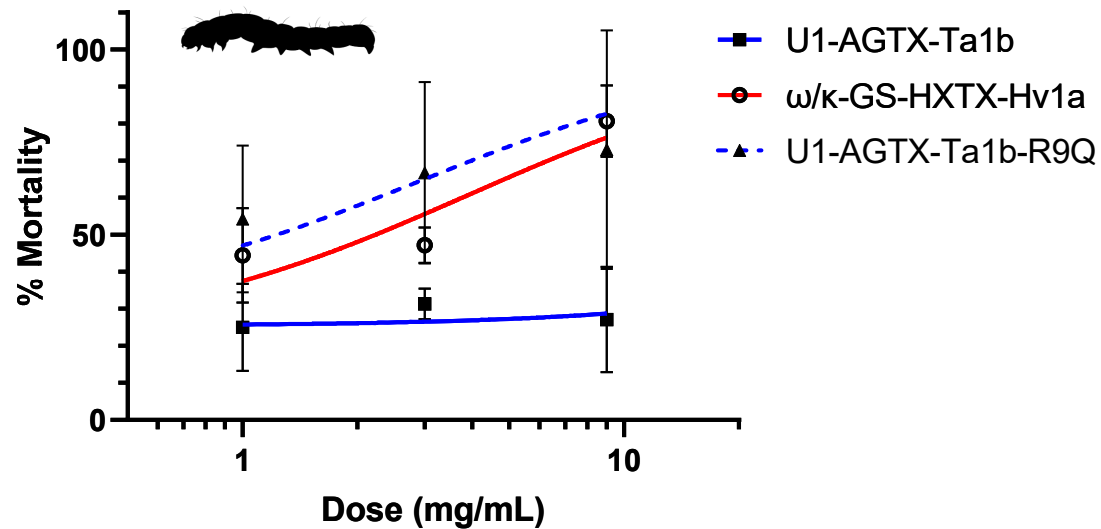


Corn Earworm (CEW)





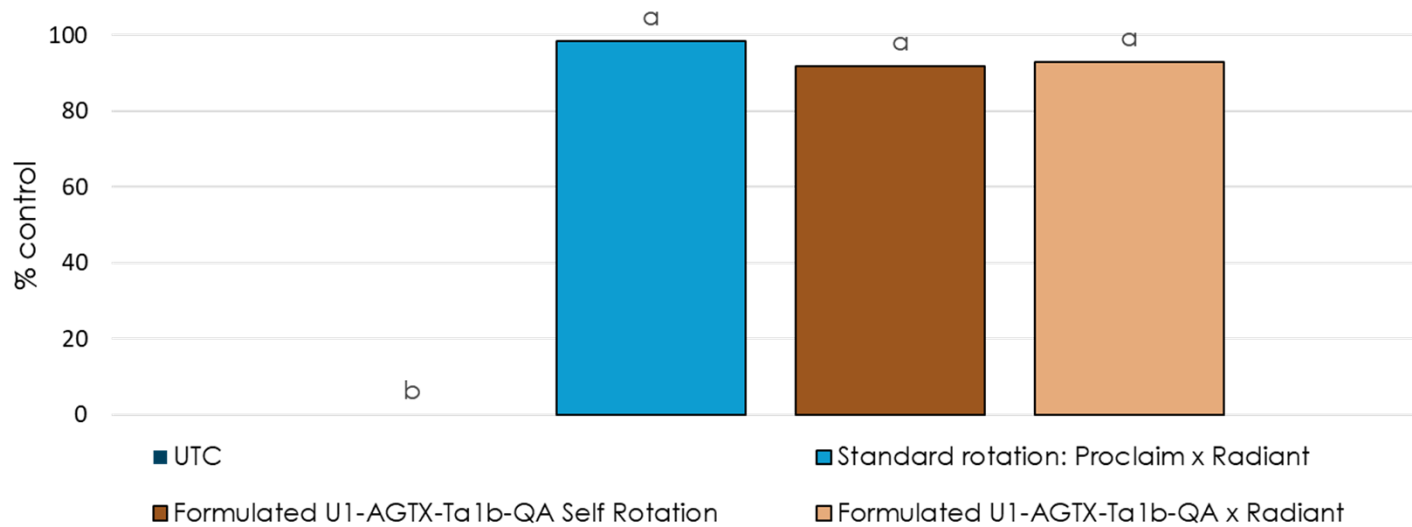
CEW Leaf Disk Feeding Assay



Stabilizing Basin to proteases results in orally bioavailable peptide



Percent control of larvae relative to UTC

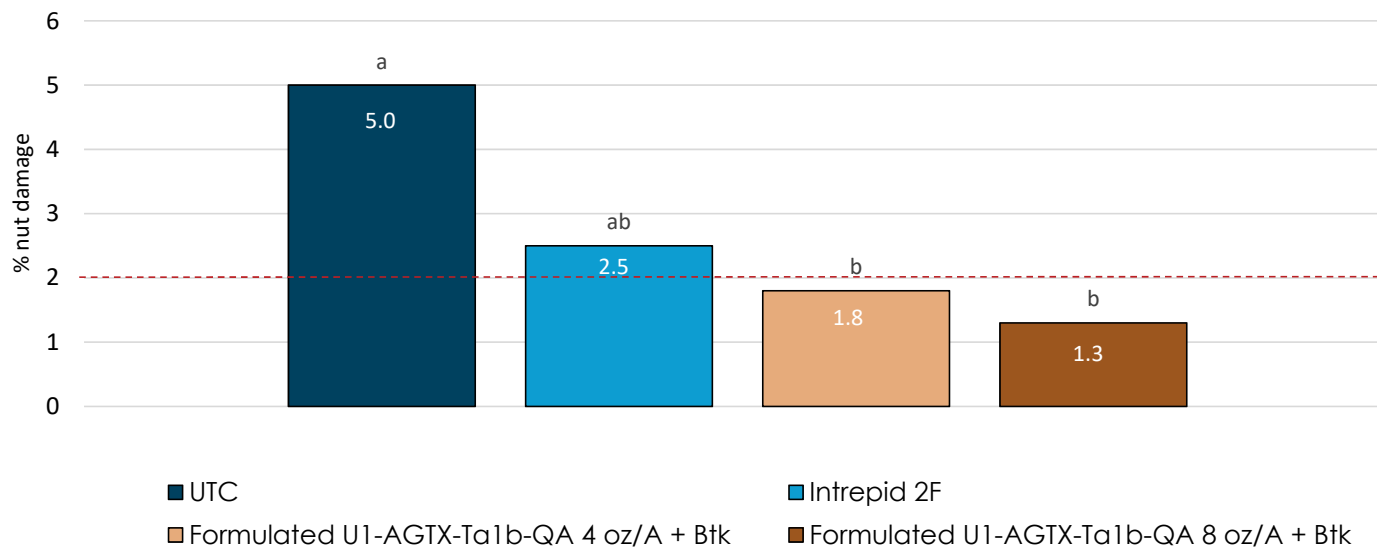


% control based on SAUDPC of total larvae counts
UTC SAUDPC = 1.77/5 leaves

Basin Flex shows commercial standard level of control in the field



Percent nut damage at harvest



Nut damage protection as good as industry standard
Numerical but not statistically-significant rate response



- Characterization and stabilization of **U1-AGTX-Ta1b** to trypsin-like proteases resulted in an orally active insecticide
- **Basin Flex** is currently under evaluation by EPA
- Expected initial commercial activity in 2024

BASIN®
FLEX



The Vestaron Pipeline

VST – 7300 (Basin) – Q4 2023

VST – 6700

VST – 7900

VST – 8400

VST – 8500

A rich pipeline of new, novel AIs with defined modes of action for insecticidal & fungicidal activity. **All new MOAs!**

