# MODE OF ACTION OF BACILLUS THURINGIENSIS (BT) CRY AND CYT TOXINS

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BS20B005

# BACILLUS THURINGIENSIS TOXINS

- Bacillus thuringiensis (Bt) is a gram-positive, spore-forming soil bacterium.
- Produces insecticidal parasporal crystal proteins (Cry and Cyt) during sporulation.
- Cry toxins: Highly specific and effective against insects in Lepidoptera, Coleoptera, Diptera, and nematodes.
- Cyt toxins: Show strong activity mainly against Dipteran larvae (e.g., mosquitoes).
- Mechanism: These toxins form pores in the insect midgut epithelium, leading to cell lysis and death.
- Advantages:
  - High specificity: Do not affect humans, vertebrates, or beneficial insects.
  - Environmentally safe and biodegradable.
  - Widely used in biopesticides and GM crops.

# TYPES, STRUCTURE, & EVOLUTION OF CRY

- Cry toxins are highly diverse: over 200 types in more than 50 subgroups.
- Three-domain structure:
  - Domain I: Composed of a-helices; responsible for membrane insertion and pore formation.
  - Domain II: β-sheet-rich; mediates binding to midgut receptors.
  - Domain III: β-sandwich structure; enhances receptor specificity and toxin stability.
- Evolution involves:
  - Independent domain evolution.
  - Swapping of domain III across toxins.
  - Result: Novel toxins with enhanced or dual specificities (e.g., active against both Lepidoptera and Coleoptera).
- Cry proteins resemble carbohydrate-binding modules, indicating possible receptor interaction through glycoconjugates.

# MODE OF ACTION : LEPIDOPTERAN INSECTS

- Bt Cry toxins exert toxicity via a multi-step process:
  - Ingestion: Larvae consume Bt spores and crystals.
  - Solubilization: Alkaline midgut environment dissolves crystal proteins.
  - Activation: Midgut proteases cleave protoxins (~130 kDa) to active toxins (~60-70 kDa).
  - Receptor Binding: Active toxin binds to receptors like Cadherin (Bt-R1), APN, ALP, and GCR on midgut epithelial cells.
  - Oligomerization: Toxin forms pre-pore structures, improving receptor binding.
  - Membrane Insertion: Oligomers insert into lipid rafts of microvilli, forming pores.
  - Cell Lysis and Death: Disruption of gut epithelium leads to septicemia and insect death.

# MODE OF ACTION : MOSQUITOES

- Cry toxins used: Cry4Aa, Cry4Ba, Cry11Aa. Cyt toxins: Cyt1Aa, Cyt2Ba.
- Activation: Proteolytic cleavage results in active fragments (e.g., Cry11Aa → 34 & 32 kDa).
- Receptors:
  - GPI-anchored alkaline phosphatase (ALP)
  - GPI-anchored aminopeptidase-N (APN)
- Cyt toxins:
  - Bind directly to membrane lipids; form pores or act detergent-like.
  - Function independently of protein receptors.
- Shared features with lepidopteran model:
  - Alkaline midgut pH.
  - Receptor diversity.
  - Oligomerization and pore formation.

# SYNERGISM OF CYT AND CRY TOXINS

- Cyt1Aa plays a pivotal role in delaying or preventing resistance in mosquitoes.
- Mechanism of synergism:
  - Cyt1Aa inserts into mosquito midgut membranes.
  - Functions as a receptor for Cry11Aa, enhancing its binding and pore formation.
- Evidence:
  - Cyt1Aa enhances Cry11Aa binding to Ae. aegypti midgut vesicles.
  - Mutagenesis studies confirm interaction via specific toxin regions (loop a8, b4, b6–aE).
- Importance:
  - Explains why mosquito resistance to Bti is rare.
  - Highlights the role of Cyt1Aa as both a toxin and co-receptor.

# APPLICATIONS AND FINAL REMARKS

- Agriculture:
  - Bt sprays for forest pests (e.g., spruce budworm).
  - Bt-transgenic crops (e.g., Bt cotton, maize): Express Cry proteins for continuous pest protection.
- Public Health:
  - Control of mosquito vectors (dengue, malaria, onchocerciasis) using Bti formulations, over 80% of West Africa uses Bti for blackfly control.
- Benefits:
  - Reduction in chemical insecticide use.
  - Environmentally sustainable pest management.
  - Long-term effectiveness with minimal resistance.
- Future Directions:
  - Discovery of new Cry toxins with novel specificities.
  - Structural studies of receptor-toxin interaction.
  - Development of next-gen bioinsecticides.

# THANK YOU