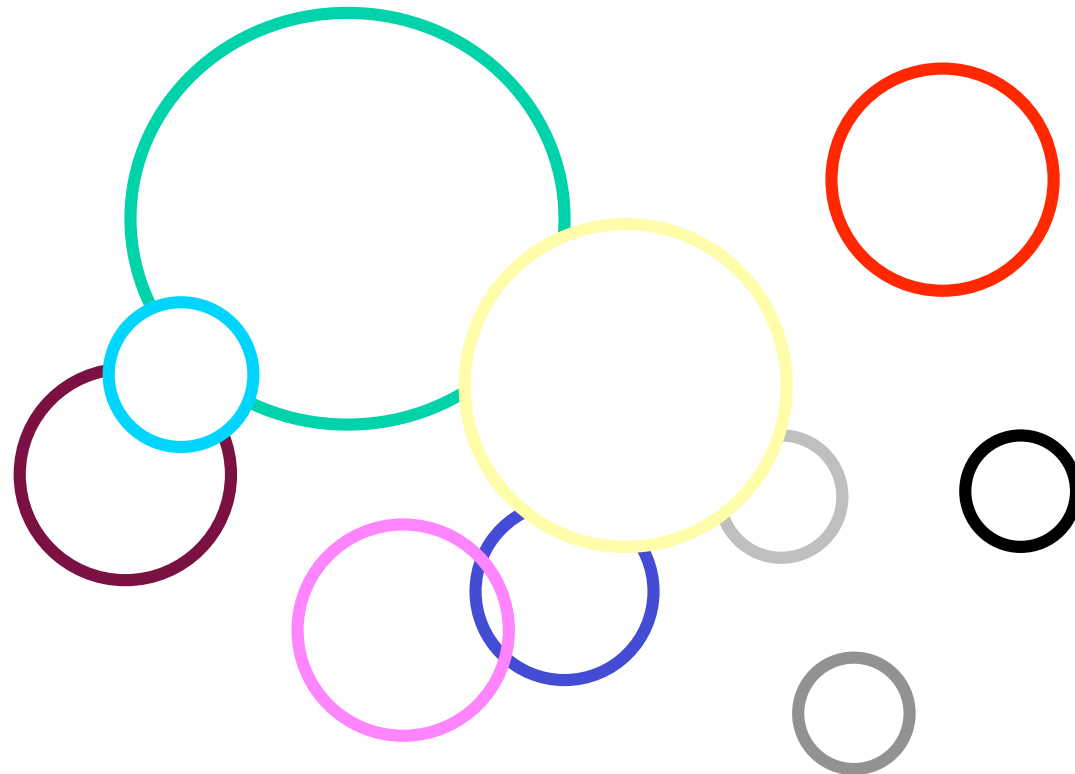


# Natural variation in *Bt* Cry toxins

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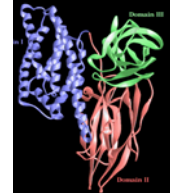


# The Bt toxins

Cry1Aa	Cry1Ab	Cry1Ac	Cry1Ad	Cry1Ae	Cry1Af	Cry1Ag	Cry1Ah	Cry1Ai	Cry1Ba
Cry1Bb	Cry1Bc	Cry1Bd	Cry1Be	Cry1Bf	Cry1Bg	Cry1Ca	Cry1Cb	Cry1Da	Cry1Db
Cry1Dc	Cry1Ea	Cry1Eb	Cry1Fa	Cry1Fb	Cry1Ga	Cry1Gb	Cry1Gc	Cry1Ha	Cry1Hb
Cry1Ia	Cry1Ib	Cry1Ic	Cry1Id	Cry1Ie	Cry1If	Cry1Ja	Cry1Jb	Cry1Jc	Cry1Jd
Cry1Ka	Cry1La	Cry2Aa	Cry2Ab	Cry2Ac	Cry2Ad	Cry2Ae	Cry2Af	Cry3Aa	Cry3Ba
Cry3Bb	Cry3Ca	Cry4Aa	Cry4Ba	Cry5Aa	Cry5Ab	Cry5Ac	Cry5Ad	Cry5Ba	Cry6Aa
Cry6Ba	Cry7Aa	Cry7Ab	Cry7Ba	Cry7Ca	Cry8Aa	Cry8Ba	Cry8Bb	Cry8Bc	Cry8Ca
Cry8Da	Cry8Ea	Cry8Fa	Cry8Ga	Cry8Ha	Cry9Aa	Cry9Ba	Cry9Bb	Cry9Ca	Cry9Da
Cry9Db	Cry9Ea	Cry9Eb	Cry9Ec	Cry9Ed	Cry10Aa	Cry11Aa	Cry11Ba	Cry11Bb	Cry12Aa
Cry13Aa	Cry14Aa	Cry15Aa	Cry16Aa	Cry17Aa	Cry18Aa	Cry18Ba	Cry18Ca	Cry19Aa	Cry19Ba
Cry20Aa	Cry21Aa	Cry21Ba	Cry22Aa	Cry22Ab	Cry22Ba	Cry23Aa	Cry24Aa	Cry24Ba	Cry24Ca
Cry25Aa	Cry26Aa	Cry27Aa	Cry28Aa	Cry29Aa	Cry30Aa	Cry30Ba	Cry30Ca	Cry30Da	Cry31Aa
Cry31Ab	Cry31Ac	Cry32Aa	Cry32Ba	Cry32Ca	Cry32Da	Cry33Aa	Cry34Aa	Cry34Ab	Cry34Ac
Cry34Ba	Cry35Aa	Cry35Ab	Cry35Ac	Cry35Ba	Cry36Aa	Cry37Aa	Cry38Aa	Cry39Aa	Cry40Aa
Cry40Ba	Cry41Aa	Cry41Ab	Cry42Aa	Cry43Aa	Cry43Ab	Cry43Ba	Cry44Aa	Cry45Aa	Cry46Aa
Cry46Ab	Cry47Aa	Cry48Aa	Cry48Ab	Cry49Aa	Cry49Ab	Cry50Aa	Cry51Aa		
Cyt1Aa	Cyt1Ab	Cyt1Ba	Cyt1Ca	Cyt2Aa	Cyt2Ba	Cyt2Bb	Cyt2Bc	Cyt2Ca	
Vip1Aa	Vip1Ab	Vip1Ba	Vip1Bb	Vip1Ca	Vip1Da				
Vip2Aa	Vip2Ab	Vip2Ac	Vip2Ad	Vip2Ba	Vip2Bb				
Vip3Aa	Vip3Ab	Vip3Ac	Vip3Ad	Vip3Ae	Vip3Af	Vip3Ag	Vip3Ah	Vip3Ba	Vip3Bb



# The 3-domain toxins



Cry1Aa	Cry1Ab	Cry1Ac	Cry1Ad	Cry1Ae	Cry1Af	Cry1Ag	Cry1Ah	Cry1Ai	Cry1Ba
Cry1Bb	Cry1Bc	Cry1Bd	Cry1Be	Cry1Bf	Cry1Bg	Cry1Ca	Cry1Cb	Cry1Da	Cry1Db
Cry1Dc	Cry1Ea	Cry1Eb	Cry1Fa	Cry1Fb	Cry1Ga	Cry1Gb	Cry1Gc	Cry1Ha	Cry1Hb
Cry1Ia	Cry1Ib	Cry1Ic	Cry1Id	Cry1Ie	Cry1If	Cry1Ja	Cry1Jb	Cry1Jc	Cry1Jd
Cry1Ka	Cry1La	Cry2Aa	Cry2Ab	Cry2Ac	Cry2Ad	Cry2Ae	Cry2Af	Cry3Aa	Cry3Ba
Cry3Bb	Cry3Ca	Cry4Aa	Cry4Ba	Cry5Aa	Cry5Ab	Cry5Ac	Cry5Ad	Cry5Ba	Cry6Aa
Cry6Ba	Cry7Aa	Cry7Ab	Cry7Ba	Cry7Ca	Cry8Aa	Cry8Ba	Cry8Bb	Cry8Bc	Cry8Ca
Cry8Da	Cry8Ea	Cry8Fa	Cry8Ga	Cry8Ha	Cry9Aa	Cry9Ba	Cry9Bb	Cry9Ca	Cry9Da
Cry9Db	Cry9Ea	Cry9Eb	Cry9Ec	Cry9Ed	Cry10Aa	Cry11Aa	Cry11Ba	Cry11Bb	Cry12Aa
Cry13Aa	Cry14Aa	Cry15Aa	Cry16Aa	Cry17Aa	Cry18Aa	Cry18Ba	Cry18Ca	Cry19Aa	Cry19Ba
Cry20Aa	Cry21Aa	Cry21Ba	Cry22Aa	Cry22Ab	Cry22Ba	Cry23Aa	Cry24Aa	Cry24Ba	Cry24Ca
Cry25Aa	Cry26Aa	Cry27Aa	Cry28Aa	Cry29Aa	Cry30Aa	Cry30Ba	Cry30Ca	Cry30Da	Cry31Aa
Cry31Ab	Cry31Ac	Cry32Aa	Cry32Ba	Cry32Ca	Cry32Da	Cry33Aa	Cry34Aa	Cry34Ab	Cry34Ac
Cry34Ba	Cry35Aa	Cry35Ab	Cry35Ac	Cry35Ba	Cry36Aa	Cry37Aa	Cry38Aa	Cry39Aa	Cry40Aa
Cry40Ba	Cry41Aa	Cry41Ab	Cry42Aa	Cry43Aa	Cry43Ab	Cry43Ba	Cry44Aa	Cry45Aa	Cry46Aa
Cry46Ab	Cry47Aa	Cry48Aa	Cry48Ab	Cry49Aa	Cry49Ab	Cry50Aa	Cry51Aa		
Cyt1Aa	Cyt1Ab	Cyt1Ba	Cyt1Ca	Cyt2Aa	Cyt2Ba	Cyt2Bb	Cyt2Bc	Cyt2Ca	
Vip1Aa	Vip1Ab	Vip1Ba	Vip1Bb	Vip1Ca	Vip1Da				
Vip2Aa	Vip2Ab	Vip2Ac	Vip2Ad	Vip2Ba	Vip2Bb				
Vip3Aa	Vip3Ab	Vip3Ac	Vip3Ad	Vip3Ae	Vip3Af	Vip3Ag	Vip3Ah	Vip3Ba	Vip3Bb

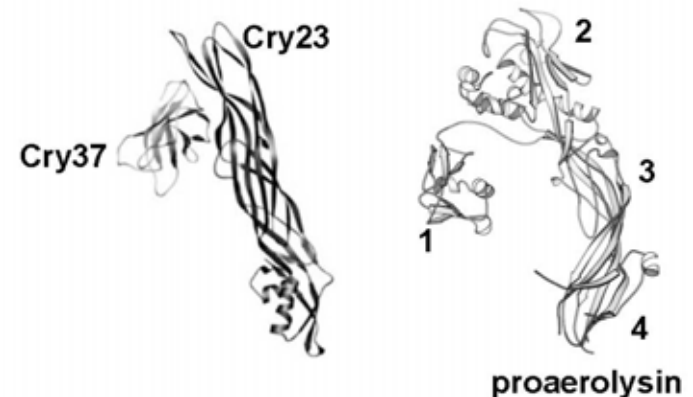
# The Mtx Group

Cry 1Aa	Cry 1Ab	Cry 1Ac	Cry 1Ad	Cry 1Ae	Cry 1Af	Cry 1Ag	Cry 1Ah	Cry 1Ai	Cry 1Ba
Cry 1Bb	Cry 1Bc	Cry 1Bd	Cry 1Be	Cry 1Bf	Cry 1Bg	Cry 1Ca	Cry 1Cb	Cry 1Da	Cry 1Db
Cry 1Dc	Cry 1Ea	Cry 1Eb	Cry 1Fa	Cry 1Fb	Cry 1Ga	Cry 1Gb	Cry 1Gc	Cry 1Ha	Cry 1Hb
Cry 1Ia	Cry 1Ib	Cry 1Ic	Cry 1Id	Cry 1Ie	Cry 1If	Cry 1Ja	Cry 1Jb	Cry 1Jc	Cry 1Jd
Cry 1Ka	Cry 1La	Cry 2Aa	Cry 2Ab	Cry 2Ac	Cry 2Ad	Cry 2Ae	Cry 2Af	Cry 3Aa	Cry 3Ba
Cry 3Bb	Cry 3Ca	Cry 4Aa	Cry 4Ba	Cry 5Aa	Cry 5Ab	Cry 5Ac	Cry 5Ad	Cry 5Ba	Cry 6Aa
Cry 6Ba	Cry 7Aa	Cry 7Ab	Cry 7Ba	Cry 7Ca	Cry 8Aa	Cry 8Ba	Cry 8Bb	Cry 8Bc	Cry 8Ca
Cry 8Da	Cry 8Ea	Cry 8Fa	Cry 8Ga	Cry 8Ha	Cry 9Aa	Cry 9Ba	Cry 9Bb	Cry 9Ca	Cry 9Da
Cry 9Db	Cry 9Ea	Cry 9Eb	Cry 9Ec	Cry 9Ed	Cry 10Aa	Cry 11A a	Cry 11Ba	Cry 11Bb	Cry 12A a
Cry 13Aa	Cry 14Aa	Cry 15Aa	Cry 16Aa	Cry 17Aa	Cry 18Aa	Cry 18Ba	Cry 18Ca	Cry 19Aa	Cry 19Ba
Cry 20Aa	Cry 21Aa	Cry 21Ba	Cry 22Aa	Cry 22Ab	Cry 22Ba	Cry 23Aa	Cry 24Aa	Cry 24Ba	Cry 24Ca
Cry 25Aa	Cry 26Aa	Cry 27Aa	Cry 28Aa	Cry 29Aa	Cry 30Aa	Cry 30Ba	Cry 30Ca	Cry 30Da	Cry 31Aa
Cry 31Ab	Cry 31Ac	Cry 32Aa	Cry 32Ba	Cry 32Ca	Cry 32Da	Cry 33Aa	Cry 34Aa	Cry 34Ab	Cry 34Ac
Cry 34Ba	Cry 35Aa	Cry 35Ab	Cry 35Ac	Cry 35Ba	Cry 36Aa	Cry 37Aa	Cry 38Aa	Cry 39Aa	Cry 40Aa
Cry 40Ba	Cry 41Aa	Cry 41Ab	Cry 42Aa	Cry 43Aa	Cry 43Ab	Cry 43Ba	Cry 44Aa	Cry 45Aa	Cry 46Aa
Cry 46Ab	Cry 47Aa	Cry 48Aa	Cry 48Ab	Cry 49Aa	Cry 49Ab	Cry 50Aa	Cry 51Aa		
Cyt1Aa	Cyt1Ab	Cyt1Ba	Cyt1Ca	Cyt2Aa	Cyt2Ba	Cyt2Bb	Cyt2Bc	Cyt2Ca	
Vip1Aa	Vip1Ab	Vip1Ba	Vip1Bb	Vip1Ca	Vip1Da				
Vip2Aa	Vip2Ab	Vip2Ac	Vip2Ad	Vip2Ba	Vip2Bb				
Vip3Aa	Vip3Ab	Vip3Ac	Vip3Ad	Vip3Ae	Vip3Af	Vip3Ag	Vip3Ah	Vip3Ba	Vip3Bb

# The Mtx Group

Mtx2 and Mtx3 are widely distributed among mosquitoicidal *Bacillus sphaericus* strains. They are related to each other and also to various other bacterial toxins such as the cytotoxin of *Pseudomonas aeruginosa*, the epsilon toxin of *Clostridium perfringens*, the alpha toxin of *Clostridium septicum* and aerolysin from *Aeromonas hydrophila*.

Cry23A resembles the Mtx toxins and is active against certain Coleoptera (eg boll weevil) but only in combination with the smaller Cry37 toxin. The structure of the Cry23/Cry37 complex resembles that of proaerolysin.



Other Bt toxins/proteins in this group include:

Cry15A + 40KDa	From <i>Bt thompsoni</i> both proteins required for crystallisation and full toxicity
Cry33A + NT32	Homologues of the <i>thompsoni</i> proteins
C53	From <i>Bt cameroun 273B</i> very little information available
Cry38	Isolated from Cry34/35 containing Bt strain – homologue of Cry23
Cry46	A parasporin with no known insecticidal activity
Cry51	Related to Cry15A and Cry33A – unknown toxicity

Note Mtx1 is not a member of this family – a putative ADP-ribosylation enzyme from *B. sphaericus*

# The Bin Group

Cry1Aa	Cry1Ab	Cry1Ac	Cry1Ad	Cry1Ae	Cry1Af	Cry1Ag	Cry1Ah	Cry1Ai	Cry1Ba
Cry1Bb	Cry1Bc	Cry1Bd	Cry1Be	Cry1Bf	Cry1Bg	Cry1Ca	Cry1Cb	Cry1Da	Cry1Db
Cry1Dc	Cry1Ea	Cry1Eb	Cry1Fa	Cry1Fb	Cry1Ga	Cry1Gb	Cry1Gc	Cry1Ha	Cry1Hb
Cry1Ia	Cry1Ib	Cry1Ic	Cry1Id	Cry1Ie	Cry1If	Cry1Ja	Cry1Jb	Cry1Jc	Cry1Jd
Cry1Ka	Cry1La	Cry2Aa	Cry2Ab	Cry2Ac	Cry2Ad	Cry2Ae	Cry2Af	Cry3Aa	Cry3Ba
Cry3Bb	Cry3Ca	Cry4Aa	Cry4Ba	Cry5Aa	Cry5Ab	Cry5Ac	Cry5Ad	Cry5Ba	Cry6Aa
Cry6Ba	Cry7Aa	Cry7Ab	Cry7Ba	Cry7Ca	Cry8Aa	Cry8Ba	Cry8Bb	Cry8Bc	Cry8Ca
Cry8Da	Cry8Ea	Cry8Fa	Cry8Ga	Cry8Ha	Cry9Aa	Cry9Ba	Cry9Bb	Cry9Ca	Cry9Da
Cry9Db	Cry9Ea	Cry9Eb	Cry9Ec	Cry9Ed	Cry10Aa	Cry11Aa	Cry11Ba	Cry11Bb	Cry12Aa
Cry13Aa	Cry14Aa	Cry15Aa	Cry16Aa	Cry17Aa	Cry18Aa	Cry18Ba	Cry18Ca	Cry19Aa	Cry19Ba
Cry20Aa	Cry21Aa	Cry21Ba	Cry22Aa	Cry22Ab	Cry22Ba	Cry23Aa	Cry24Aa	Cry24Ba	Cry24Ca
Cry25Aa	Cry26Aa	Cry27Aa	Cry28Aa	Cry29Aa	Cry30Aa	Cry30Ba	Cry30Ca	Cry30Da	Cry31Aa
Cry31Ab	Cry31Ac	Cry32Aa	Cry32Ba	Cry32Ca	Cry32Da	Cry33Aa	Cry34Aa	Cry34Ab	Cry34Ac
Cry34Ba	Cry35Aa	Cry35Ab	Cry35Ac	Cry35Ba	Cry36Aa	Cry37Aa	Cry38Aa	Cry39Aa	Cry40Aa
Cry40Ba	Cry41Aa	Cry41Ab	Cry42Aa	Cry43Aa	Cry43Ab	Cry43Ba	Cry44Aa	Cry45Aa	Cry46Aa
Cry46Ab	Cry47Aa	Cry48Aa	Cry48Ab	Cry49Aa	Cry49Ab	Cry50Aa	Cry51Aa		
Cyt1Aa	Cyt1Ab	Cyt1Ba	Cyt1Ca	Cyt2Aa	Cyt2Ba	Cyt2Bb	Cyt2Bc	Cyt2Ca	
Vip1Aa	Vip1Ab	Vip1Ba	Vip1Bb	Vip1Ca	Vip1Da				
Vip2Aa	Vip2Ab	Vip2Ac	Vip2Ad	Vip2Ba	Vip2Bb				
Vip3Aa	Vip3Ab	Vip3Ac	Vip3Ad	Vip3Ae	Vip3Af	Vip3Ag	Vip3Ah	Vip3Ba	Vip3Bb

# Binary Toxins

BinA and BinB are homologous proteins found in many strains of *Bacillus sphaericus*. Both toxins are required for full mosquitocidal activity although BinA has limited toxicity alone. BinA is believed to act as a pore-forming toxin whose binding to the cell surface is facilitated by BinB

Cry36Aa (ET69) shares significant sequence similarity with the Bin proteins, it was isolated from a *B. thuringiensis* strain and showed weak activity against western corn root worm. There is no evidence of there being a binary partner.

Cry34Aa1 – Cry35Aa1  
Cry34Aa2 – Cry35Aa2  
Cry34Aa3 – Cry35Aa3  
Cry34Aa4 – Cry35Aa4  
Cry34Ab1 – Cry35Ab1  
Cry34Ac1 – Cry35Ac1  
Cry34Ac2 – Cry35Ab2  
Cry34Ac3 – Cry35Ab3  
Cry34Ba1 – Cry35Ba1  
Cry34Ba2 – Cry35Ba2  
Cry34Ba3 – Cry35Ba3

## Cry34/35

The two genes encoding the binary pair are located together in an operon. The smaller Cry34 toxins show little or no activity themselves, the larger Cry35 toxins show limited toxicity towards the western corn rootworm. Both proteins are required for full toxicity.

Bacteria expressing these toxins are spread widely and are often found in locations in which the western corn rootworm is absent. Cry35Ab1 contains regions homologous to the beta-trefoil carbohydrate-binding domain found in other toxins such as ricin. Mechanism of action is believed to be that of pore-formation

## Cry48/49

Binary toxins isolated from *Bacillus sphaericus* with mosquitocidal activity. The Cry48 toxins are part of the three-domain group of Cry toxins, the Cry49 ones are related to the Bin group toxins. Full activity is only observed though if both proteins are present.

Cry48Aa1-Cry49Aa1  
Cry48Aa2-Cry49Aa2  
Cry48Aa3-Cry49Aa3  
Cry48Ab1-Cry49Ab1  
Cry49Ab2-Cry49Aa4

# The Cry6 Group

Cry1Aa	Cry1Ab	Cry1Ac	Cry1Ad	Cry1Ae	Cry1Af	Cry1Ag	Cry1Ah	Cry1Ai	Cry1Ba
Cry1Bb	Cry1Bc	Cry1Bd	Cry1Be	Cry1Bf	Cry1Bg	Cry1Ca	Cry1Cb	Cry1Da	Cry1Db
Cry1Dc	Cry1Ea	Cry1Eb	Cry1Fa	Cry1Fb	Cry1Ga	Cry1Gb	Cry1Gc	Cry1Ha	Cry1Hb
Cry1Ia	Cry1Ib	Cry1Ic	Cry1Id	Cry1Ie	Cry1If	Cry1Ja	Cry1Jb	Cry1Jc	Cry1Jd
Cry1Ka	Cry1La	Cry2Aa	Cry2Ab	Cry2Ac	Cry2Ad	Cry2Ae	Cry2Af	Cry3Aa	Cry3Ba
Cry3Bb	Cry3Ca	Cry4Aa	Cry4Ba	Cry5Aa	Cry5Ab	Cry5Ac	Cry5Ad	Cry5Ba	Cry6Aa
Cry6Ba	Cry7Aa	Cry7Ab	Cry7Ba	Cry7Ca	Cry8Aa	Cry8Ba	Cry8Bb	Cry8Bc	Cry8Ca
Cry8Da	Cry8Ea	Cry8Fa	Cry8Ga	Cry8Ha	Cry9Aa	Cry9Ba	Cry9Bb	Cry9Ca	Cry9Da
Cry9Db	Cry9Ea	Cry9Eb	Cry9Ec	Cry9Ed	Cry10Aa	Cry11Aa	Cry11Ba	Cry11Bb	Cry12Aa
Cry13Aa	Cry14Aa	Cry15Aa	Cry16Aa	Cry17Aa	Cry18Aa	Cry18Ba	Cry18Ca	Cry19Aa	Cry19Ba
Cry20Aa	Cry21Aa	Cry21Ba	Cry22Aa	Cry22Ab	Cry22Ba	Cry23Aa	Cry24Aa	Cry24Ba	Cry24Ca
Cry25Aa	Cry26Aa	Cry27Aa	Cry28Aa	Cry29Aa	Cry30Aa	Cry30Ba	Cry30Ca	Cry30Da	Cry31Aa
Cry31Ab	Cry31Ac	Cry32Aa	Cry32Ba	Cry32Ca	Cry32Da	Cry33Aa	Cry34Aa	Cry34Ab	Cry34Ac
Cry34Ba	Cry35Aa	Cry35Ab	Cry35Ac	Cry35Ba	Cry36Aa	Cry37Aa	Cry38Aa	Cry39Aa	Cry40Aa
Cry40Ba	Cry41Aa	Cry41Ab	Cry42Aa	Cry43Aa	Cry43Ab	Cry43Ba	Cry44Aa	Cry45Aa	Cry46Aa
Cry46Ab	Cry47Aa	Cry48Aa	Cry48Ab	Cry49Aa	Cry49Ab	Cry50Aa	Cry51Aa		
Cyt1Aa	Cyt1Ab	Cyt1Ba	Cyt1Ca	Cyt2Aa	Cyt2Ba	Cyt2Bb	Cyt2Bc	Cyt2Ca	
Vip1Aa	Vip1Ab	Vip1Ba	Vip1Bb	Vip1Ca	Vip1Da				
Vip2Aa	Vip2Ab	Vip2Ac	Vip2Ad	Vip2Ba	Vip2Bb				
Vip3Aa	Vip3Ab	Vip3Ac	Vip3Ad	Vip3Ae	Vip3Af	Vip3Ag	Vip3Ah	Vip3Ba	Vip3Bb

# The Cry6 Group

Consisting of just Cry6A and Cry6B – these were originally identified as nematocidal toxins although the toxicity of Cry6B to nematodes has not proved to be reproducible.

The toxins have no sequence similarity to any other Bt toxin although do appear homologous to various hypothetical proteins from *B. subtilis* and other bacteria.

A truncated form of Cry6A has reported activity against various Coleoptera including corn rootworm and alfalfa weevil.

# The Cry22 Group

Cry1Aa	Cry1Ab	Cry1Ac	Cry1Ad	Cry1Ae	Cry1Af	Cry1Ag	Cry1Ah	Cry1Ai	Cry1Ba
Cry1Bb	Cry1Bc	Cry1Bd	Cry1Be	Cry1Bf	Cry1Bg	Cry1Ca	Cry1Cb	Cry1Da	Cry1Db
Cry1Dc	Cry1Ea	Cry1Eb	Cry1Fa	Cry1Fb	Cry1Ga	Cry1Gb	Cry1Gc	Cry1Ha	Cry1Hb
Cry1Ia	Cry1Ib	Cry1Ic	Cry1Id	Cry1Ie	Cry1If	Cry1Ja	Cry1Jb	Cry1Jc	Cry1Jd
Cry1Ka	Cry1La	Cry2Aa	Cry2Ab	Cry2Ac	Cry2Ad	Cry2Ae	Cry2Af	Cry3Aa	Cry3Ba
Cry3Bb	Cry3Ca	Cry4Aa	Cry4Ba	Cry5Aa	Cry5Ab	Cry5Ac	Cry5Ad	Cry5Ba	Cry6Aa
Cry6Ba	Cry7Aa	Cry7Ab	Cry7Ba	Cry7Ca	Cry8Aa	Cry8Ba	Cry8Bb	Cry8Bc	Cry8Ca
Cry8Da	Cry8Ea	Cry8Fa	Cry8Ga	Cry8Ha	Cry9Aa	Cry9Ba	Cry9Bb	Cry9Ca	Cry9Da
Cry9Db	Cry9Ea	Cry9Eb	Cry9Ec	Cry9Ed	Cry10Aa	Cry11Aa	Cry11Ba	Cry11Bb	Cry12Aa
Cry13Aa	Cry14Aa	Cry15Aa	Cry16Aa	Cry17Aa	Cry18Aa	Cry18Ba	Cry18Ca	Cry19Aa	Cry19Ba
Cry20Aa	Cry21Aa	Cry21Ba	Cry22Aa	Cry22Ab	Cry22Ba	Cry23Aa	Cry24Aa	Cry24Ba	Cry24Ca
Cry25Aa	Cry26Aa	Cry27Aa	Cry28Aa	Cry29Aa	Cry30Aa	Cry30Ba	Cry30Ca	Cry30Da	Cry31Aa
Cry31Ab	Cry31Ac	Cry32Aa	Cry32Ba	Cry32Ca	Cry32Da	Cry33Aa	Cry34Aa	Cry34Ab	Cry34Ac
Cry34Ba	Cry35Aa	Cry35Ab	Cry35Ac	Cry35Ba	Cry36Aa	Cry37Aa	Cry38Aa	Cry39Aa	Cry40Aa
Cry40Ba	Cry41Aa	Cry41Ab	Cry42Aa	Cry43Aa	Cry43Ab	Cry43Ba	Cry44Aa	Cry45Aa	Cry46Aa
Cry46Ab	Cry47Aa	Cry48Aa	Cry48Ab	Cry49Aa	Cry49Ab	Cry50Aa	Cry51Aa		
Cyt1Aa	Cyt1Ab	Cyt1Ba	Cyt1Ca	Cyt2Aa	Cyt2Ba	Cyt2Bb	Cyt2Bc	Cyt2Ca	
Vip1Aa	Vip1Ab	Vip1Ba	Vip1Bb	Vip1Ca	Vip1Da				
Vip2Aa	Vip2Ab	Vip2Ac	Vip2Ad	Vip2Ba	Vip2Bb				
Vip3Aa	Vip3Ab	Vip3Ac	Vip3Ad	Vip3Ae	Vip3Af	Vip3Ag	Vip3Ah	Vip3Ba	Vip3Bb

# The Cry22 Group

The three members of this group were originally isolated on the basis of having activity against certain Hymenoptera, and in particular ants. Later Coleopteran activity was also found against corn rootworm and boll weevil.

No significant sequence similarities to other toxins

The structure of one of these proteins was solved at Monsanto revealing an elongated six domain protein including four cadherin-like domains and a C-terminal domain resembling domain III of the three-domain Cry toxins.

# The Vip toxins

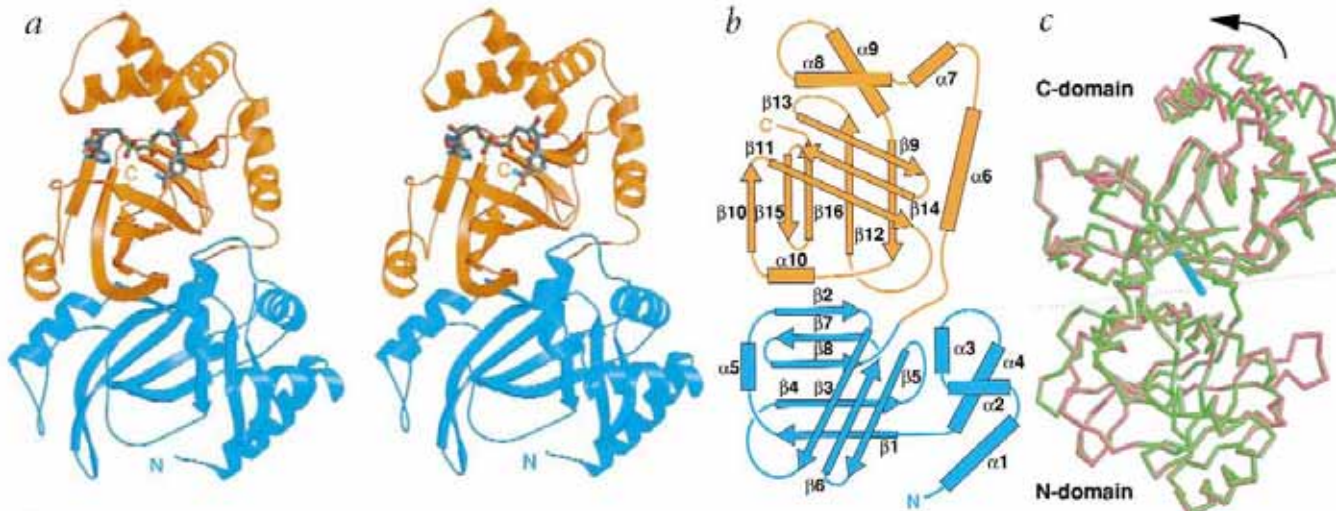
Cry1Ka	Cry1La	Cry2Aa	Cry2Ab	Cry2Ac	Cry2Ad	Cry2Ae	Cry2Af	Cry3Aa	Cry3Ba
Cry3Bb	Cry3Ca	Cry4Aa	Cry4Ba	Cry5Aa	Cry5Ab	Cry5Ac	Cry5Ad	Cry5Ba	Cry6Aa
Cry6Ba	Cry7Aa	Cry7Ab	Cry7Ba	Cry7Ca	Cry8Aa	Cry8Ba	Cry8Bb	Cry8Bc	Cry8Ca
Cry8Da	Cry8Ea	Cry8Fa	Cry8Ga	Cry8Ha	Cry9Aa	Cry9Ba	Cry9Bb	Cry9Ca	Cry9Da
Cry9Db	Cry9Ea	Cry9Eb	Cry9Ec	Cry9Ed	Cry10Aa	Cry11Aa	Cry11Ba	Cry11Bb	Cry12Aa
Cry13Aa	Cry14Aa	Cry15Aa	Cry16Aa	Cry17Aa	Cry18Aa	Cry18Ba	Cry18Ca	Cry19Aa	Cry19Ba
Cry20Aa	Cry21Aa	Cry21Ba	Cry22Aa	Cry22Ab	Cry22Ba	Cry23Aa	Cry24Aa	Cry24Ba	Cry24Ca
Cry25Aa	Cry26Aa	Cry27Aa	Cry28Aa	Cry29Aa	Cry30Aa	Cry30Ba	Cry30Ca	Cry30Da	Cry31Aa
Cry31Ab	Cry31Ac	Cry32Aa	Cry32Ba	Cry32Ca	Cry32Da	Cry33Aa	Cry34Aa	Cry34Ab	Cry34Ac
Cry34Ba	Cry35Aa	Cry35Ab	Cry35Ac	Cry35Ba	Cry36Aa	Cry37Aa	Cry38Aa	Cry39Aa	Cry40Aa
Cry40Ba	Cry41Aa	Cry41Ab	Cry42Aa	Cry43Aa	Cry43Ab	Cry43Ba	Cry44Aa	Cry45Aa	Cry46Aa
Cry46Ab	Cry47Aa	Cry48Aa	Cry48Ab	Cry49Aa	Cry49Ab	Cry50Aa	Cry51Aa		
Cyt1Aa	Cyt1Ab	Cyt1Ba	Cyt1Ca	Cyt2Aa	Cyt2Ba	Cyt2Bb	Cyt2Bc	Cyt2Ca	
Vip1Aa	Vip1Ab	Vip1Ba	Vip1Bb	Vip1Ca	Vip1Da				
Vip2Aa	Vip2Ab	Vip2Ac	Vip2Ad	Vip2Ba	Vip2Bb				
Vip3Aa	Vip3Ab	Vip3Ac	Vip3Ad	Vip3Ae	Vip3Af	Vip3Ag	Vip3Ah	Vip3Ba	Vip3Bb

# The Vip toxins

Discovered through screening the supernatant of vegetatively growing Bt strains for insecticidal activity

With no similarity to Cry toxins they were termed Vegetative Insecticidal Proteins (Vips)

Vip1 and Vip2 comprise a binary toxin of the classical AB type where Vip1 is the receptor-binding B domain and Vip2 the catalytic A domain. Vip2 has ADP-ribosylation activity with actin as the likely target. The toxin has activity against the corn rootworms. It has significant similarities to the iota toxin of *Clostridium perfringens* and the Cdt toxin of *C. difficile*.



## Vip3

The Vip3 toxins have Lepidopteran activity. Like Vip1/2 they are secreted during vegetative growth yet have no obvious signal sequence. Like the Cry toxins they seem to cause death via the formation of pores in the midgut epithelial cells.

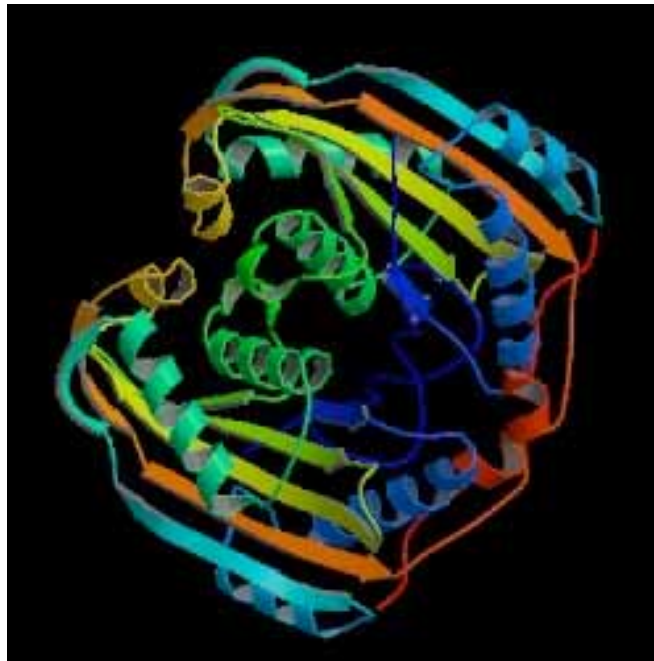
## Sip1

From Monsanto, a toxin secreted by Bt during vegetative growth – thus really a Vip toxin? Has coleopteran activity particularly against Colorado potato beetle. Some sequence similarity to the Mtx class of toxins including the *Pseudomonas aeruginosa* cytotoxin and the *Clostridium perfringens* alpha-toxin

# The Cyt Toxins

Specifically mosquitocidal in vivo they exhibit haemolytic and general cytolytic activity in vitro. Cyt1Aa is a major component of the Bti strain used extensively for mosquito control.

The toxins act either as a pore-formers or as a more general membrane detergent. It has been hypothesised that they can also act as receptors for other Bt toxins resulting in a synergistic interaction.



# The Parasporins

Cry 1Aa	Cry 1Ab	Cry 1Ac	Cry 1Ad	Cry 1Ae	Cry 1Af	Cry 1Ag	Cry 1Ah	Cry 1Ai	Cry 1Ba
Cry 1Bb	Cry 1Bc	Cry 1Bd	Cry 1Be	Cry 1Bf	Cry 1Bg	Cry 1Ca	Cry 1Cb	Cry 1Da	Cry 1Db
Cry 1Dc	Cry 1Ea	Cry 1Eb	Cry 1Fa	Cry 1Fb	Cry 1Ga	Cry 1Gb	Cry 1Gc	Cry 1Ha	Cry 1Hb
Cry 1Ia	Cry 1Ib	Cry 1Ic	Cry 1Id	Cry 1Ie	Cry 1If	Cry 1Ja	Cry 1Jb	Cry 1Jc	Cry 1Jd
Cry 1Ka	Cry 1La	Cry 2Aa	Cry 2Ab	Cry 2Ac	Cry 2Ad	Cry 2Ae	Cry 2Af	Cry 3Aa	Cry 3Ba
Cry 3Bb	Cry 3Ca	Cry 4Aa	Cry 4Ba	Cry 5Aa	Cry 5Ab	Cry 5Ac	Cry 5Ad	Cry 5Ba	Cry 6Aa
Cry 6Ba	Cry 7Aa	Cry 7Ab	Cry 7Ba	Cry 7Ca	Cry 8Aa	Cry 8Ba	Cry 8Bb	Cry 8Bc	Cry 8Ca
Cry 8Da	Cry 8Ea	Cry 8Fa	Cry 8Ga	Cry 8Ha	Cry 9Aa	Cry 9Ba	Cry 9Bb	Cry 9Ca	Cry 9Da
Cry 9Db	Cry 9Ea	Cry 9Eb	Cry 9Ec	Cry 9Ed	Cry 10Aa	Cry 11Aa	Cry 11Ba	Cry 11Bb	Cry 12Aa
Cry 13Aa	Cry 14Aa	Cry 15Aa	Cry 16Aa	Cry 17Aa	Cry 18Aa	Cry 18Ba	Cry 18Ca	Cry 19Aa	Cry 19Ba
Cry 20Aa	Cry 21Aa	Cry 21Ba	Cry 22Aa	Cry 22Ab	Cry 22Ba	Cry 23Aa	Cry 24Aa	Cry 24Ba	Cry 24Ca
Cry 25Aa	Cry 26Aa	Cry 27Aa	Cry 28Aa	Cry 29Aa	Cry 30Aa	Cry 30Ba	Cry 30Ca	Cry 30Da	Cry 31Aa
Cry 31Ab	Cry 31Ac	Cry 32Aa	Cry 32Ba	Cry 32Ca	Cry 32Da	Cry 33Aa	Cry 34Aa	Cry 34Ab	Cry 34Ac
Cry 34Ba	Cry 35Aa	Cry 35Ab	Cry 35Ac	Cry 35Ba	Cry 36Aa	Cry 37Aa	Cry 38Aa	Cry 39Aa	Cry 40Aa
Cry 40Ba	Cry 41Aa	Cry 41Ab	Cry 42Aa	Cry 43Aa	Cry 43Ab	Cry 43Ba	Cry 44Aa	Cry 45Aa	Cry 46Aa
Cry 46Ab	Cry 47Aa	Cry 48Aa	Cry 48Ab	Cry 49Aa	Cry 49Ab	Cry 50Aa	Cry 51Aa		
Cyt 1Aa	Cyt 1Ab	Cyt 1Ba	Cyt 1Ca	Cyt 2Aa	Cyt 2Ba	Cyt 2Bb	Cyt 2Bc	Cyt 2Ca	
Vip 1Aa	Vip 1Ab	Vip 1Ba	Vip 1Bb	Vip 1Ca	Vip 1Da				
Vip 2Aa	Vip 2Ab	Vip 2Ac	Vip 2Ad	Vip 2Ba	Vip 2Bb				
Vip 3Aa	Vip 3Ab	Vip 3Ac	Vip 3Ad	Vip 3Ae	Vip 3Af	Vip 3Ag	Vip 3Ah	Vip 3Ba	Vip 3Bb

# The Parasporins

From the labs of Fukuoka, Japan

Solubilised and protease treated crystals from a wide variety of Bt strains were tested for activity against human T-cells from leukaemic and non-leukaemic sources.

In an initial screen 60/1744 strains showed activity against leukaemia cells

16 of these 60 had a general cytolytic activity as measured by haemolysis

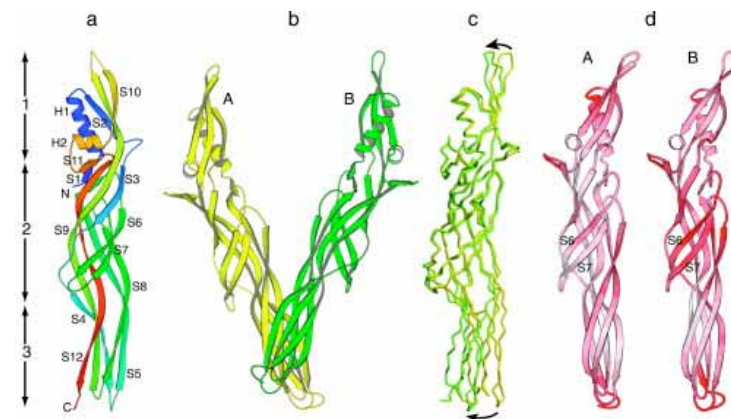
42 were non-haemolytic, none showed activity against 11 insects from 5 different orders

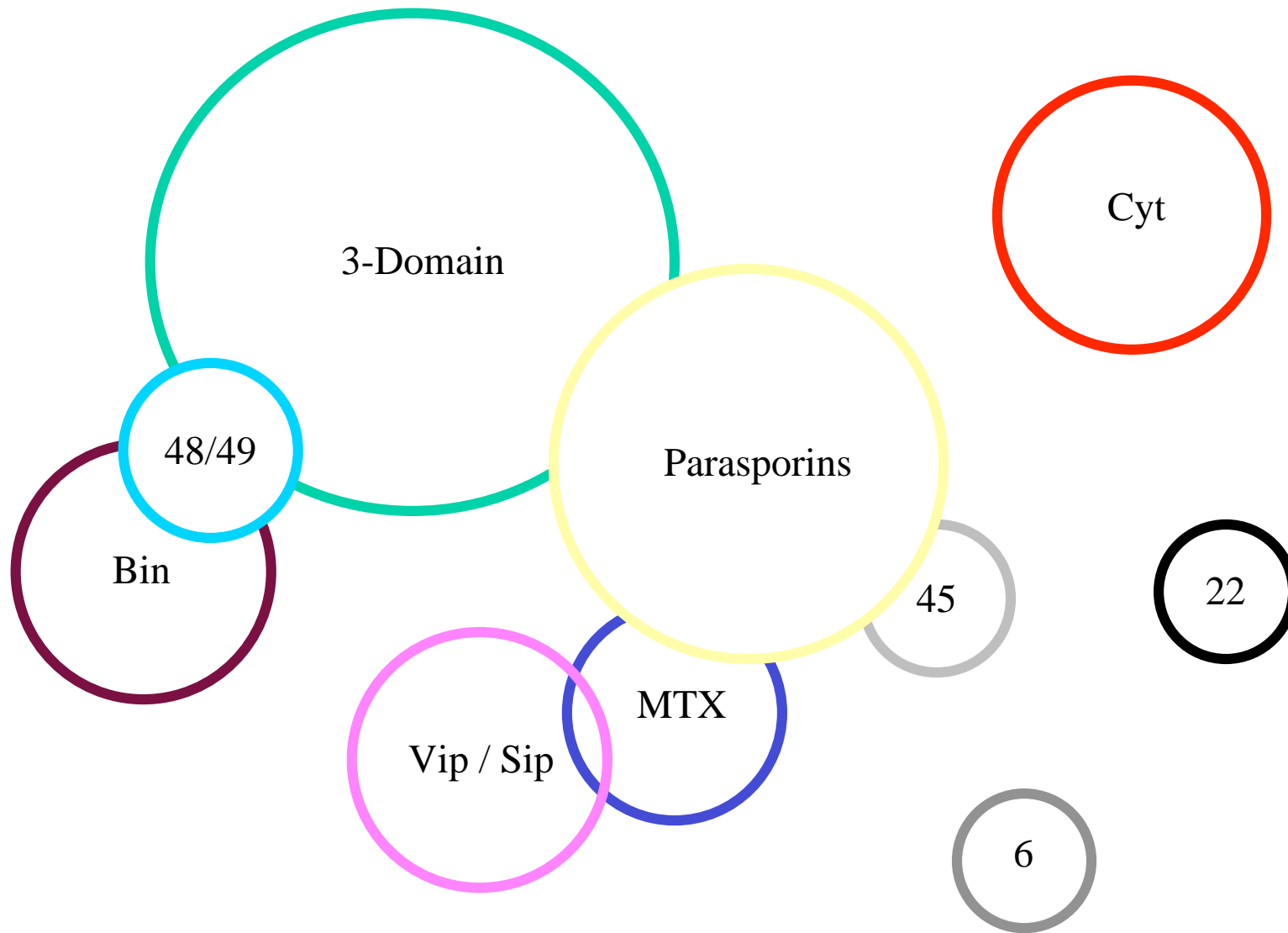
At least two could distinguish between normal and leukaemic cell lines

Parasporin 1	Cry31Aa/b/c	Three-domain Cry toxin
Parasporin 2	Cry46Aa	Mtx-like toxin
Parasporin 3	Cry41Aa/b	Three domain Cry toxin
Parasporin 4	Cry45Aa	epsilon toxin like
	Cry42Aa	Three domain Cry toxin

## Cry45

A parasporin with no known insecticidal target but with high cytolytic activity against human T-cells. Structurally almost identical to the epsilon toxin from *Clostridium perfringens* – a pore-forming toxin.





# Diversity exists – so what?

There are many diverse insecticidal Bt toxins out there but does this knowledge lead to an increased optimism in the search for improved strains?

Not necessarily – such a diversity gives us more potential to design improved toxins through directed evolution for example, or to provide alternative toxins for GM crops to combat resistance etc. Cryptic genes can be activated or poorly expressed ones can be manipulated to give a better yield, but as the companies tell us large improvements in efficacy are required to overcome regulatory problems.

Is the only way to develop a new Bt strain as a product to stick to the traditional approach of large screening programs. This may still work for specific pests but for the main targets of HD1 or Bti?

Although there are many problems concerned with the development of recombinant Bt products are there any more acceptable modifications that can be made to improve the efficacy of a given toxin? Considerable literature exists on the effect of protease treatment of toxins for examples, some treatments enhance toxicity towards a given pest population or release otherwise dormant activities, other treatments reduce toxicity. Can we use this knowledge to improve the efficacy, specificity or environmental safety of a given Bt strain?