

The use of the genetic diversity of *Cydia pomonella granulovirus* (CpGV) to overcome CpGV resistance

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Abstract

*The *Cydia pomonella granulovirus* (CpGV) is the most important microbial control agent of codling moth in organic pome fruit production. Since the first reports on organic orchards with codling moth populations resistant to CpGV products, new CpGV products overcoming CpGV resistance and new types of CpGV resistance were described, resulting in a complex and sometimes confusing variety of CpGV isolate names and resistance types reported in the literature. The following review aims to provide a summary on the current status of CpGV resistance research and product development.*

Introduction

In organic as well as in integrated production of pome fruits and walnuts, the codling moth (CM, *Cydia pomonella* L.) is one of the most severe pest insects. Female moth lay their egg on developing leaves or fruits and the neonate larvae tunnel into the fruits where they feed and grow until the final larval instar. Uncontrolled, CM causes significant damage, rendering the fruits unmarketable. In organic production, control of CM is heavily depending on the use of *Cydia pomonella granulovirus* (CpGV) (Lacey et al., 2008). CpGV belongs to the virus species *Betabaculovirus cypomonellae* of the *Baculoviridae* family, and has a dsDNA genome of about 120-124 kbp (Wennmann et al., 2017). The virus itself is protected against chemical and physical degradation by a proteinaceous occlusion body (OB). OBs can be sprayed with conventional field sprayers, leaving CpGV easy to formulate and to apply. Especially in combination with pheromone mating disruption, CpGV application is an indispensable corner stone of CM control in organic pome fruit production.

Since its first registration in 1989 in Switzerland by Andermatt Biocontrol, CpGV has proven to be one of the most sustainable CM control agents worldwide. CpGV is highly effective, environmentally safe, and non-toxic, non-pathogenic and non-detrimental to non-target organisms (OECD, 2023). In the EU, CpGV is classified as a low-risk (EU) substance, ideally suited for an effective but environmentally sound pest control in organic and integrated pome fruit production.

Today, CpGV isolates are registered basically in all countries where pome fruits are produced and where CM is present as a pest. Over the decades of successful use, some codling moth populations - especially in Europe - developed resistance towards CpGV. First reports of resistance date back to 2005 (Fritsch et al., 2005; Sauphanor et al., 2006), followed by intensive research in discovery of resistance in many European countries (Schmitt et al., 2013, Fritsch et al., 2022) as well as in the US (Fan et al., 2022). CpGV resistance is characterized by a significant reduction or nearly complete loss of susceptibility of given CM populations, which is genetically inherited by the offspring. Spread of CpGV resistance is a severe economic risk to organic farmers with unforeseeable economic uncertainty in case this pivotal control instrument becomes lost.

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Types of Resistance

Since the first report of CpGV resistance, different types and regional occurrence of resistance have been reported (Table 1). The resistance types differ in their mode of inheritance and specificity for certain CpGV isolates. The first CpGV resistance cases in Germany and France were associated with type I resistance, which was Z chromosomal and dominantly inherited, and was targeted against CpGV-M (genome group A) only. To control type I resistance several commercial products were developed and registered, such as Madex Plus, Madex Max, and Carpovirusine Evo2. In 2008, CM populations with resistance against CpGV genome group E, a major component for the first generation of resistance breaking CpGV isolates, was first identified (Jehle et al., 2017; Sauer et al., 2017a). Its inheritance was autosomal and dominant and some CpGV isolates originally identified to tackle type I resistance also failed (Sauer et al., 2017a). To overcome type II resistance further commercial products, such as Madex Top and Madex Primo, were developed. A resistance similar to type II was further reported from Washington state from the US (Fan et al., 2022). But it is not characterized in more detail yet. Also in 2008, type III resistance was found in Eastern Germany exhibiting a similar isolate specificity as type II resistance but differences in its mode of inheritance (Sauer et al., 2017b). Further types IV and V resistances were recently reported from France (Siegwart et al., 2020). Type IV resistance is poorly described and needs further investigation, since current data are somehow contradictory. It was proposed that it was resistant against CpGV of genome group A, B and E, whereas a combination of genome group A and E would overcome resistance, though no additive effect or synergism of genome groups A and E was ever reported for this resistance type. Type V resistance appeared to be linked to the Z chromosome and showed different resistance levels, depending on the CpGV isolate (Gingueneau et al., 2025). Most strikingly, CpGV isolates of the genome group B, known to break all types of resistance before, also showed a significantly reduced efficacy in resistance type V larvae when compared to its virulence for CpGV susceptible CM larvae.

Table 1: Overview on reported cases of CpGV resistance. Given are the different types of resistance, the inheritance mode, country of occurrence, commercial products overcoming resistance.

Type	Inheritance	Targeted CpGV groups	Reported from countries	References
I	Z chromosomal, dominant	A	Germany, France, Austria, Italy, Netherlands, Switzerland, Czech Republic	Asser-Kaiser et al., 2007; Schmitt et al., 2013; Zichova et al., 2013
II	Autosomal, dominant	A, E	Germany (possibly US)	Jehle et al. 2017; Sauer et al., 2017a; Fan et al., 2022
III	Autosomal and Z chromosomal, dominant	A, E	Germany	Sauer et al., 2017b
IV	n.d.	A, B and E?	France, Italy	Siegwart et al., 2020
V	X chromosomal, dominant	A, B, E	France, Italy, possibly Germany*	Siegwart et al., 2020 Gingueneau et al., 2025

* Kienzle, Biganski, Jehle (2026) unpublished, n.d. = not determined

Types of genetic diversity of CpGV

Although different geographic CpGV isolates had been reported since the early 1980s, only CpGV-M and CpGV-S (=Cp4) were developed as commercial products for codling moth control. With the emergence of CpGV resistance and its isolate specificity, scientific interest focused on other geographic isolates of CpGV including their resistance overcoming character (Rezapanah et al., 2008, Fan et al., 2020).

Genome sequencing of numerous CpGV isolates revealed a complex phylogeny with different phylogenetic lineages (= genome groups A to G) of CpGV (Fan et al. 2021) (Figure 1). Nowadays isolates from three different genome groups, i.e. genome group A, B, and E are used in commercial products, satisfying the needs of growers for effective CpGV products in the field. With the emergence of some rare cases with cross resistance to genome group A, B and E, new resistance-breaking isolates need to be developed. Beyond efficacy against codling moth, some newly selected CpGV isolates, such as CpGV-V22 and -V45, show increased virulence against the oriental fruit moth *Grapholita molesta* (Table 2).

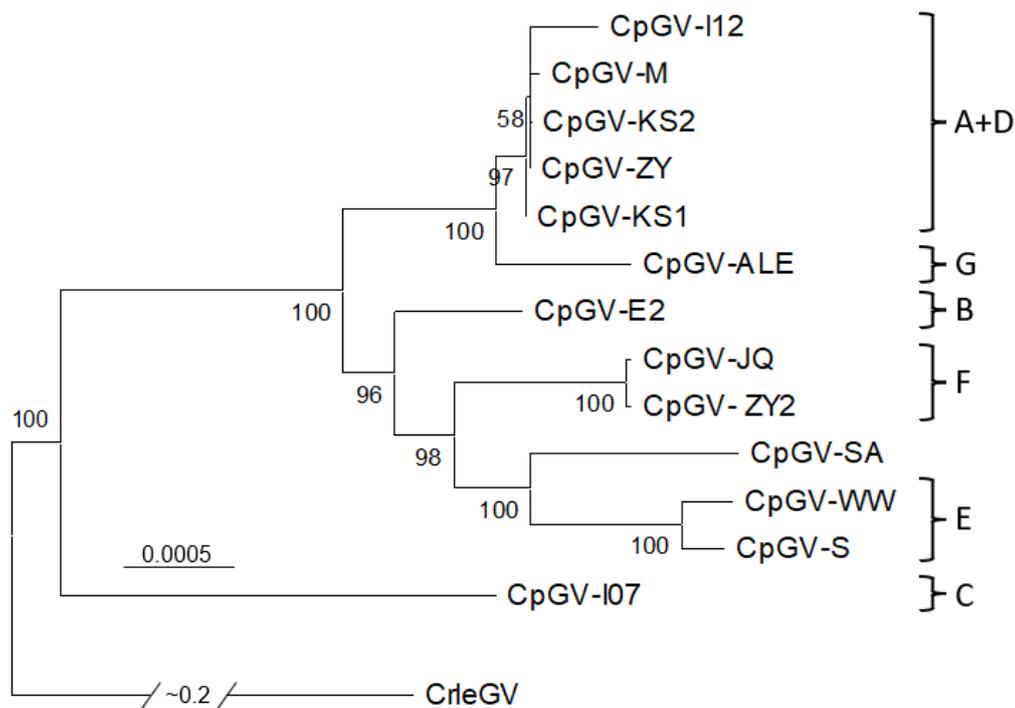


Figure 1: Maximum-likelihood phylogenetic analysis based on an alignment of thirteen CpGV genomes. CrleGV was used as the outgroup. Bootstrap values (250 replicates) are shown at the nodes. The letters A to G indicate the different CpGV genome groups. Figure adopted from Fan (2019).

Genetic diversity of baculoviruses in commercial products

As a consequence of the occurrence of resistance to CpGV improved commercial CpGV products have been developed during the last couple of years. In Table 2 an overview on the different commercially available products in Europe is given. Note that not all of these products are available in every country and some product registrations may have expired.

Table 2: CpGV isolates used in commercial products available in Europe. Given are the isolate names, the registration isolate names, product names, the genome group(s) of the active ingredient, the types of resistances the products can overcome, and further targets according to the registration.*

Isolate	Registered as	Product Name	Genome Group	Resistance-breaking of type	Further targets
CpGV-M	GV-0001	Madex, Granupom, CydX,	A	-	
CpGV-M	GV-0002	Carpovirusine, Carpovirusine Max (n.f.)	A	-	<i>Grapholita molesta</i>
CpGV-V01	GV-0003	Madex Plus	A [§]	I	
CpGV-M		Virgo, Carpostop, Carpo 600	A	-	
CpGV-V03	GV-0006	Madex Max	A, E	I	
CpGV-R5	GV-0007	Carpovirusine Evo2, Carpovirusine Ultra	A, E	I, IV	
CpGV-V15	GV-0013	Madex Top, Madex Pro	E, B	I, II, III	
CpGV-V22	GV-0014	Madex Twin	n.a.	n.a.	<i>Grapholita molesta</i>
CpGV-V14	GV-0015	Madex Primo	B	I, II, III	
CpGV-V45	GV-0017	Madex Duo	A, B, E	I, II, III	<i>Grapholita molesta</i>

*Table may not contain all commercially available products, some products may have expired registration; some data taken from Gueli Alletti et al. (2017); n.f. = new formulation, [§]mutant of CpGV-M, breaking type I resistance

Future perspectives

The availability of effective CpGV products is a corner stone for the current and future practice of organic pome fruit production worldwide. Emergence of CpGV resistance, therefore, puts organic apple production at risk. The intense research on CpGV resistance as well as on the genetic diversity of CpGV during the last 15 years has shaped our understanding of CpGV host interaction in a new dimension. By the registration of improved CpGV products with new isolates, commercial producers were able to provide reliable solutions to the growers who experienced CpGV resistance in their orchards – so far. Further research is necessary to reveal the various resistance mechanisms and to isolate further CpGV isolates with novel virulence patterns exploiting the natural genetic diversity of CpGV.

Recently, a novel baculovirus was isolated from the litchi moth, namely *Cryptophlebia peltastica* nucleopolyhedrovirus (CrpeNPV) belonging to the species *Alphabaculovirus crypeltasticae* (Marsberg et al., 2018). It was shown that CrpeNPV is not only infective for *Cryptophlebia* sp. but also for codling moth. Most importantly, it was shown in laboratory experiments, that CrpeNPV broke all types of CpGV resistance tested (Wennmann et al., 2019). Because of the phylogenetic distance of CpGV and CrpeNPV it can be expected that the infection process of CrpeNPV is not affected by CpGV resistance, offering a potentially new tool for codling moth control. CrpeNPV is currently under evaluation by the EU for active ingredient approval and product registration. First field experiments carried out at JKI in Dossenheim delivered mixed results and need further testing. Such experiments are currently carried out within the project “ÖkoapfelForward”.

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