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# **Foodborne outbreaks and bacteremia associated with *Bacillus thuringiensis* biopesticides: in vivo evaluation and modeling of the virulence potential**

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# Votre projet Académie 3

**A RENSEIGNER EN ANGLAIS**

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## **Title**

Foodborne outbreaks and bacteremia associated with *Bacillus thuringiensis* biopesticides: *in vivo* evaluation and modeling of the virulence potential

## **Acronym** (obligatoire)

VIRBT

## **Teaser text/Tagline**

Court sous-titre « accrocheur » Une phrase décrivant le projet de façon attractive  
Biopesticides: are natural and organic pesticides really safe?

## **Academy 3 highlight**

Expliquez en 2-3 lignes max. comment votre projet s'inscrit dans les thématiques transdisciplinaires de l'A3 (400 et 500 caractères espaces compris max)

*Bacillus thuringiensis* is a bacterium increasingly used as microbial insecticide to fight lepidopteran larvae, a major crop pest. Recently, this bacterium has also been involved in food poisoning and systemic infections, affecting humans, wildlife and the environment indiscriminately. As part of the "One Health" concept, our project tackles the mechanism of virulence of this bacterium using insects, mice and human cell culture and combining medicine, immunology, cell biology, genetics and bioinformatics. It contributes to the topic "*Assessment and detection of anthropogenic risks to human health*"

## **Brief information on the project**

### **Scientific domain**

Environmental and Human Health  
Biology

### **Key words**

Un mot par ligne (5 mots maximum)  
Bacillus thuringiensis  
One Health  
Bioinsecticides  
Agriculture  
Food poisoning

### **PI Laboratory(ies)**

Un laboratoire par ligne  
ISA - Université Côte d'Azur, CNRS, INRAE

**Total budget and Academy 3 contribution** (et autres Académies et/ou Bureau Idex si le cas)  
€266,500 including, €66,500 from Academy 3

### **Start of the project**

2022

### **Partner laboratories**

Noms des laboratoires (ou structures) partenaires

Un partenaire par ligne

C3M - *Université Côte d'Azur, Inserm*

CHU de Nice l'Archet - *Université Côte d'Azur*

ANSES - *Maisons-Alfort*

### **Logos of partner laboratories (or structures)**

Merci de déposer une archive ZIP contenant les logos en bonne qualité (1000px minimum, format JPEG ou PNG de préférence)

.....  
.....

### **Project members and e-mail**

Un nom et email par ligne

Armel Gallet, [Armel.GALLET@univ-cotedazur.fr](mailto:Armel.GALLET@univ-cotedazur.fr)

Mathilde Bonis, [mathilde.bonis@anses.fr](mailto:mathilde.bonis@anses.fr)

Laurent Boyer, [Laurent.BOYER@univ-cotedazur.fr](mailto:Laurent.BOYER@univ-cotedazur.fr)

Raymond Ruimy, [Raymond.RUIMY@univ-cotedazur.fr](mailto:Raymond.RUIMY@univ-cotedazur.fr)

### **International collaborations**

Une collaboration par ligne

.....

### **Students involved**

Un étudiant par ligne

Fatima Tleiss (PhD)

Claire Guillebon (Master/PhD)

Arnaud Fichant (PhD)

### **The project**

Résumez le projet de manière vulgarisée : contexte, objectifs, aspects inter-disciplinaires et structurants (si justifié), aspects novateurs, résultats majeurs (5000 caractères espaces compris max)

The use of chemical pesticides is controversial, mainly because of their harmful effects on the environment and human health. The emerging solution is the use of biocontrol agents, also called biopesticides. Like chemical pesticides, biopesticides are used to combat certain organisms considered harmful, but by means of natural substances (plant extracts, pheromones, essential oils, etc.) or organisms (predators such as ladybirds, bacteria, viruses, etc.). These natural pesticides are a good alternative to chemical ones, but not without a risk to human health. The microbial insecticide *Bacillus thuringiensis* (Bt), although an "organic" pesticide, is involved in almost 20% of cases of food poisoning caused by the *Bacillus cereus* group of bacteria to which it belongs (Bonis et al., PLOS One, 2021). Some strains of the *Bacillus cereus* group have also been found responsible for nosocomial diseases (such as septicemia) in weakened individuals (e.g., immunocompromised individuals, the elderly, newborns). So far, we have ignored how this group of bacteria displays its virulence and to what extent the hazard coming from Bt in food originates from agriculture. This is what the consortium of researchers working on the VirBt project is trying to investigate and understand. Focusing on Bt and its

effects, biologists from ISA, C3M, Nice CHU and the Laboratory for Food Safety of the ANSES Maisons-Alfort are working together to assess the virulence of Bt strains. They are also investigating the extent to which weakened individuals are prone to Bt infection and more broadly to infection by the *Bacillus cereus* group. To achieve this, three models are being used in the experiments: *Drosophila* (fruit fly), mice and human intestinal cell cultures. *Drosophila* is a well-established model for studying the innate immune system because it presents strong similarities with mammals, including mice and humans. Furthermore, the use of *Drosophila* complies with ethical requirements by first testing the virulence of many *Bacillus* strains on *Drosophila*, before selecting a limited number of strains and testing them on mice. The data obtained from these models will then be correlated with those recovered from human patient samples. Initial results from tests on *Drosophila* show that Bt storage is most concentrated in the intestinal tract, sporadically leading to diarrhea and intestinal disorders as early as 8 to 24 hours after ingestion.

While Bt strains are the most effective of all pesticides, they are also the ones to which people are most exposed. The survey conducted by ANSES as part of the project highlights this exposure. After collecting and testing 161 fruits and vegetables commercially certified "Organic Agriculture", almost 50% of the products tested came up positive for Bt. Peppers, tomatoes, apples, cucumbers, aromatic herbs, etc., were all in the same basket! Importantly, no Bt of agricultural origin has been identified in any of the 45 patients analyzed so far with septicemia caused by bacteria from the *Bacillus cereus* group. This observation suggests that Bt used as a microbial pesticide, though present in fruits and vegetables, may be partly responsible for food poisoning but is unlikely to be involved in septicemia in weakened patients. Research conducted jointly by biologists and public health professionals should lead to the development of tools to assess and detect these Bt strains more easily in food and in the body, and should make it safer to use them in agriculture, since today neither dose limits nor a delay before harvest are imposed.

### **The +**

Point(s) saillant(s) du projet (référence notamment aux points discuté(s) avec le comité de suivi de l'Académie 3) (250 et 300 caractères espaces compris max)

The project consortium includes public health authorities (ANSES), and it has led to two doctoral theses.

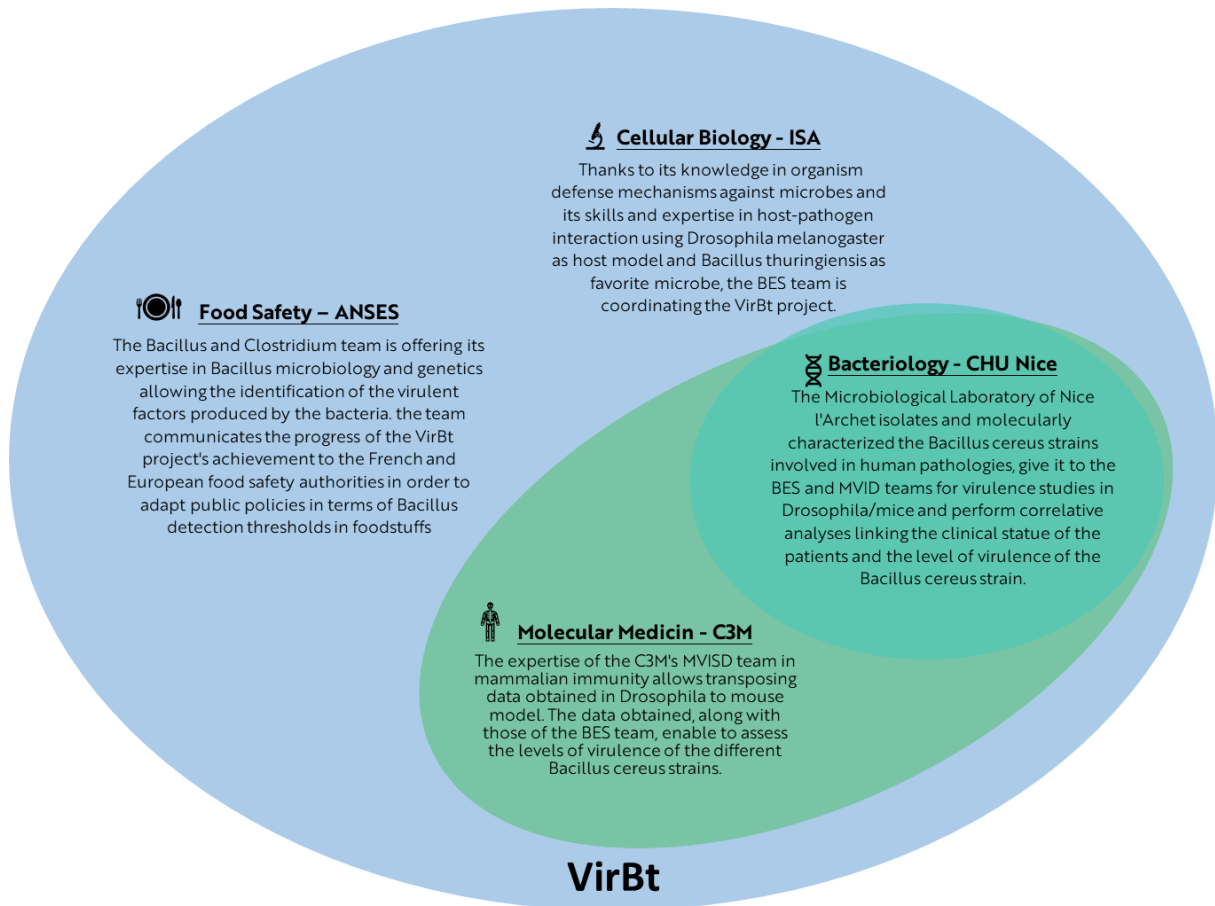
### **What's next?**

Les perspectives d'évolution future du projet (400 et 500 caractères espaces compris max)

The consortium of researchers is now focusing on sequencing the results obtained with technical support (a ten-month fixed-term contract) funded by Academy 3. The Ecophyto grant obtained in January 2023 will expand the project, making it a major project in the field of bio-pesticides and health.

### **How does the project contribute to the transdisciplinary ambition?**

Chaque partenaire spécifie l'apport de sa discipline au sein du projet (200 caractères espaces compris max par partenaire)



### Cellular Biology - ISA

The BES team is coordinating the VirBt project and bringing its knowledge in organism defense mechanisms against microbes and its skills and expertise in host-pathogen interaction using *Drosophila melanogaster* as host model and *Bacillus thuringiensis* as favorite microbe.

### Bacteriology - CHU Nice

The Microbiological Laboratory of the Nice l'Archet University Hospital isolated and molecularly characterized the Bacillus cereus strains involved in human pathologies, shared them with the BES and MVID teams for virulence studies in *Drosophila* and mice, and performed correlative analyses linking the clinical state of the patients with the level of virulence of the Bacillus cereus strain.

### Molecular Medicine - C3M

The expertise of C3M's MVID team in mammalian immunity was useful in transposing data obtained in *Drosophila* to the mouse model. The data obtained, along with those from the BES team, were used to assess the levels of virulence of the different Bacillus cereus strains.

### Food Safety – ANSES

The Bacillus and Clostridium team has been contributing its expertise in Bacillus microbiology and genetics to help identify the virulent factors produced by the bacteria. The team has been communicating the achievements of the VirBt project to the French and European food safety authorities who need to adapt public policies regarding Bacillus detection thresholds in foodstuffs.

## Illustration

Une ou deux images parlantes, attrayantes, pédagogiques (format portrait si possible)  
Image #1 Image de bonne qualité (1500px minimum, format JPEG ou PNG de préférence)



Image #2 Image de bonne qualité (1500px minimum, format JPEG ou PNG de préférence)

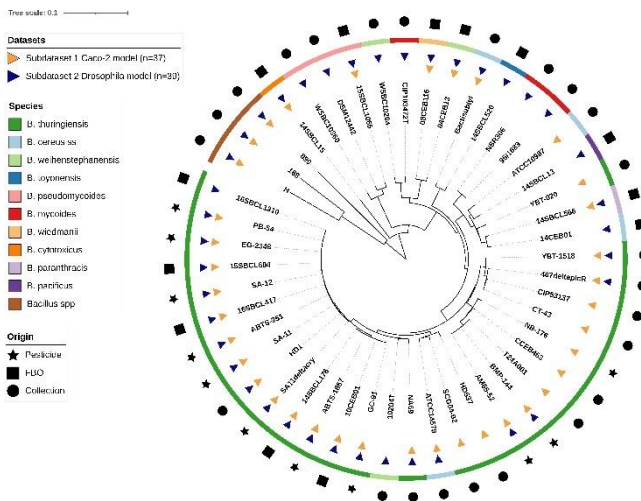
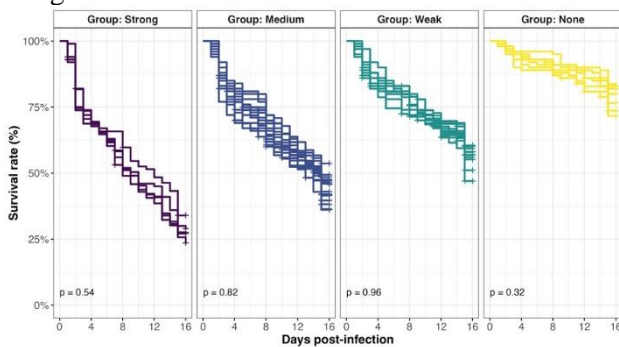


Image 3 :



**Legend(s)** (1 ligne max.)

- 1) Infected *Drosophila* producing an immune response visible by the appearance of red, green and blue fluorescence.

- 2) Phylogenetic tree representing and classifying the different Bacillus strains tested in the project.
- 3) Bacillus strains tested in Drosophila by level of virulence

### **Information about the Project initiator(s)**

*Possibilité de renseigner plusieurs Porteurs*

Nom & prénom : [Armel Gallet](#)

Photo



Lien vers page professionnelle : <https://www.researchgate.net/profile/Armel-Gallet>

Laurent Boyer



<https://www.researchgate.net/profile/Laurent-Boyer-3>

Raymond Ruimy

<https://www.researchgate.net/profile/Raymond-Ruimy>

Mathilde Bonis



<https://www.researchgate.net/profile/Mathilde-Bonis>

Nom & prénom

Photo

Lien vers page professionnelle

### **Scientific promotion of the project**

Liste de publications, conférences, etc. découlant du projet

Lien(s) si page(s) existante(s)

Tleiss F., Montanari M., Pierre O., Royet J., Osman D., Gallet A. and Kurz C.L.: "Spatial and temporal coordination of Duox/TrpA1/Dh31 and IMD pathways is required for the efficient elimination of pathogenic bacteria in the intestine of *Drosophila larvæ*". *eLife*, June 17, 13:RP98716 (2024)

<https://doi.org/10.7554/eLife.98716.1>

Fichant A., Lanceleur R., Hachfi S., Brun-Barale A., Blier A.L., Firmesse O., Gallet A., Fessard V. and Bonis M.: "New approach methods to assess the enteropathogenic potential of strains of the *Bacillus cereus* group including *Bacillus thuringiensis*". *Foods* 13(8), 1140 (2024).

<https://doi.org/10.3390/foods13081140>

Fichant A., Felten A., Gallet A., Firmesse O., Bonis M.: "Identification of genetic markers for the discrimination of *Bacillus thuringiensis* within the *Bacillus cereus* group, in the context of foodborne outbreaks". *Foods* 11(23), 3924 (2022)

<https://doi.org/10.3390/foods11233924>

Armel GALLET Seminar at the invitation of Léopold Kurz: "Bacillus, Environnement et Santé", UMR 7288, Institut de Biologie du Développement de Marseille (France, October 6, 2023)

- Armel GALLET Chairperson: Symbionts session, Jacques Monod conference, Insect Models For Infection Biology, (Roscoff, France, June 26 to 30, 2023)

- Armel GALLET Poster: "Ingestion of *Bacillus cereus* spores dampens the immune response to favor bacterial persistence". Jacques Monod conference, Insect Models For Infection Biology, (Roscoff, France, June 26 to 30, 2023)

- Armel GALLET Seminar at the invitation of V. Broussolle: "Ingestion of *Bacillus cereus* spores dampens the intestinal immune response to favor bacterial persistence". UMR408 Sécurité et Qualité des Produits d'Origine Végétale, Centre INRAE PACA (Avignon, France, May 31, 2023).

-Arnaud FICHANT communication: "Characterization of the virulence potential of spore-forming *Bacillus cereus* in *Drosophila melanogaster*", 10th European Spores Conference (Cambridge, United Kingdom, April 2023)

- Mathilde BONIS, communication: "New approach methodologies to assess the virulence potency of enteropathogenic *Bacillus cereus*" (BSPIT congress: Bactéries sporulantes pathogènes ou d'intérêt technologique; November 2023)

- Fichant, A.; Lanceleur, R.; Hachfi, S.; Brun-Barale, A.; Blier, A.-L.; Firmesse, O.; Gallet, A.; Fessard, V.; Bonis, M. New Approach Methods to Assess the Enteropathogenic Potential of Strains of the *Bacillus cereus* Group, including *Bacillus thuringiensis*. *Foods* 2024, 13, 1140. <https://doi.org/10.3390/foods13081140>

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