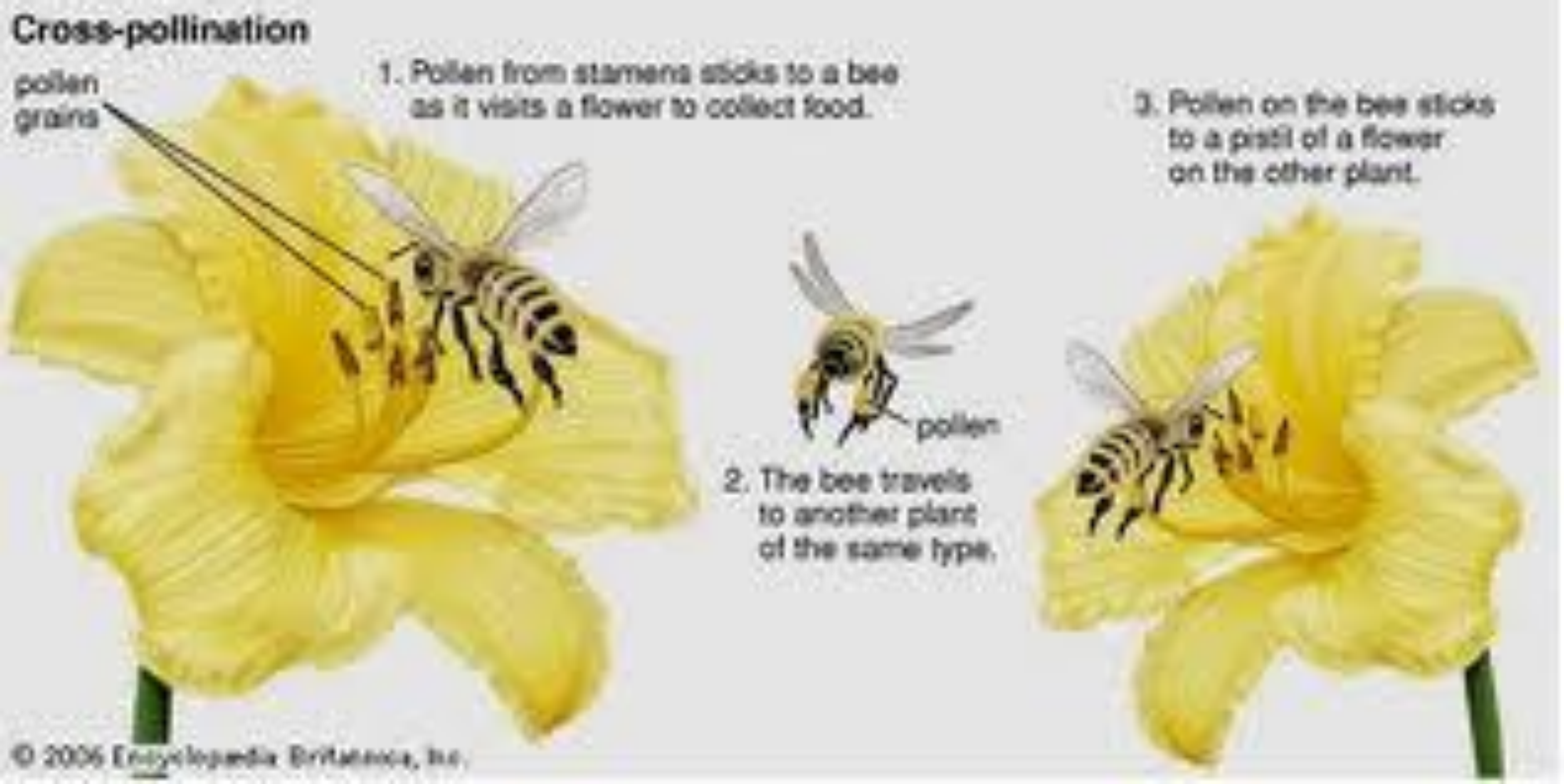
Non-antibiotic Treatment for Honey Bee Diseases in the Era of Omics

Yanping (Judy) Chen

U.S. Department of Agriculture
Agricultural Research Service
Bee Research Laboratory, Beltsville, Maryland, USA

European honey bee, *Apis mellifera*

CROP POLLINATION

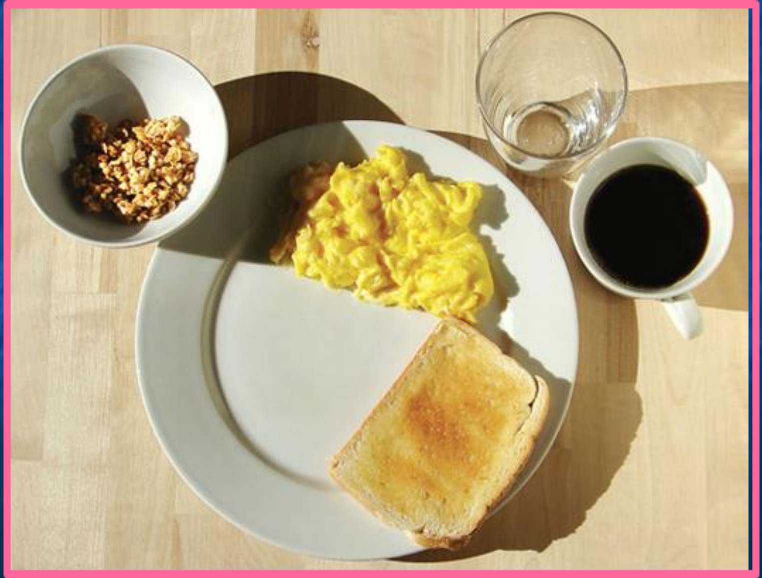


<u>Pollination</u>: The transfer of pollen from the male anther to the female stigma, which results in fertilization of plant ovaries and the production of seeds.

Grocery Shelves With or Without Honey Bees

http://www.fastcodesign.com/1672866/this-is-what-our-grocery-shelves-would-look-like-without-bees

The Breakfast With or Without Honey Bees



http://www.scientificamerican.com/article/breakfast-without-bees/








The total economic values of pollination worldwide amounted to €153 billion, which represented 9.5% of the value of the world agricultural production used for human food in 2005.

Gallai et al. **2009 Economic valuation of the vulnerability of world agriculture confronted with pollinator decline. Ecological Economics. 68(3):810-821.**

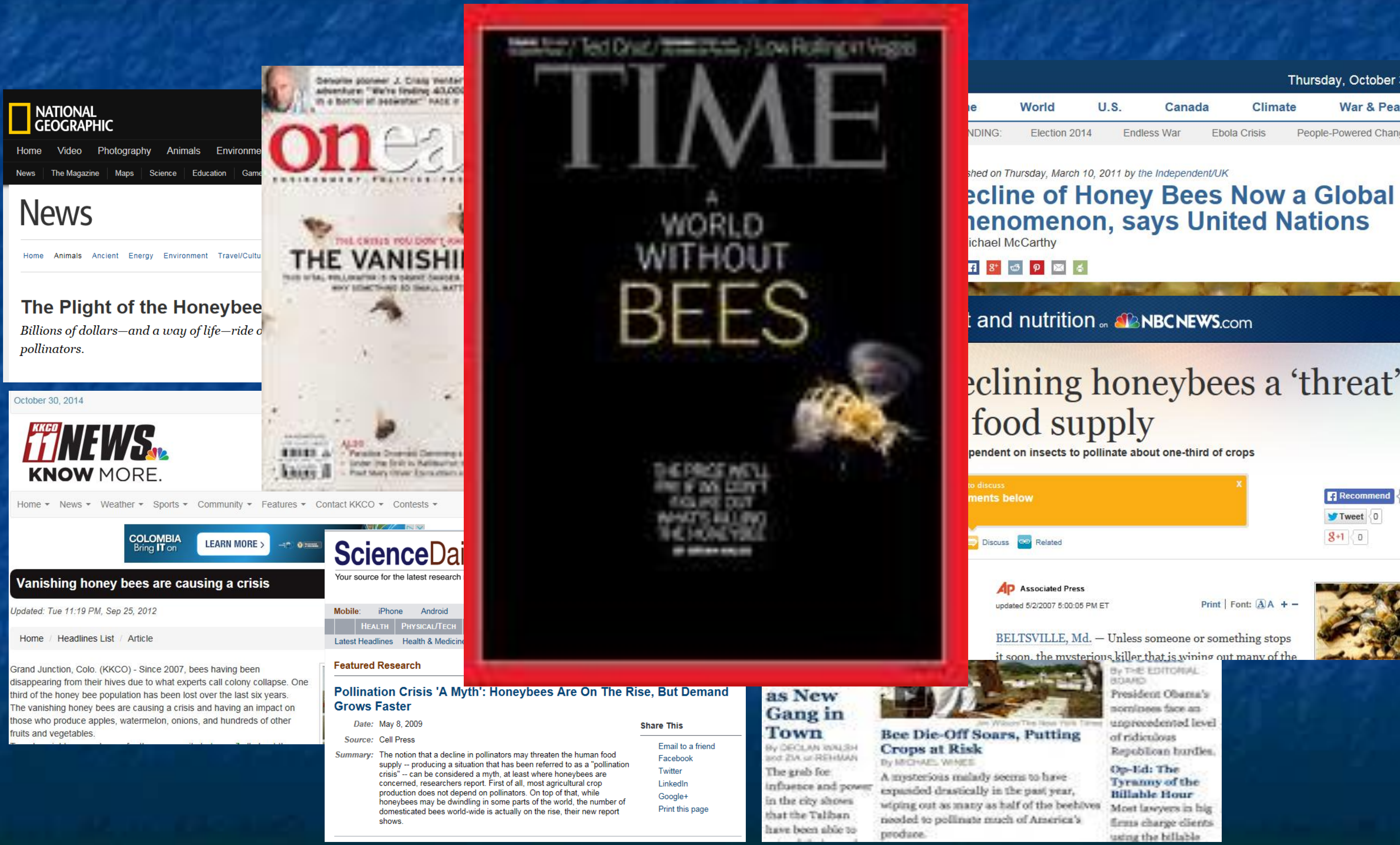








AGRICULTURE SUFFERS FROM DECLINE IN BEES



Colony Collapse Disorder (CCD)


The New York Times

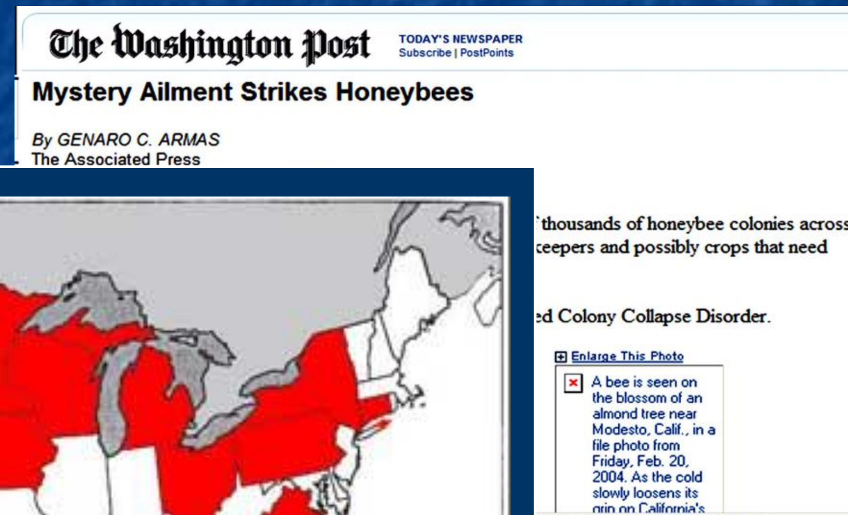
February 27, 2007

Honeybees Vanish, Leaving Keepers in Peril

By ALEXEI BARRIONUEV

VISALIA, Calif., Feb. 23 —
beekeeper, but he got the
half of his 100 million bee

In 24 states throughout th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Mystery Ailment Strikes Honeybees

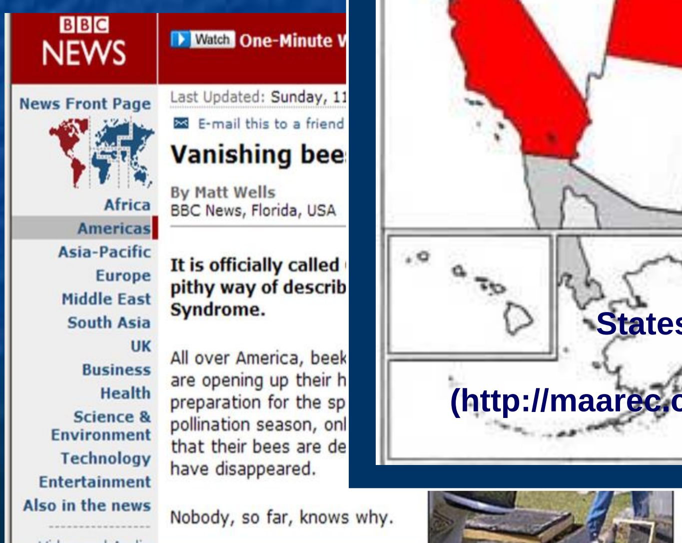
By GENARO C. ARMAS
The Associated Press

thousands of honeybee colonies across
keepers and possibly crops that need

ed Colony Collapse Disorder.

Enlarge This Photo

A bee is seen on the blossom of an almond tree near Modesto, Calif., in a file photo from Friday, Feb. 20, 2004. As the cold slowly loosens its grip on California's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Last Updated: Sunday, 11

E-mail this to a friend

Vanishing bee

By Matt Wells
BBC News, Florida, USA

It is officially called
pithy way of describ
Syndrome.

All over America, beek
are opening up their h
preparation for the sp
pollination season, onl
that their bees are de
have disappeared.

Nobody, so far, knows why.


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g extinction

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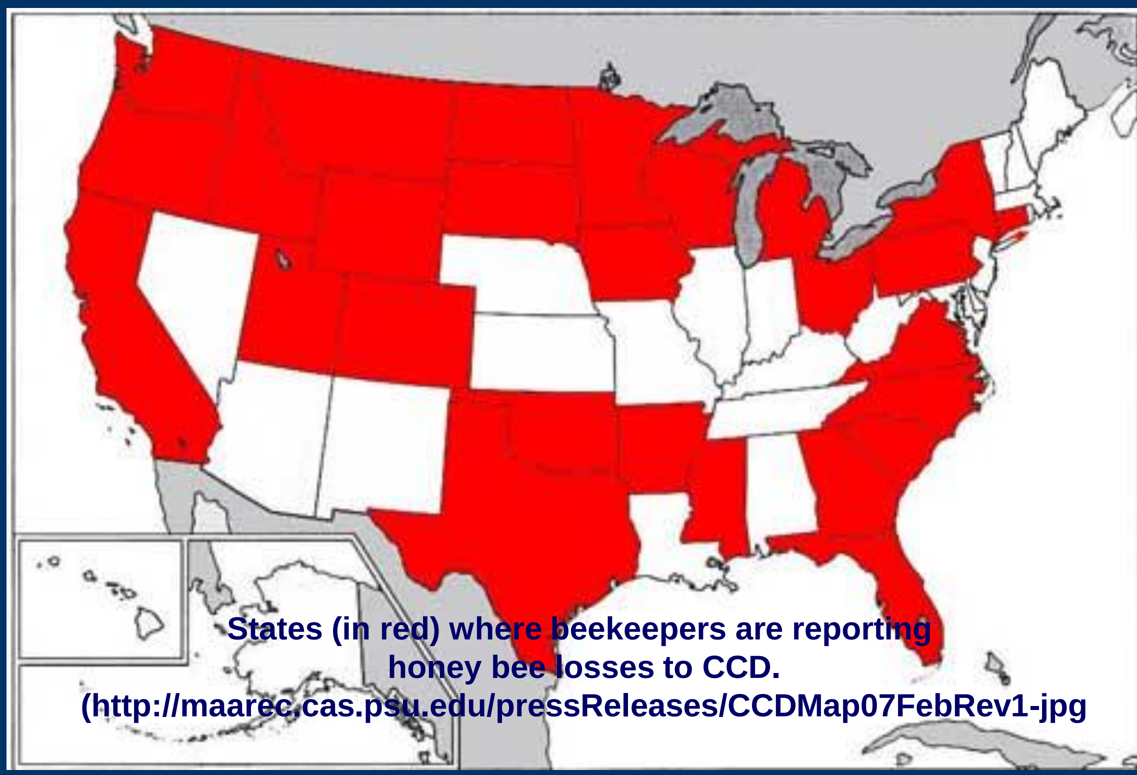
ppear, man would follow

ysterious condition that
States over the last 35

lain the fall in honey bee
fears of that a new
disease, the effects of pollution or the increased use
of pesticides could be to blame for "colony collapse
disorder". From 1971 to 2006 approximately one half
of the US honey bee colonies have vanished.

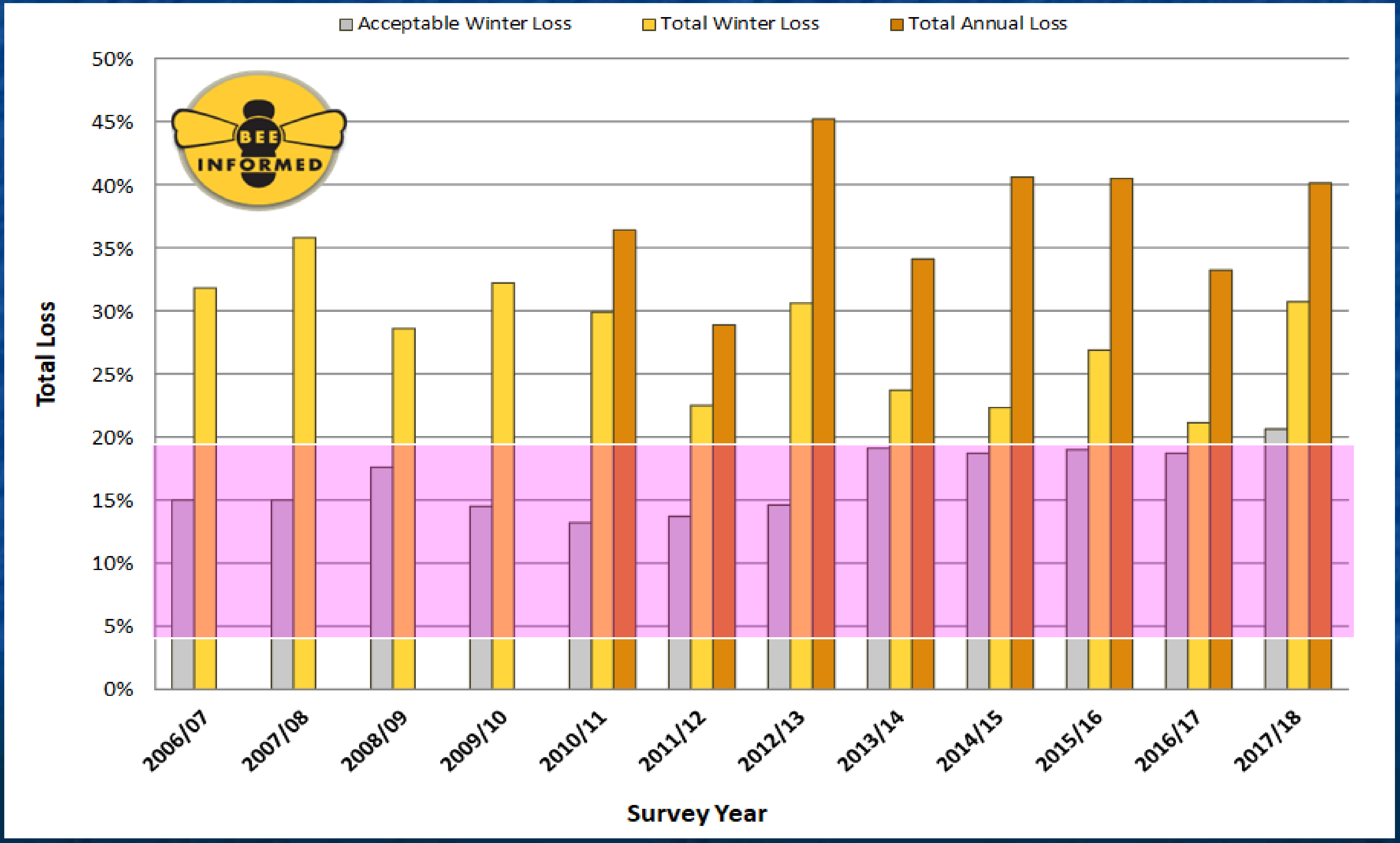
Honey bee collapse could cost country £200 million, say MPs

BBC iPlayer choices - Thursday 23 April



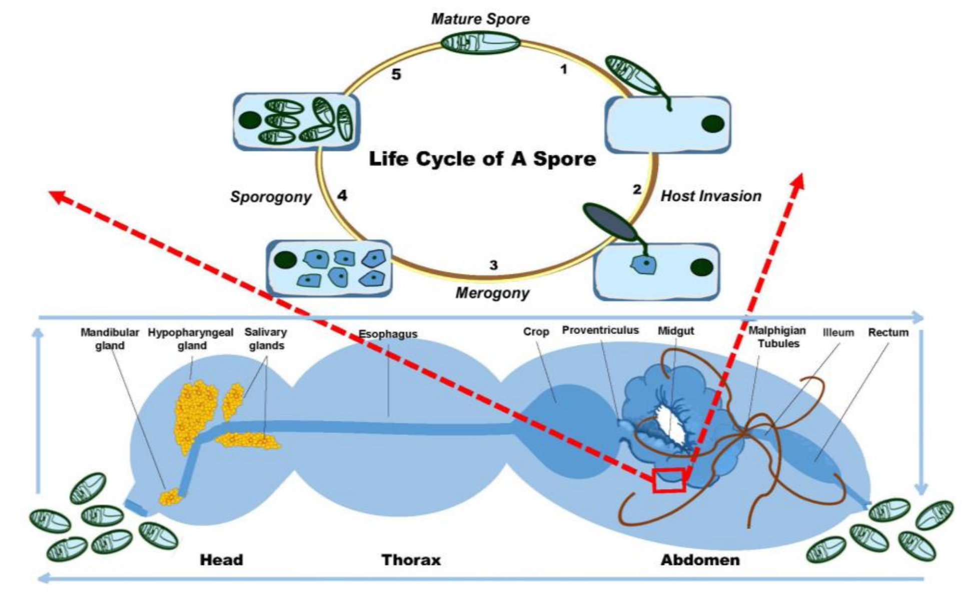
States (in red) where beekeepers are reporting honey bee losses to CCD.
(http://maarec.cas.psu.edu/pressReleases/CCDMap07FebRev1-jpg

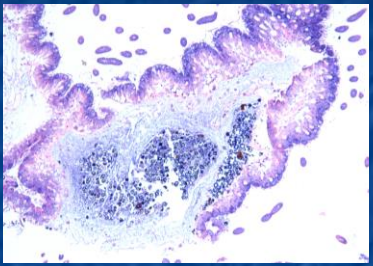
TOTAL US MANAGED HONEY BEE COLONIES LOSS ESTIMATES

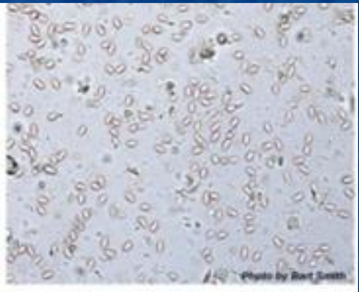


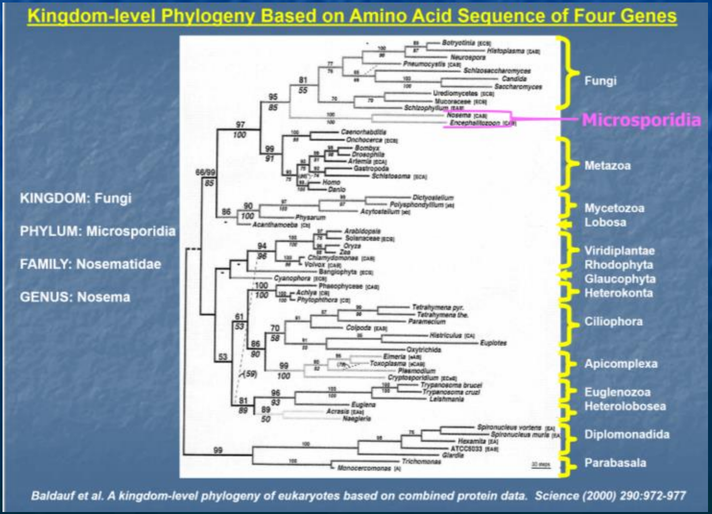
Source: *The Bee Informed Partnership (http://beeinformed.org/)*

NOSEMOSIS IN HONEY BEES









***Nosema apis*:**

Found in the European honey bee, *Apis mellifera* (Zander. 1907)

***Nosema ceranae*:**

First described in the Asian honey bee, *Apis cerana* (Fries et al., 1996) and later identified as a disease of *A. mellifera* in Taiwan and Spain (Higes et al., 2006; Huang et al., 2007).

Science
Reprint

A Metagenomic Survey of Microbes in Honey Bee Colony Collapse Disorder

Diana L. Cox-Foster, Sean Conlan, Edward C. Holmes, Gustavo Palacios, Jay D. Evans, Nancy A. Moran, Phenix-Lan Quan, Thomas Briese, Mady Hornig, David M. Geiser, Vince Martinson, Dennis vanEngelsdorp, Abby L. Kalkstein, Andrew Drysdale, Jeffrey Hui, Junhui Zhai, Liwang Cui, Stephen K. Hutchison, Jan Fredrik Simons, Michael Egholm, Jeffery S. Pettis, W. Ian Lipkin

12 October 2007
Volume 318, pp.283-287

AAAS
ADVANCING SCIENCE, SERVING SOCIETY

Table 1. Closest sequenced relatives identified through BLAST analysis of the high-throughput sequence data. *Indicates viruses not yet classified by the International Committee on the Taxonomy of Viruses but that exhibit the key features of the indicated taxon. [1]Found in Jeyaprakash *et al*. (2003). [2]Found in Babendreier *et al*. (2007).

Kingdom	**Taxon (rank)**	**Organism**
Bacteria	*Firmicutes* (phylum)	*Lactobacillus* sp.[1,2] Uncultured Firmicutes[2]
Bacteria	*Actinobacteria* (class)	*Bifidobacterium* sp.[1]
Bacteria	*Alphaproteobacteria* (class)	*Bartonella* sp.[1,2] *Gluconacetobacter* sp.[1,2]
Bacteria	*Betaproteobacteria* (class)	*Simonsiella* sp.[1,2]
Bacteria	*Gammaproteobacteria* (class)	Two uncultured species[1,2]
Fungus	Entomophthorales (order)	*Pandora delphacis*
Fungus	Mucorales (order)	*Mucor* spp.
Fungus / Microsporidian	*Nosematidae* (family)	*Nosema ceranae*
Fungus / Microsporidian	*Nosematidae* (family)	*Nosema apis*
Eukaryota	*Trypanosomatidae* (family)	*Leishmania*/*Leptomonas* sp.
Metazoan	*Varroidae* (family)	*Varroa destructor*
Virus	(unclassified)	Chronic bee paralysis virus*
Virus	*Iflavirus* (genus)	*Sacbrood virus*
Virus	*Iflavirus* (genus)	Deformed wing virus*
Virus	*Dicistroviridae* (family)	*Black queen cell virus*
Virus	*Dicistroviridae* (family)	Kashmir bee virus*
Virus	*Dicistroviridae* (family)	*Acute bee paralysis virus*
Virus	*Dicistroviridae* (family)	Israeli acute paralysis virus of bees*

Agent	Number of positive samples n (% positive of samples tested)			Positive Predictive Value (%)	Sensitivity (%)	Specificity (%)
	CCD (n = 30)	non-CCD (n = 21)	Total (n = 51)			
IAPV	25 (83.3%)	1 (4.8%)	26 (51.0%)	96.1	83.3	95.2
KBV	30 (100%)	16 (76.2%)	46 (90.2%)	65.2	100	23.8
N. apis	27 (90%)	10 (47.6%)	37 (72.5%)	73.0	90.0	52.4
N. ceranae	30 (100%)	17 (80.9%)	47 (92.1%)	63.8	100	19.0
All 4 agents	23 (76.7%)	0 (0%)	23 (45.0%)	100	76.7	100

NOSEMA INFECTION CAUSES NEGATIVE IMPACTS ON HONEY BEE HEALTH

Environmental Microbiology (2009) doi:10.1111/j.1462-2920.2009.01953.x

Immune suppression in the honey bee (*Apis mellifera*) following infection by *Nosema ceranae* (*Microsporidia*)

Karina Antúnez,[1] Raquel Martín-Hernández,[2] Lourdes Prieto,[3] Aránzazu Meana,[4] Pablo Zunino[1] and Mariano Higes[2]*
[1]Departamento de Microbiología, Instituto de Investigaciones Biológicas Clemente Estable, Montevideo, Uruguay.
[2]Bee Pathology Laboratory, Centro Apícola Regional, JCCM, 19180 Marchamalo, Spain.
[3]Instituto Universitario de Investigación en Ciencias Policiales (IUICP), Comisaría General de Policía Científica (Forensic Police), DNA Laboratory, Madrid, Spain.
[4]Animal Health Department, Facultad de Veterinaria, Universidad Complutense de Madrid, 28040 Madrid, Spain.

two broad categories, cellular and humoral immunity (Gillespie *et al.*, 1997; Lavine and Strand, 2002; Boman, 2003). Cellular immunity involves processes such as phagocytosis, nodulation and encapsulation. Both nodulation and encapsulation are often accompanied by melanization, which is catalysed by the (prophenol-) phenoloxidase (PO) (Ashida and Brey, 1998) and this PO-mediated melanin synthesis plays a major role in an insect's immune defence. The cellular response also requires the participation of glucose dehydrogenase (GLD), both during the encapsulation reaction and the insect killing response to fungal invaders. Indeed, GLD may be used as a marker of the initial activation of the cellular immune response (Lovallo and Cox-Foster, 1999). In addition, lysozyme (LYS) is also important in

---

VETERINARY RESEARCH

Nosema spp. infection and its negative effects on honey bees (*Apis mellifera iberiensis*) at the colony level

Botías *et al.*

BioMed Central
Botías *et al. Veterinary Research* 2013, **44**:25
http://www.veterinaryresearch.org/content/44/1/25

OPEN ACCESS Freely available online PLOS ONE

Crop Pollination Exposes Honey Bees to Pesticides Which Alters Their Susceptibility to the Gut Pathogen *Nosema ceranae*

Jeffery S. Pettis[1], Elinor M. Lichtenberg[2], Michael Andree[3], Jennie Stitzinger[2], Robyn Rose[4], Dennis vanEngelsdorp[2]*
1 Bee Research Laboratory, USDA-ARS, Beltsville, Maryland, United States of America, 2 Department of Entomology, University of Maryland, College Park, College Park, Maryland, United States of America, 3 Cooperative Extension Butte County, University of California, Oroville, California, United States of America, 4 USDA-APHIS, Riverdale, Maryland, United States of America

Journal of Invertebrate Pathology 106 (2011) 380–385
Contents lists available at ScienceDirect
Journal of Invertebrate Pathology

Pathological effects of the microsporidium *Nosema ceranae* on honey bee queen physiology (*Apis mellifera*)

Cédric Alaux[a,*], Morgane Folschweiller[a], Cynthia McDonnell[a], Dominique Beslay[a], Marianne Cousin[b], Claudia Dussaubat[a], Jean-Luc Brunet[b], Yves Le Conte[a]
[a] INRA, UMR 406 Abeilles et Environnement, Laboratoire Biologie et Protection de l'abeille, Site Agroparc, Domaine Saint-Paul, 84914 Avignon, France
[b] INRA, UMR 406 Abeilles et Environnement, Laboratoire de Toxicologie Environnementale, Site Agroparc, Domaine Saint-Paul, 84914 Avignon, France

ARTICLE INFO

Article history:
Received 27 September 2010
Accepted 7 December 2010
Available online 13 December 2010

ABSTRACT

Nosema ceranae, a microsporidian parasite originally described in the Asian honey bee *Apis cerana*, has recently been found to be cross-infective and to also parasitize the European honey bee *Apis mellifera*. Since this discovery, many studies have attempted to characterize the impact of this parasite in *A. mellifera* honey bees...

Contents lists available at ScienceDirect
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journal homepage: www.elsevier.com/locate/yjipa
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Energetic stress in the honeybee *Apis mellifera* from *Nosema ceranae* infection

Christopher Mayack, Dhruba Naug*
Department of Biology, Colorado State University, Fort Collins, CO 80523, USA

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environmental microbiology
sfam
Environmental Microbiology (2010) **12**(3), 774–782 doi:10.1111/j.1462-2920.2009.02123.x

Interactions between *Nosema* microspores and a neonicotinoid weaken honeybees (*Apis mellifera*)

Cédric Alaux,[1]* Jean-Luc Brunet,[2] Claudia Dussaubat,[1] Fanny Mondet,[2] Sylvie Tchamitchan,[2] Marianne Cousin,[2] Julien Brillard,[3] Aurelie Baldy,[1] Luc P. Belzunces[2] and Yves Le Conte[1]
[1]INRA, UMR 406 Abeilles et Environnement, Laboratoire

interactions that are widely used to eliminate insect pests in integrative pest management.

Introduction

The current decline in abundance and diversity of wild

Journal of Apicultural Research 53(5): 545-554 (2014)
DOI 10.3896/IBRA.1.53.5.09

ORIGINAL RESEARCH ARTICLE

IBRA INTERNATIONAL BEE RESEARCH ASSOCIATION

Nosema ceranae and queen age influence the reproduction and productivity of the honey bee colony

Predrag Simeunovic[1*], Jevrosima Stevanovic[1], Dragan Cirkovic[3], Sonja Radojicic[2], Nada Lakic[4], Ljubodrag Stanisic[1], Zoran Stanimirovic[1]
[1]Department of Biology, Faculty of Veterinary Medicine, University of Belgrade, Bul. Oslobodjenja 18, 11000 Belgrade, Serbia.
[2]Department of Infectious Diseases and Diseases of Bees, Faculty of Veterinary Medicine, University of Belgrade, Bul. Oslobodjenja 18, 11000 Belgrade, Serbia.
[3]Department of Chemical-Technological Sciences, State University of Novi Pazar, Vuka Karadzica bb, 36300 Novi Pazar, Serbia
[4]Department of Statistics, Faculty of Agriculture, University of Belgrade, Nemanjina 6, 11081 Belgrade-Zemun, Serbia.

Received 17 July 2013, accepted subject to revision 20 December 2013, accepted for publication 30 January 2014.

*Corresponding author: Email: simeunovic.p@gmail.com

Summary

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onlinelibrary.wiley.com/doi/10.1111/1758-2229.12024/pdf
...nental Microbiology Reports
...ssue 1, Version of Record online: 18 JAN 2013
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Environmental Microbiology Reports (2013) 5(1), 17–29 doi:10.1111/1758-2229.1202...

Minireview

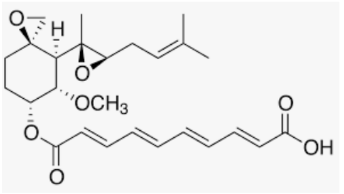
Nosema ceranae (Microsporidia), a controversial 21st century honey bee pathogen

Mariano Higes,[1]* Aránzazu Meana,[2] Carolina Bartolomé,[3] Cristina Botías[1] and Raquel Martín-Hernández[1,4]
[1]Centro Apícola Regional (CAR), Dirección General de la Producción Agropecuaria, Consejería de Agricultura,

and colony levels, but it also has significant effects on the production of honeybee products.

Introduction

LIFE WITHOUT FUMAGILIN-B



Fumagillin - Wikipedia

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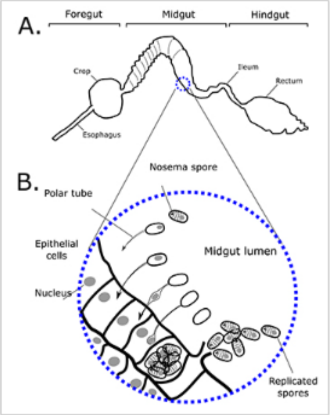
The Scientific Trenches: An Insider's Perspective

LIFE WITHOUT FUMAGILIN

- September 1, 2018 - Alison McAfee - (excerpt)



The only registered treatment for Nosema disease is no longer commercially available.

The harpoon shoots out from its egg-shaped case like a microscopic military-grade weapon. It hits its target – a honey bee midgut cell – dead on, piercing the cell membrane and latching on. But the harpoon was not built to kill (at least not right away). Instead, still attached to its case via a tubular tether, it begins injecting infectious material into the host cell, seizing the cell's resources to do its bidding in as little as two seconds. The poor cell has no choice but to comply, facilitating the mass production of more tiny, egg-shaped spores until it ruptures, releasing new spores into the gut to begin the cycle anew. More spores find more cells to infect, and the nosema infection spreads.

Nosema spores might look nondescript, but their *modus operandi* is anything but. The microscopic spore particles drift in the honey bee's midgut lumen, waiting to come across the unsuspecting epithelial cells lining the gut wall, and then they strike (Figure 1). Nosema disease, or nosemosis, is now the most globally prevalent honey bee disease, and in some regions (mainly in th
against nosemosis i

On April 12, 2018, M
shutting down produ
butter of Medivet Ph
we will dismantle ou

Medivet's ghostly w
mainly to Middle-Ea

Medivet relied on another company, CEVA Sante Animale in Libourne, France, t
outsourced manufacturer is no longer allowed to produce it, and it's unlikely that
can be produced."

Now, as we tip-toe into fall – when most beekeepers would begin treating for nos
customers. No doubt some beekeepers have a stockpile of the antibiotic at home
some labs around that are trying to test other compounds to treat nosema, but I c

IMPACT OF ANTIBIOTIC TREATMENT TO *NOSEMA* INFECTION

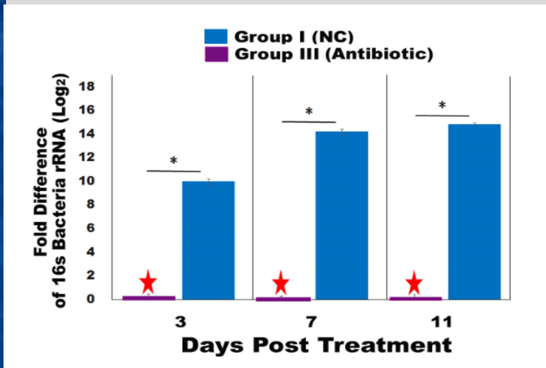


Fig 1. Disruption of bacterial activity in honey bee by antibiotic treatment

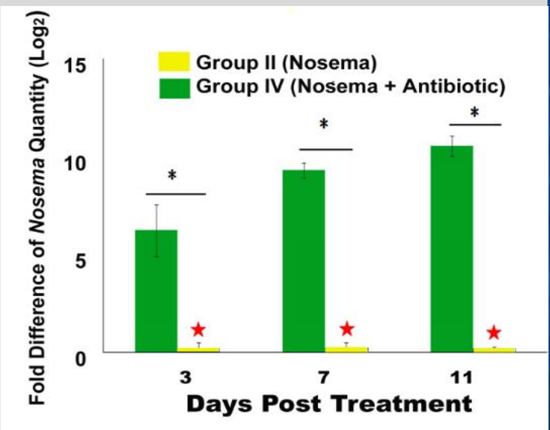


Fig 4. The relative quantities of *N. ceranae* in infected bees

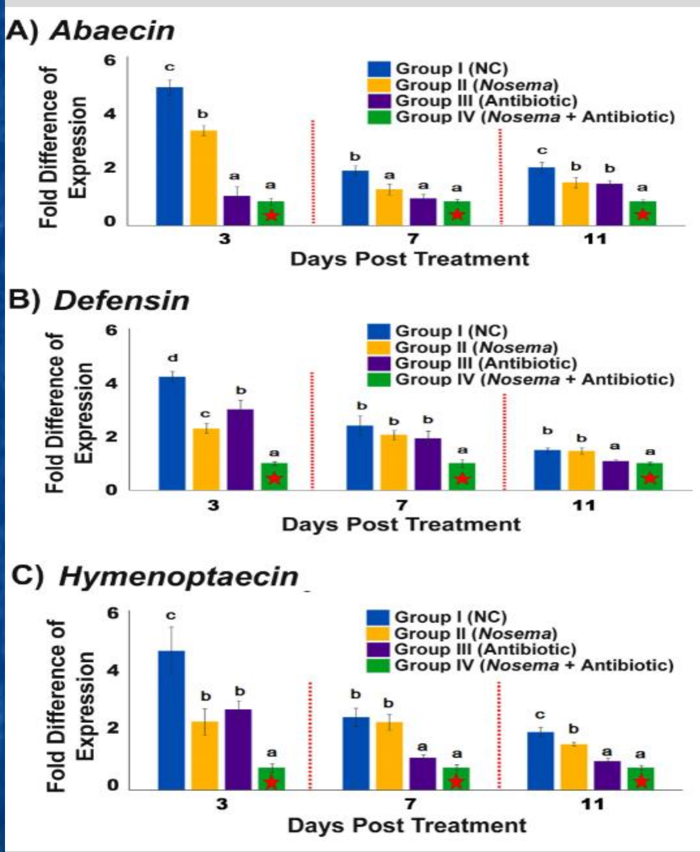


Fig 3. Effect of bacteria disruption on the expression of genes encoding antimicrobial peptides (AMPs).

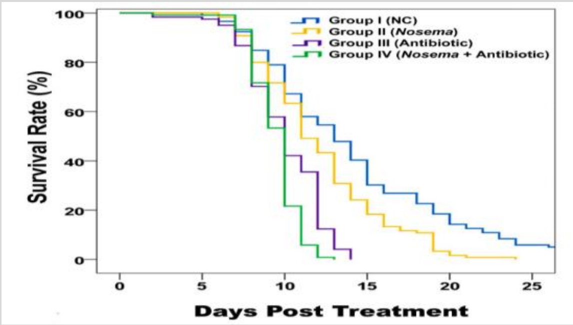
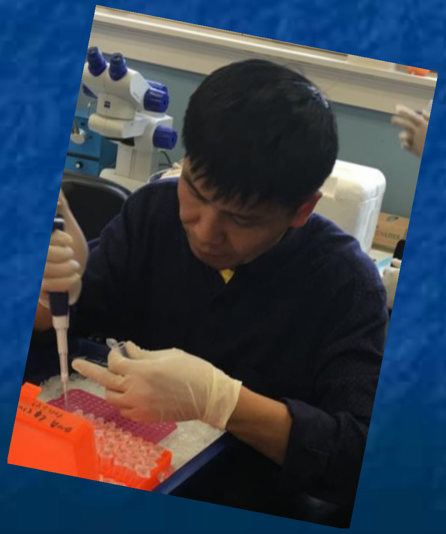
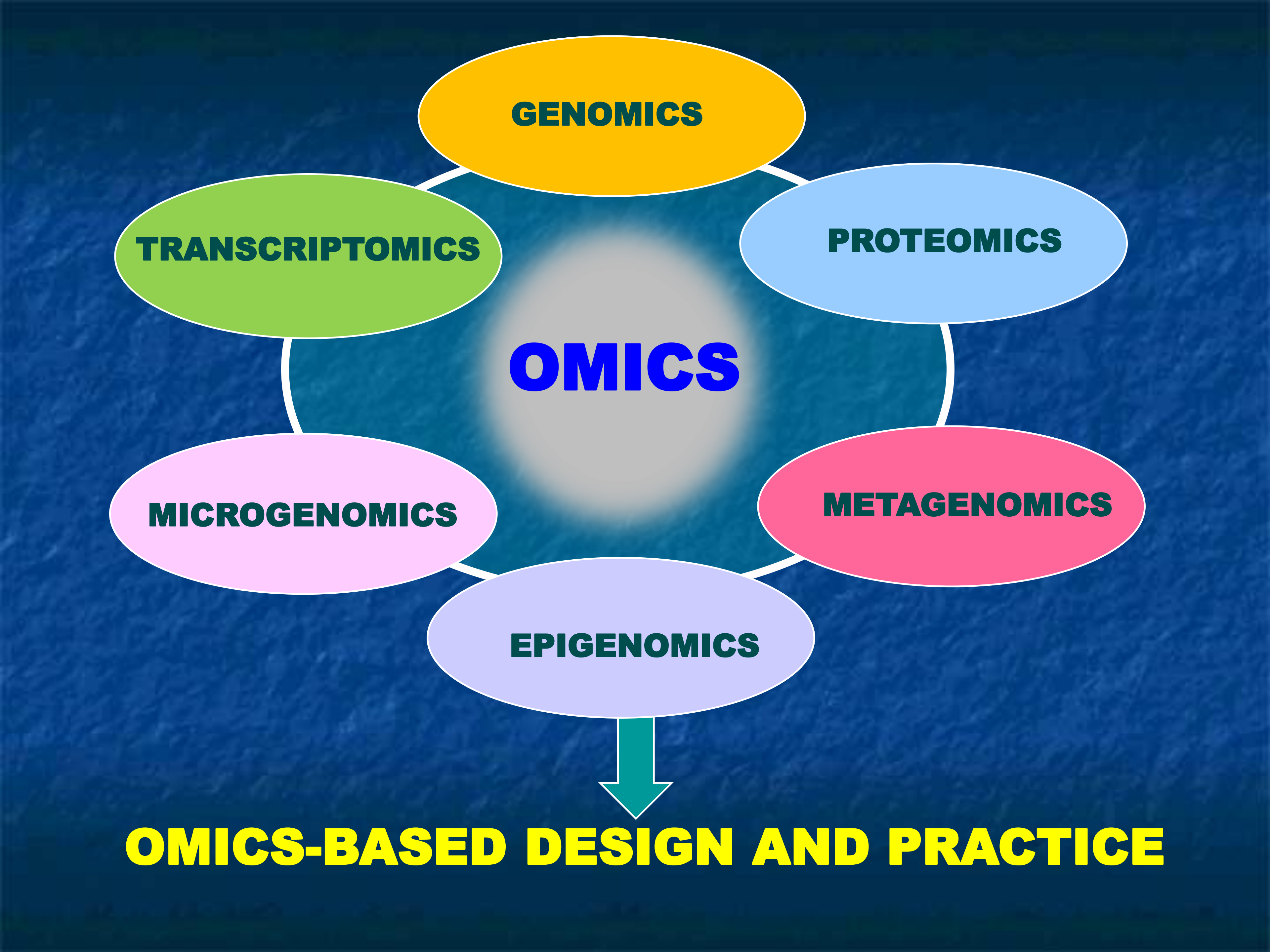


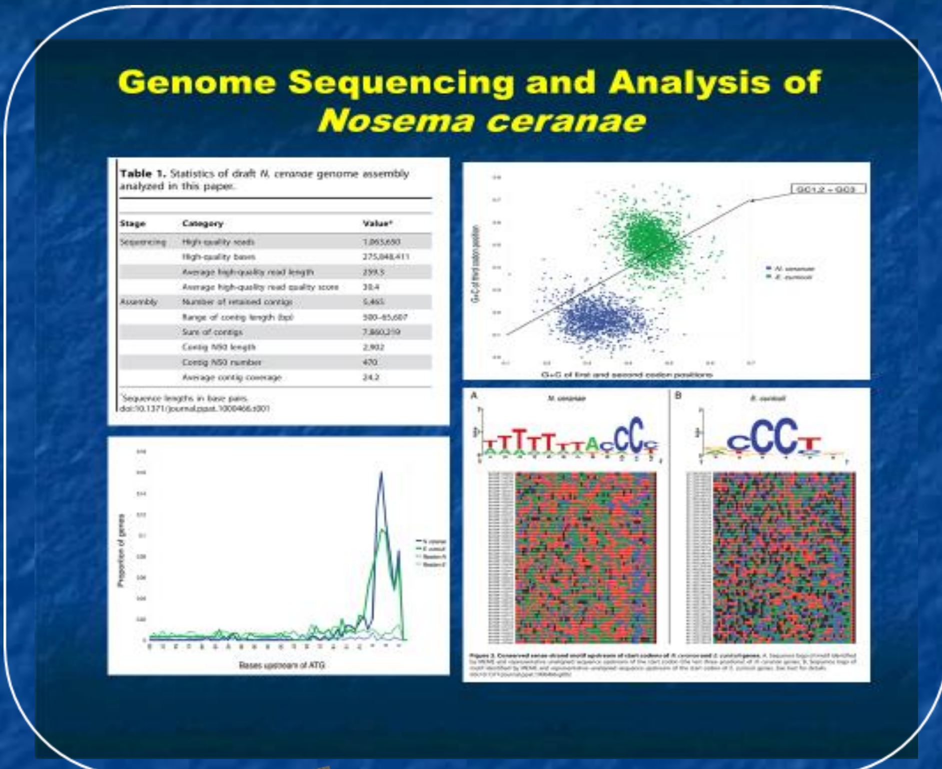
Fig 5. Effect of bacteria disruption by antibiotic and/or *Nosema* infection on the survivorship of adult workers

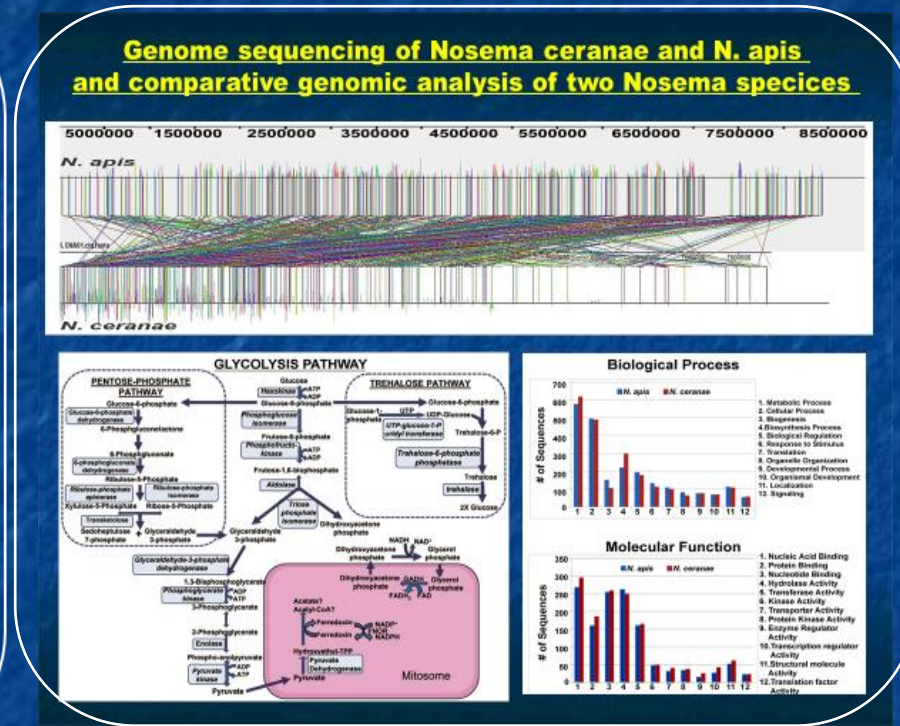


Li, J. H., et al. New evidence showing that the destruction of gut bacteria by antibiotic treatment could increase the honeybee's vulnerability to Nosema infection. PLoS ONE, 12(11): e0187505


GENOMICS
TRANSCRIPTOMICS
PROTEOMICS
OMICS
MICROGENOMICS
METAGENOMICS
EPIGENOMICS
OMICS-BASED DESIGN AND PRACTICE

A GENOMIC APPROACH





Cornman et al. (2009). Genomic analyses of the microsporidian Nosema ceranae, an emergent pathogen of honey bees. PLoS Pathog. 5(6):e100466.

Chen et al., (2013) Genome sequencing and comparative genomics of honey bee microsporidia parasite, Nosema apis reveal novel insights into host-parasite interactions. BMC Genomics. 14:451.

N. ceranae VIRULENT FACTORS

SEQ. ID	GENE/PROTEIN	FUNCTION	HOMOLOGOUS TO *N. apis*
NcORF-00063	swp25_nosbo ame/Spore wall protein	Host Cell Adhesion	No
NcORF-00064	swp25_nosbo ame//Spore wall protein	Host Cell Adhesion	No
NcORF-00308	swp26_nosbo ame/spore wall protein	Host Cell Adhesion	Yes
NcORF-00240	Spore wall protein 12	Host Cell Adhesion	Yes
NcORF-00600	swp32_nosbo ame/spore wall protein 30	Host Cell Adhesion	Yes
NCORF-00159	hypothetical spore wall protein 25 flags	Host Cell Adhesion	Yes
NcORF-00803	spore wall and anchoring disk complex	Host Cell Adhesion	No
NcORF-00159	hypothetical spore wall protein	Host Cell Adhesion	Yes
NcORF-00543	hypothetical spore wall protein 381	Host Cell Adhesion	Yes
NcORF-01130	enp1/Spore wall and anchoring disk complex	Host Cell Adhesion	Yes
NcORF-02428	y215/Spore wall protein ecu02_0150 flags	Host Cell Adhesion	Yes
NcORF-00608	swp25_nosbo ame/Spore wall protein 25 flags	Host Cell Adhesion	Yes
NcORF-00083	Polar tube protein 3	Host Cell Invasion	Yes
NcORF-00182	chitin synthase d	Spore Wall Formation	Yes
NcORF-00659	chitin synthase activator	Spore Wall Formation	Yes
NcORF-00086	protein transport protein	Energy Parasitism	Yes
NcORF-00440	transport protein Sec23	Energy Parasitism	Yes
NcORF-00537	protein transporter sec24	Energy Parasitism	No
NcORF-00316	golgi gdp-mannose transporter	Energy Parasitism	Yes
NcORF-01150	transmembrane protein	Energy Parasitism	Yes
NcORF-00170	atp adp translocase	Energy Parasitism	Yes
NcORF-00319	atp adp translocase	Energy Parasitism	Yes
NcORF-00097	atp-binding cassette sub-family	Energy Parasitism	Yes
NcORF-00461	vacuolar protein sorting-associated protein	Energy Parasitism	Yes
NcORF-00540	vesicular transport protein	Energy Parasitism	Yes
NcORF-00663	abc transporter	Energy Parasitism	Yes
NcORF-00705	abc transporter (mitochondrial type)	Energy Parasitism	Yes
NcORF-00710	abc transporter	Energy Parasitism	Yes
NcORF-00711	abc atp-binding permease protein	Energy Parasitism	Yes
NcORF-02000	mitogenactivated protein kinase organizer	Pathogenicity Regulation	No
NcORF-00738	ngg1-interacting factor 3	Pathogenicity Regulation	No
NcORF-00751	mitotic checkpoint protein bub3	Pathogenicity Regulation	Yes
Over 500	Conserved hypothetical proteins		No

Host

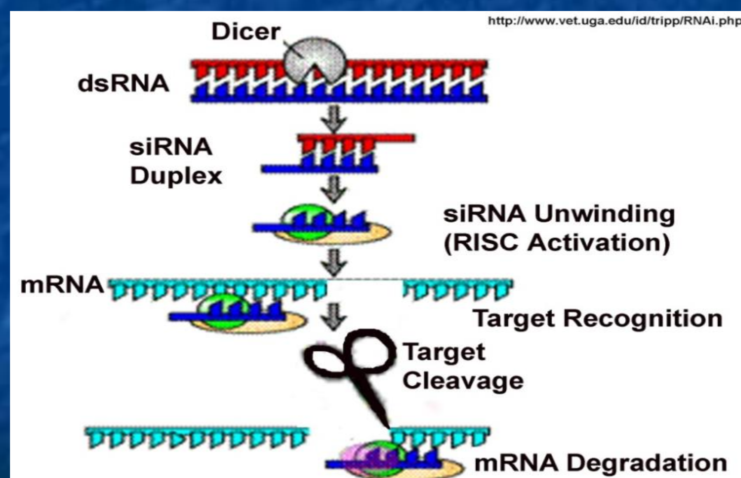
Innate Immunity
- Cellular
- Humoral

Host Defense
- Caste and age
- Behavior

Parasite

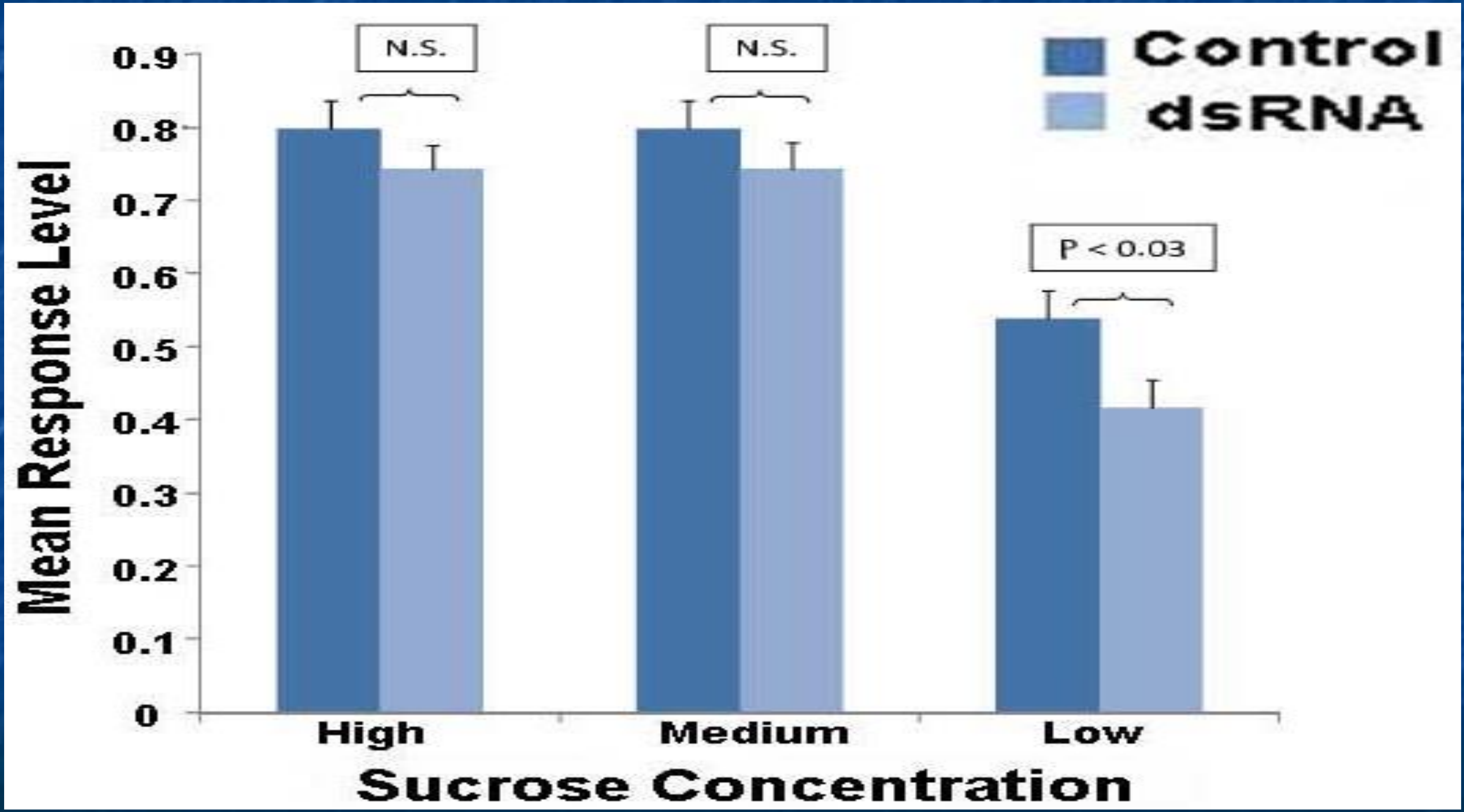
Virulent Factors:
- Invasion
- Virulence
- Defense avoidance

RNA INTERFERENCE (RNAi)



No Protein Expression

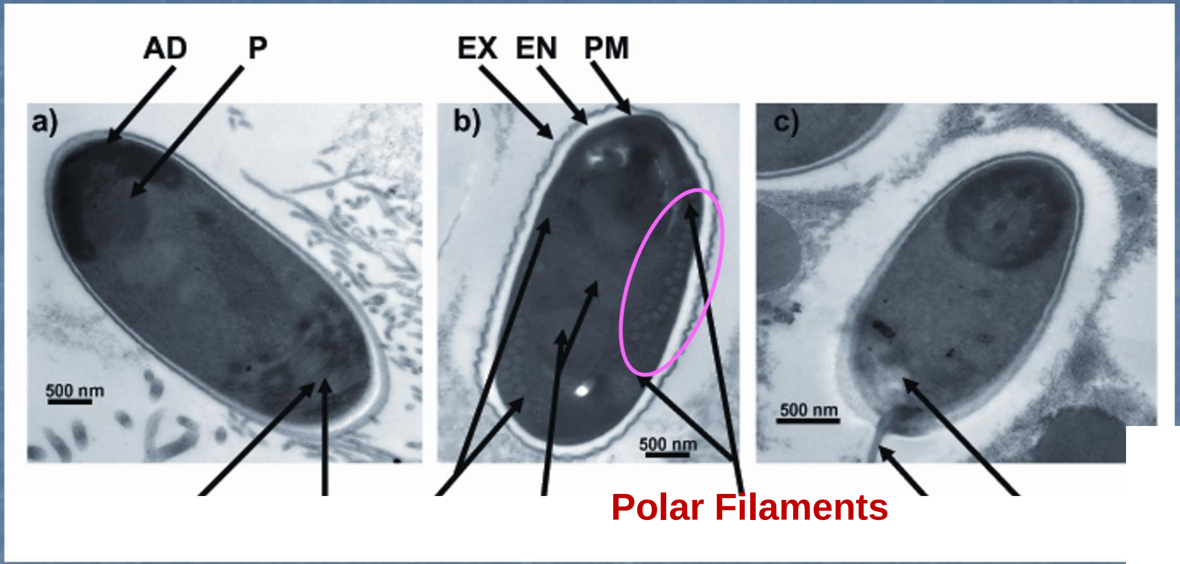
KNOCKDOWN OF *N. ceranae* ADP/ATP TRANSPORTER GENES

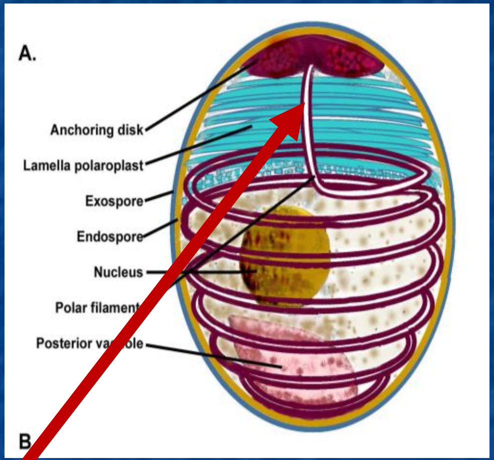


Paldi et al. (2010) Effective Gene Silencing in a Microsporidian Parasite Associated with Honeybee (Apis mellifera) Colony Declines. AEM. 76 (17): 5960–5964.

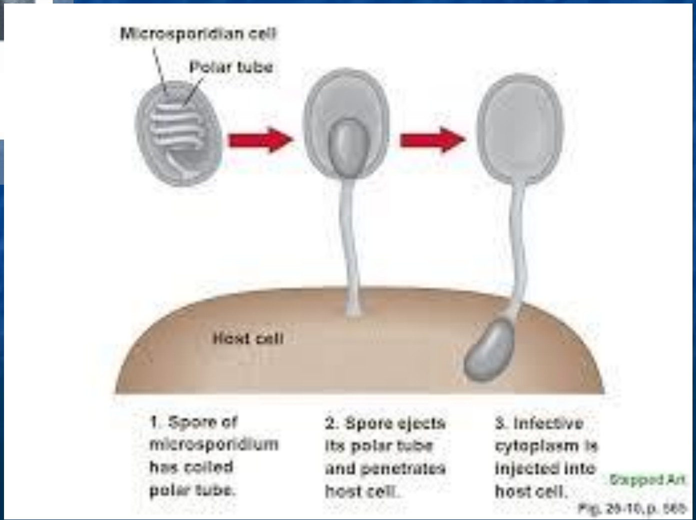
N. eeranae POLAR TUBE/FILAMENT

<u>Electron Micrograph of the *Nosema ceranae* Spore</u>





Polar Filament



Chen, Y. P. et al. 2009. . Morphological, molecular, and phylogenetic characterization of Nosema ceranae, a microsporidian parasite isolated from the European honey bee, Apis mellifera. J. Euk. Micro. 56(2): 142-147.

NOSEMOSIS CONTROL BY RNAi SILENCING GENE ENCODING POLAR TUBE PROTEIN 3 (PTP3)

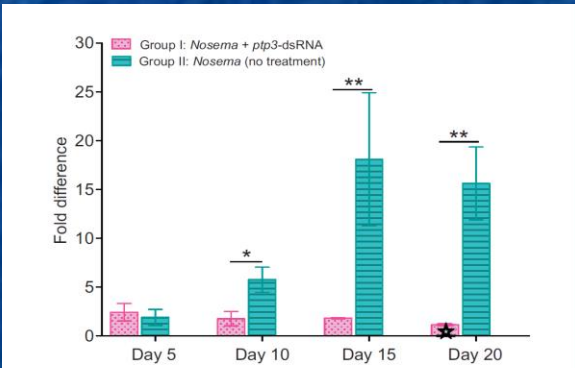


Fig. 1. Dynamic of *Nosema ceranae ptp3* expression in infected bees at different sampling points. Honey bees were inoculated with 10^6 *N. ceranae* spores first and then fed with *ptp3*-dsRNA (group I), or negative control without any treatment (group II). The fold difference is expressed as mean±s.d. The calibrator for each time interval used to normalize the gene expression was the group with the lowest expression and is represented with a grey star. A *t*-test was used to analyse the differences between data, and represented with asterisks (**P*<0.05, ***P*<0.001). Group III had no *N. ceranae* spores and was not represented.

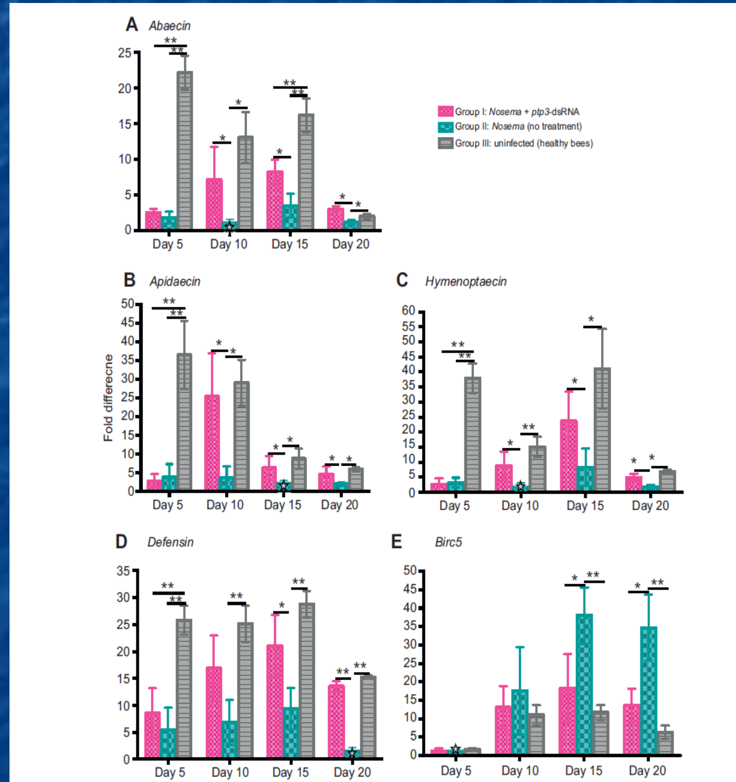


Fig. 2. Effects of *ptp3*-dsRNA treatment on the expression of genes encoding *abaecin*, *apidaecin*, *hymenoptaecin*, *defensin* and *birc5* at days 5, 10, 15 20 post-treatment. (A) *Abaecin*; (B) *apidaecin*; (C) *hymenoptaecin*; (D) *defensin-1*; (E) *birc5*. Group I, *Nosema*-infected bees with *ptp3*-dsRNA treatment; grou *Nosema*-infected bees without treatment; group III, *Nosema*-uninfected healthy bees. The relative normalized expression is expressed as mean±s.d. The calibrator for each time interval used to normalize the gene expression was the group with the lowest expression and is represented with a gray star. One-way ANC and Tukey's post hoc test was used to analyse the differences between data. Significant differences are represented with asterisks (**P*<0.05, ***P*<0.001).

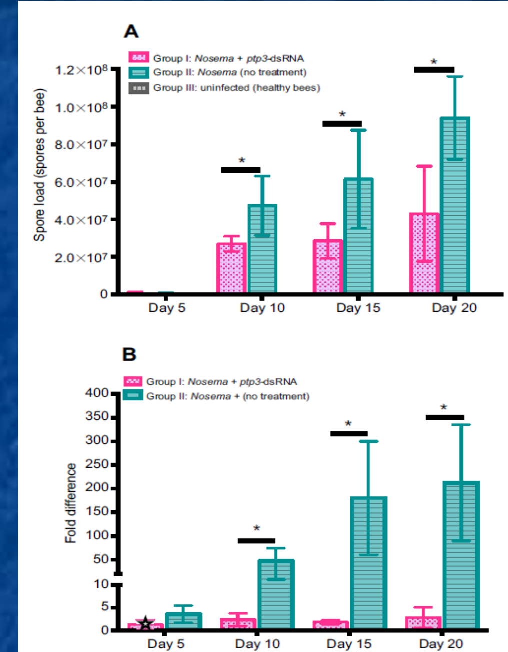


Fig. 3. Effect of *ptp3* silencing on the spore load of adult workers infected by *N. ceranae*. (A) The spore load is expressed as mean±s.d. (B) The relative normalized expression of 16S rRNA is also expressed as mean±s.d. The calibrator for each time interval used to normalize the gene expression was the group with the lowest expression and is represented with a gray star. A *t*-test was employed to analyse the differences between data, and represented with asterisks (**P*<0.05, ***P*<0.001). Group III was free of spores and without 16S rRNA expression during all sampling points, so is not represented in B.

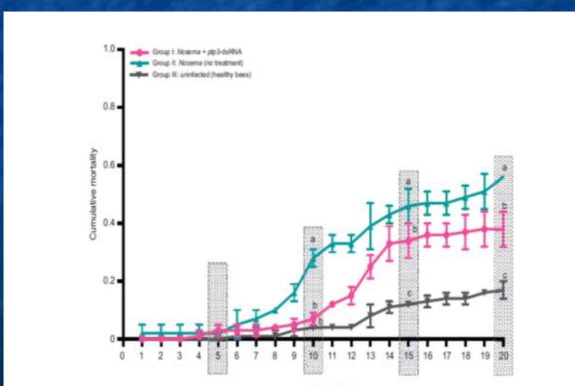
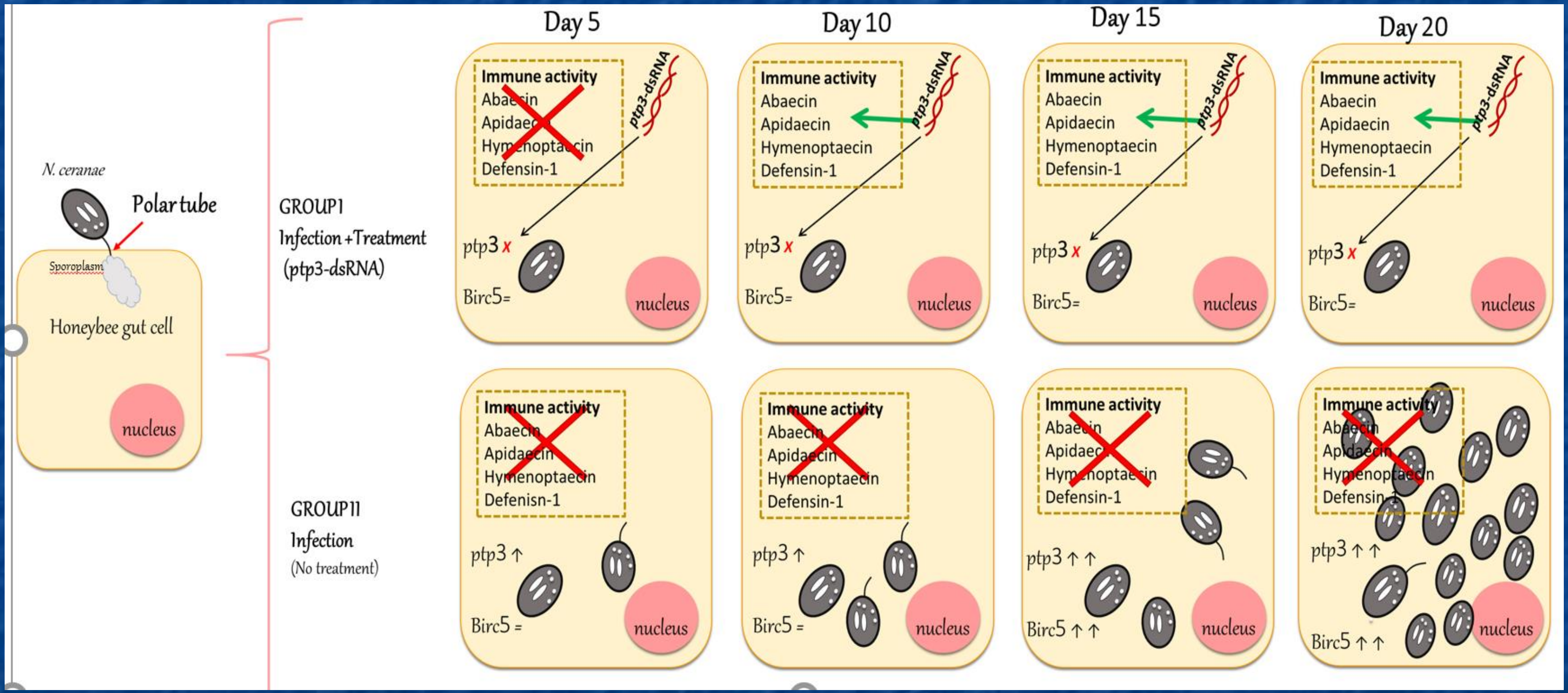


Fig. 4. Cumulative mortality for the three experimental groups. *N*=105 bees per group. Data represent the proportion of cumulative mortality (mean±s.d.) of the three groups over time (20 days). Group I, *Nosema*-infected bees treated with *ptp3*-dsRNA (pink line); group II, *Nosema*-infected bees without treatment (blue line); group III, healthy bees without *Nosema* infection (gray line). Shaded boxes show the days of mortality analysis. Knockdown of the *N. ceranae ptp3* gene reduced the incidence of death. Different letters denote significant differences (*P*<0.05 by ANOVA and Tukey's post hoc test).

Rodríguez-García et al. 2018. Nosemosis control in honey bees Apis mellifera by silencing the gene encoding Nosema ceranae polar tube protein 3. J Exp Biol.5;221(Pt 19). pii: jeb184606.

A MODEL OF SILENCING MECHANISM BY RNAi



CONCLUSION: ***N. ceranae*** **gene** ***ptp3*** **is a good candidate for the development of an innovative therapeutic strategy for large scale field application in the future.**

Host

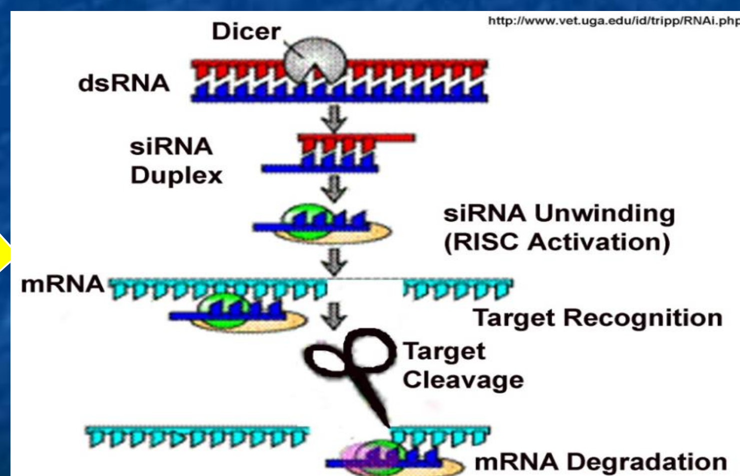
Innate Immunity
- Cellular
- Humoral

Host Defense
- Caste and age
- Behavior

Parasite

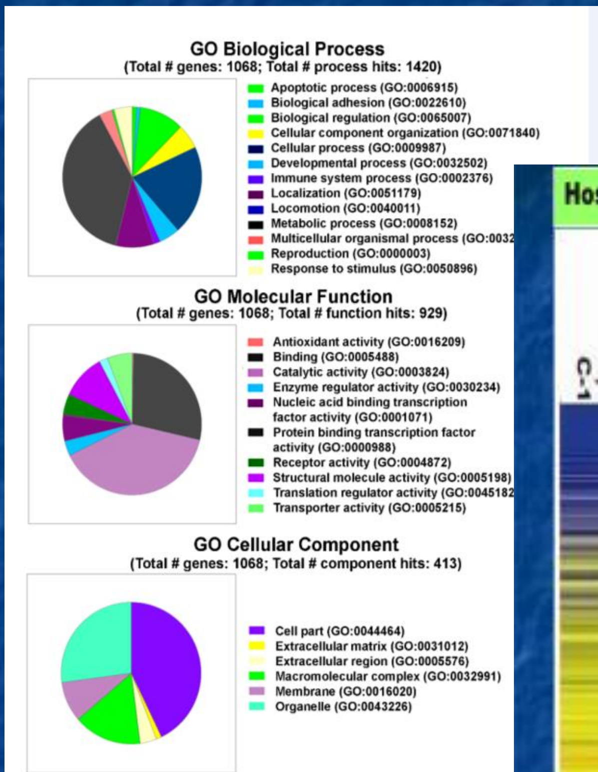
Virulent Factors:
- Invasion
- Virulence
- Defense avoidance

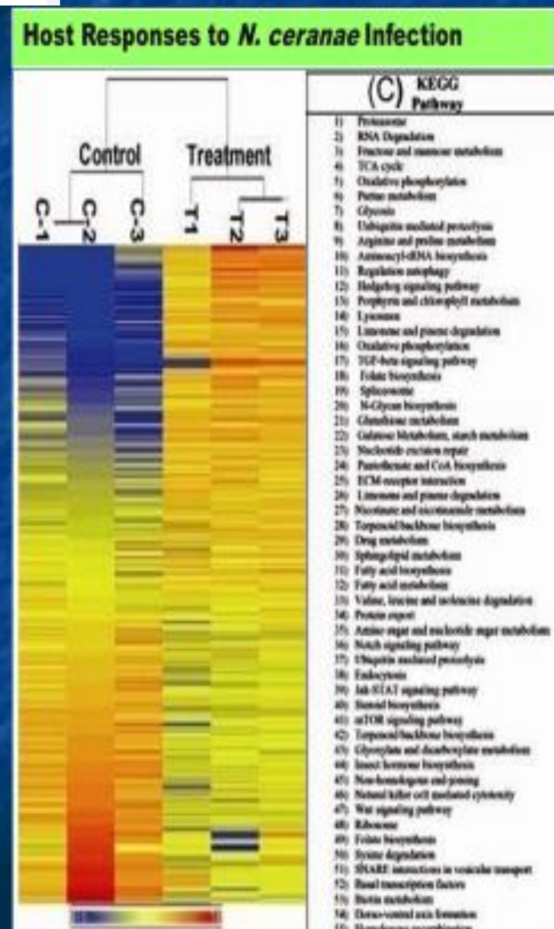
RNA INTERFERENCE (RNAi)

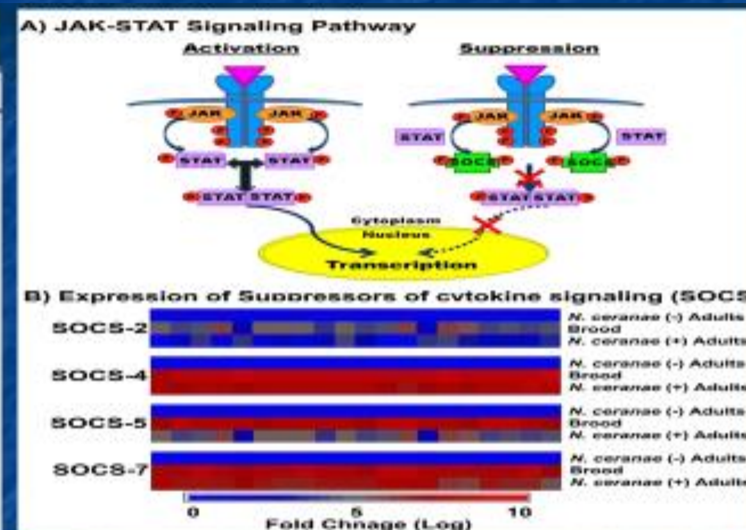


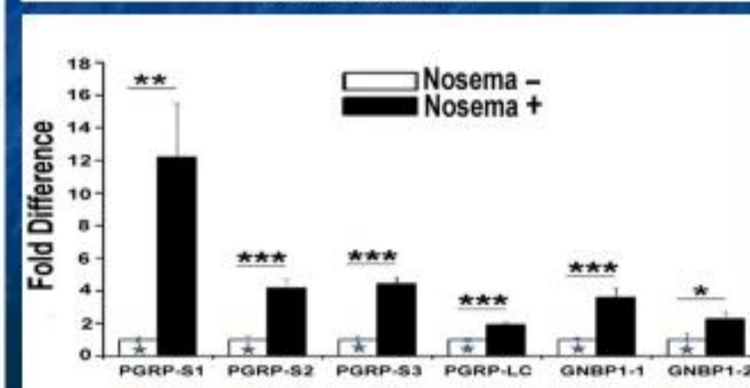
No Protein Expression

A TRANSCRIPTOMIC APPROACHE

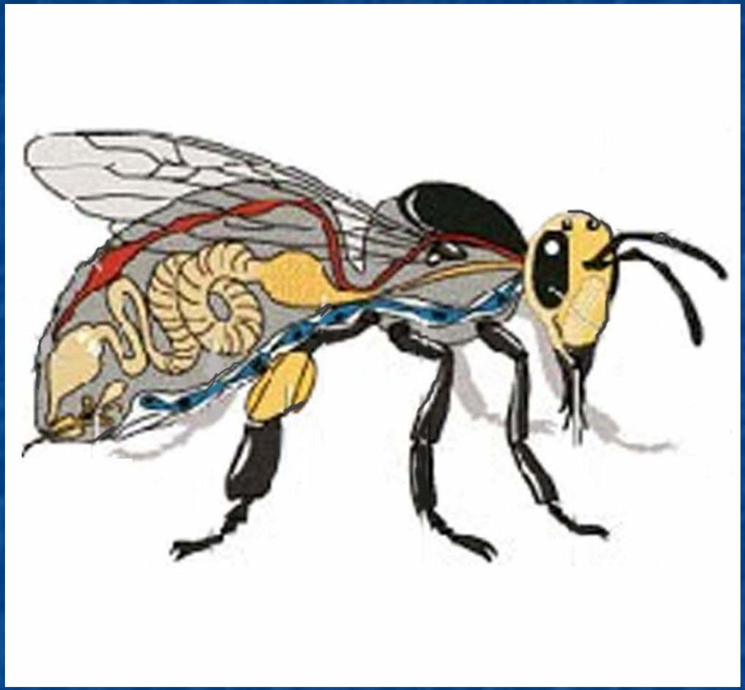








HONEY BEE IMMUNE DEFENSES



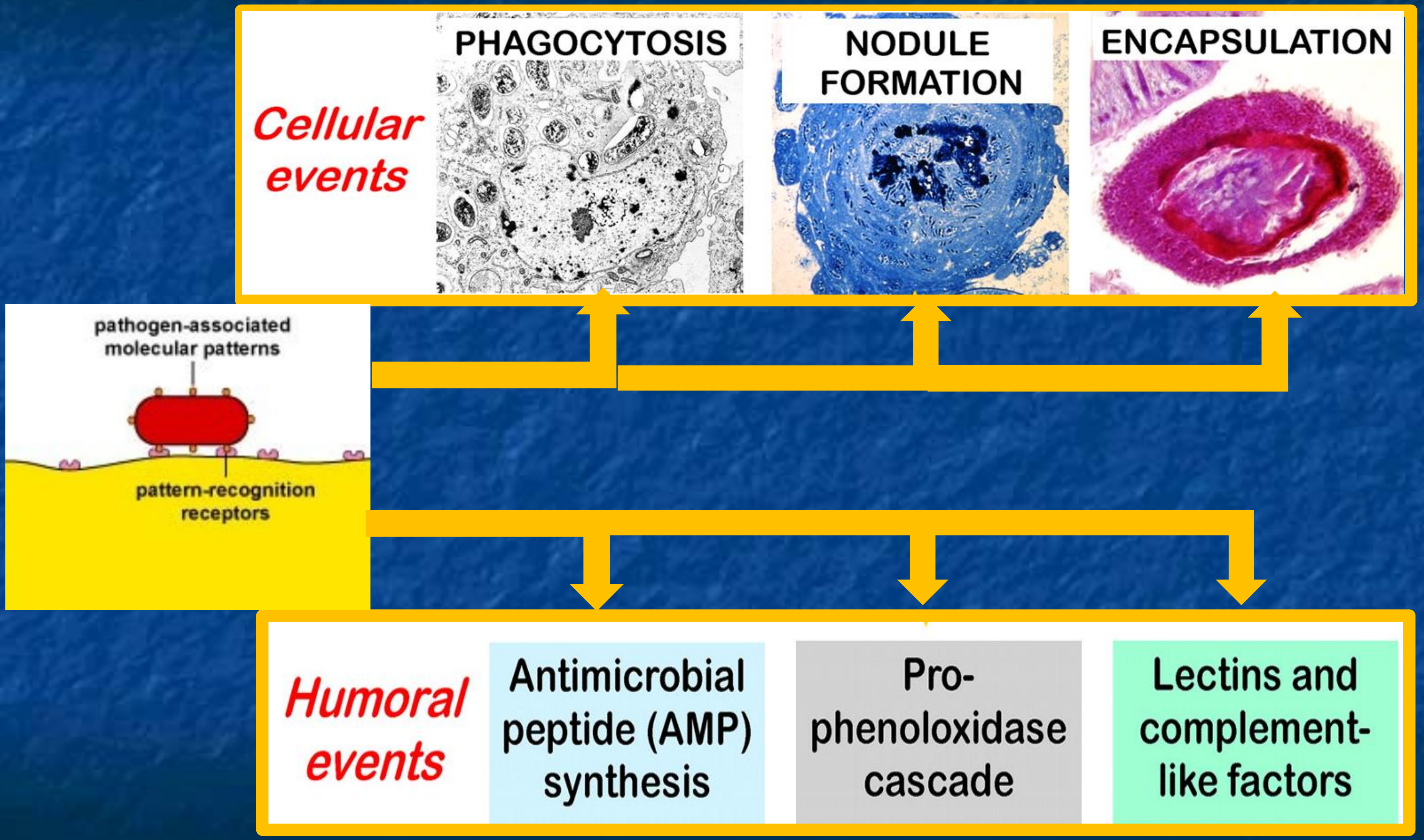
Social Immunity

- Task specialization
- Social Fever
- Grooming
- Hygienic Behaviors

Individual Immunity

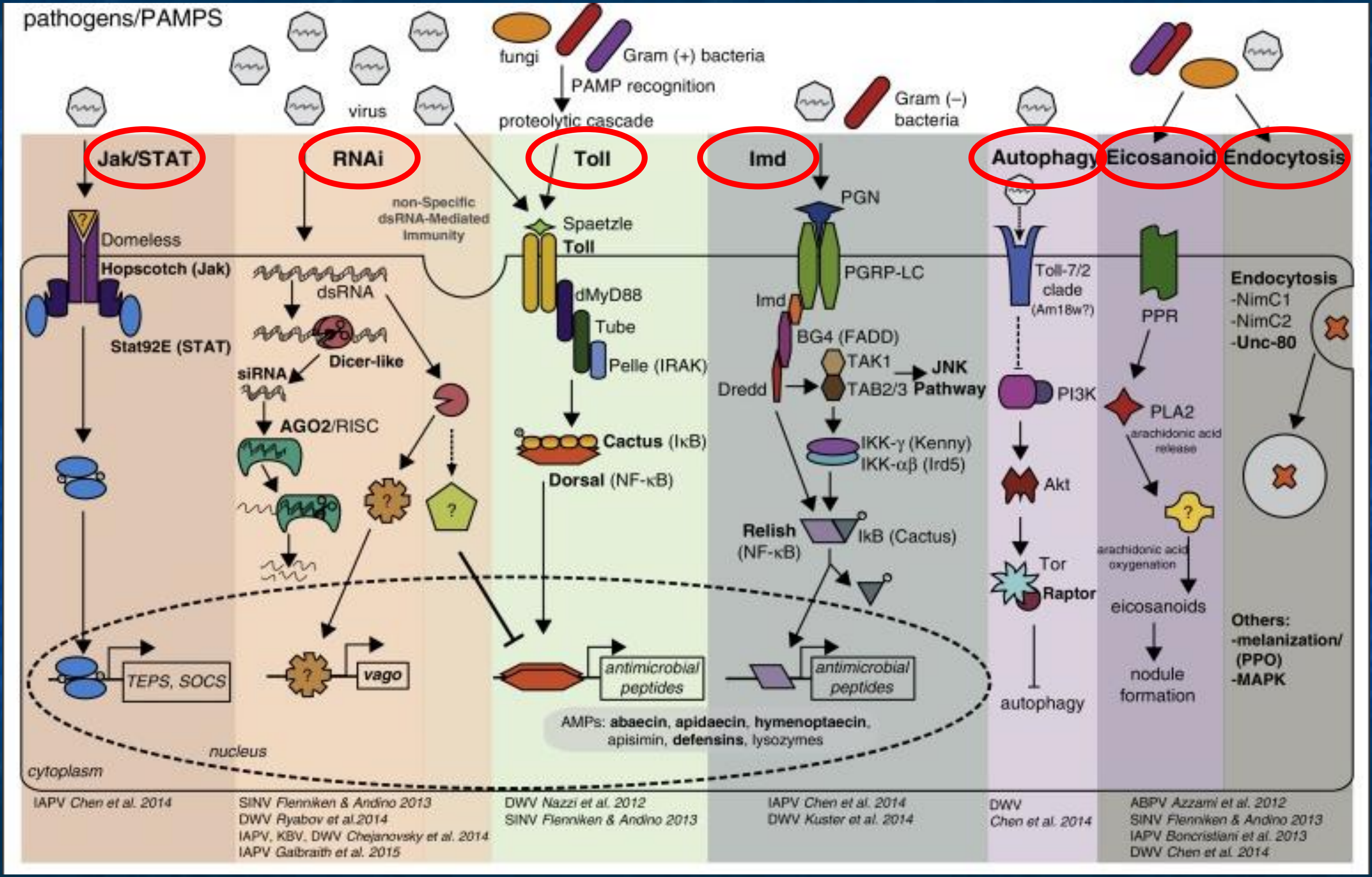
- Cuticle barrier
- Microbiota
- Cellular
- Humoral (Antimicrobial peptides)
- Apoptosis
- RNAi

SCHEMATIC OF THE DEFENSE STRATEGIES OF INSECTS



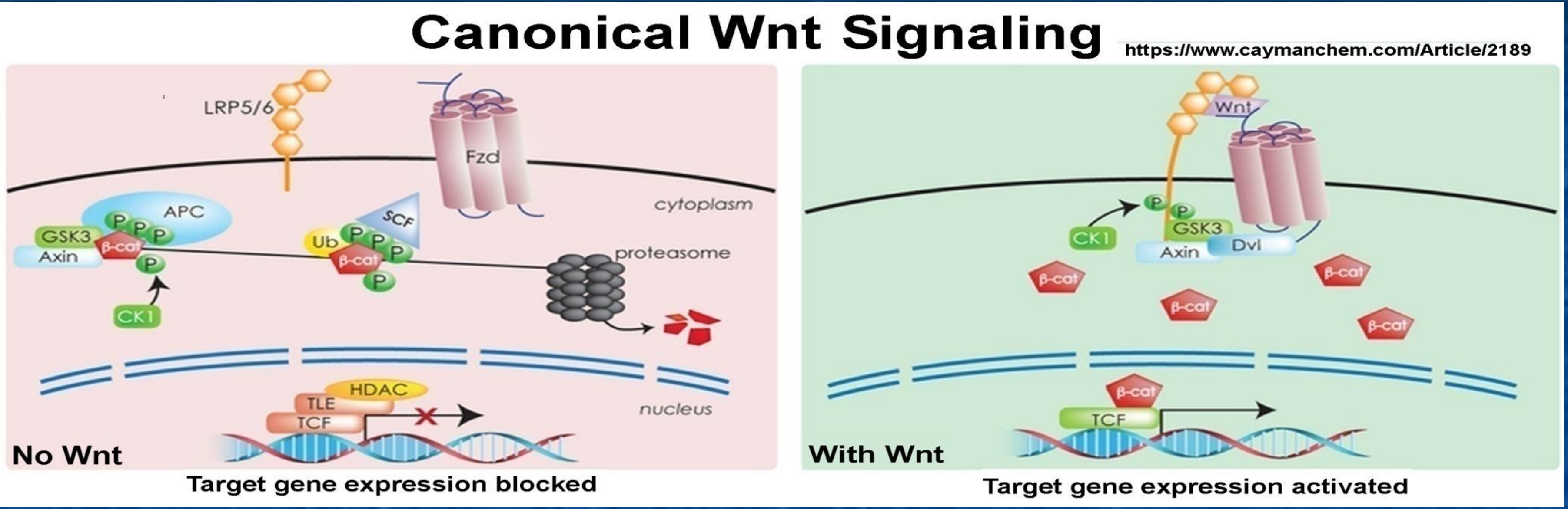
Rowley and Powell. (2007) Invertebrate Immune Systems–Specific, Quasi-Specific, or Nonspecific? J. Immunol. 179 (11) 7209-7214

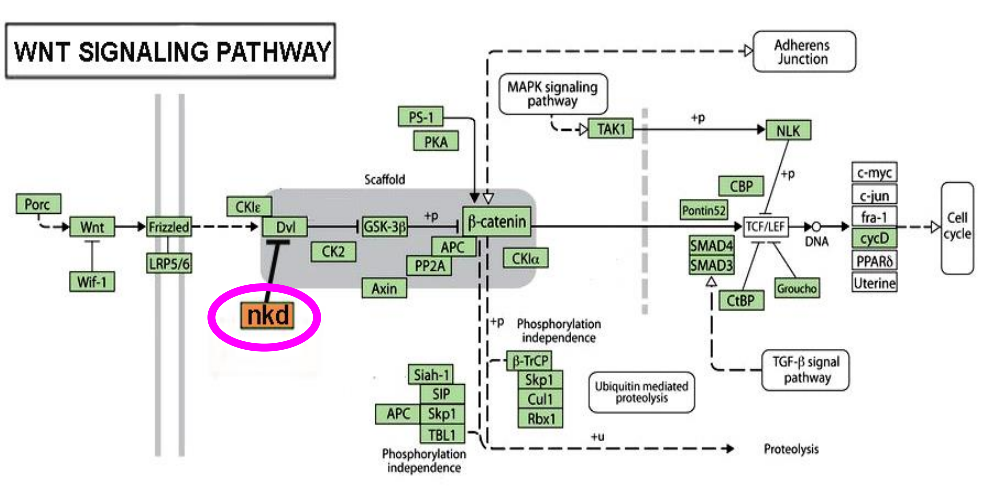
SIGNAL PATHWAYS IN THE HONEY BEE IMMUNE RESPONSES



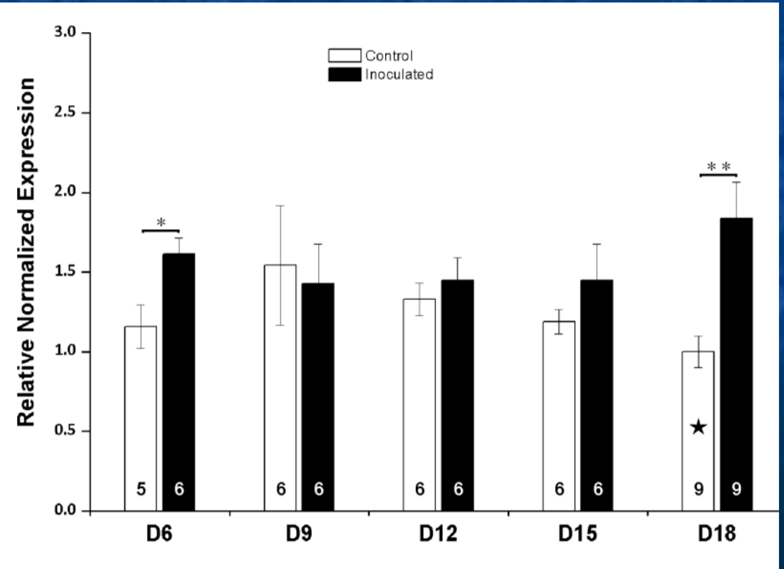
Brutscher et al., Antiviral defense mechanisms in honey bees . Current Opinion in Insect Science. 10: 71-82.

HOST IMMUNE RESPONSES TO *N. ceranae* INFECTION

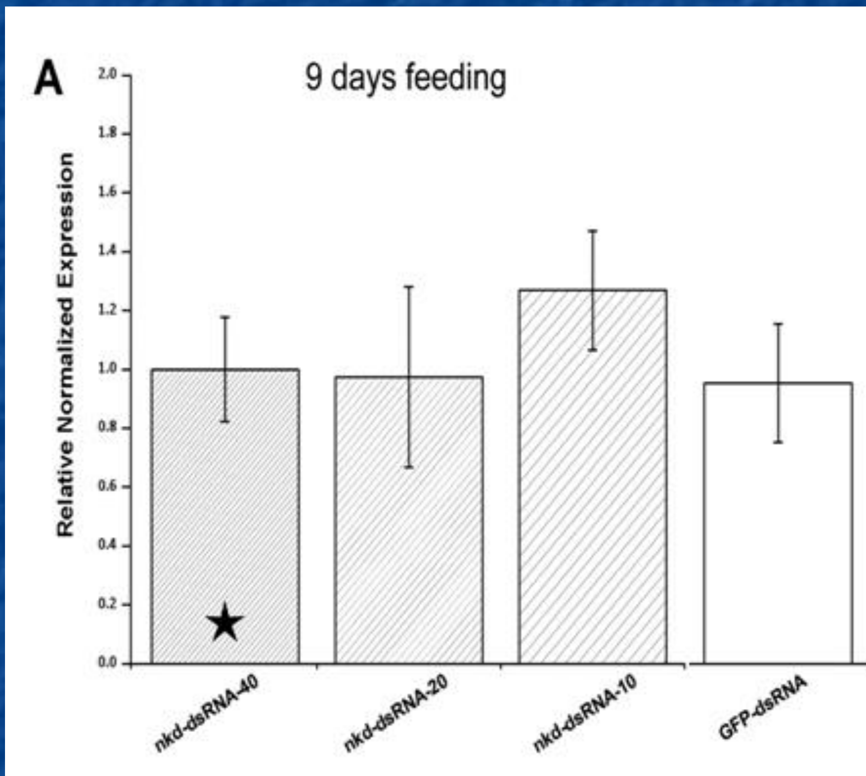


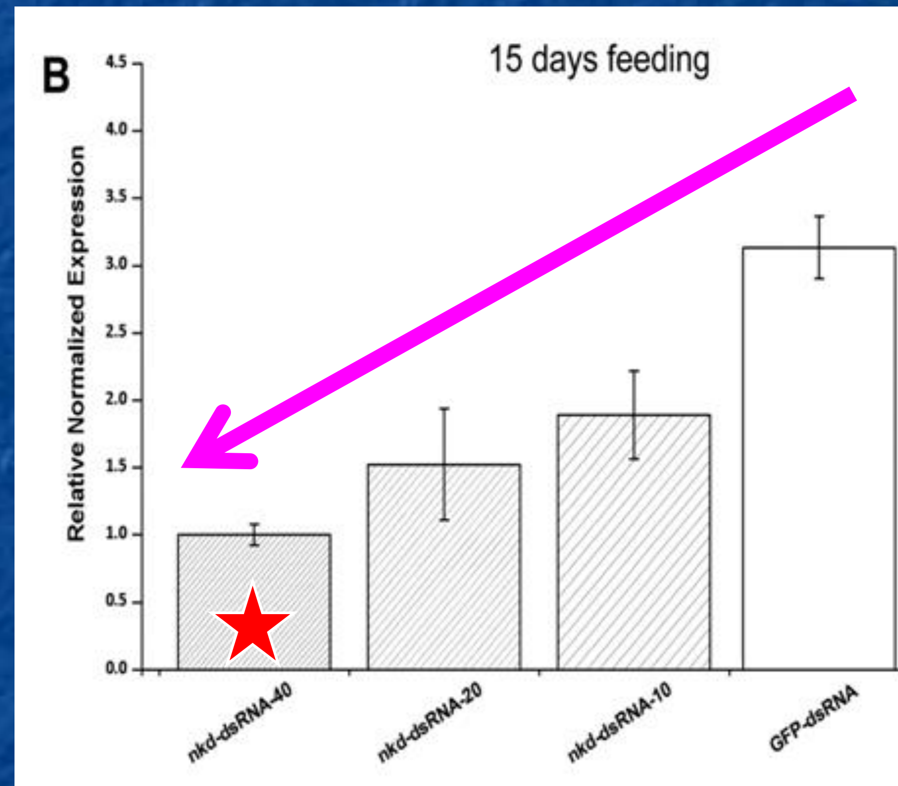


A KEGG diagram of the canonical Wnt/β-catenin pathway
(Boxes in green indicate proteins relevant to Wnt signaling in *Drosophila melanogaster*)



KNOCKDOWN OF *nkd* GENE IN ADULT BEES BY dsRNA INGESTION





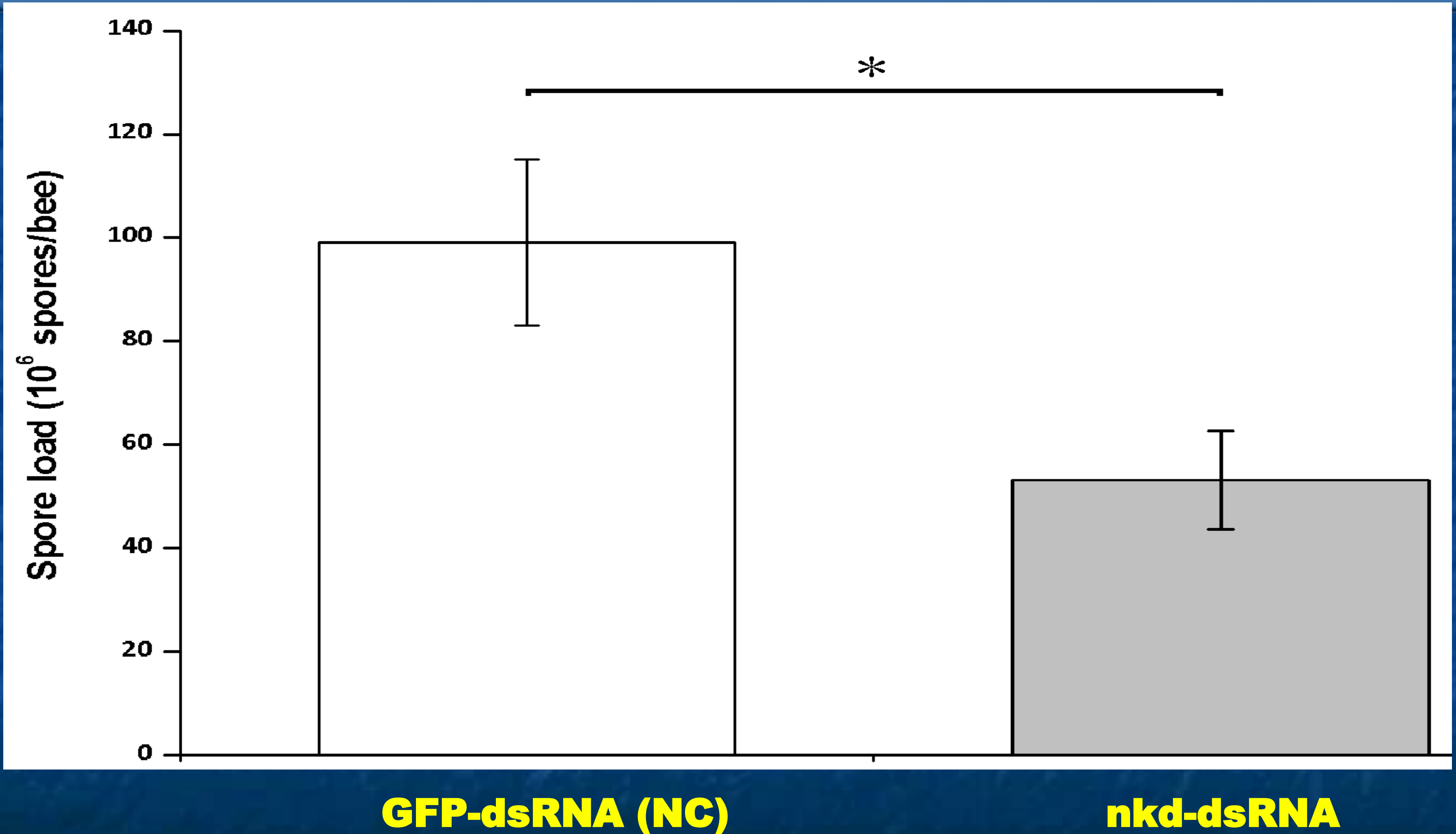
40 µg/ml **20 µg/ml** **10 µg/ml** **NC**

40 µg/ml **20 µg/ml** **10 µg/ml** **NC**

The Concentration of nkd dsRNA

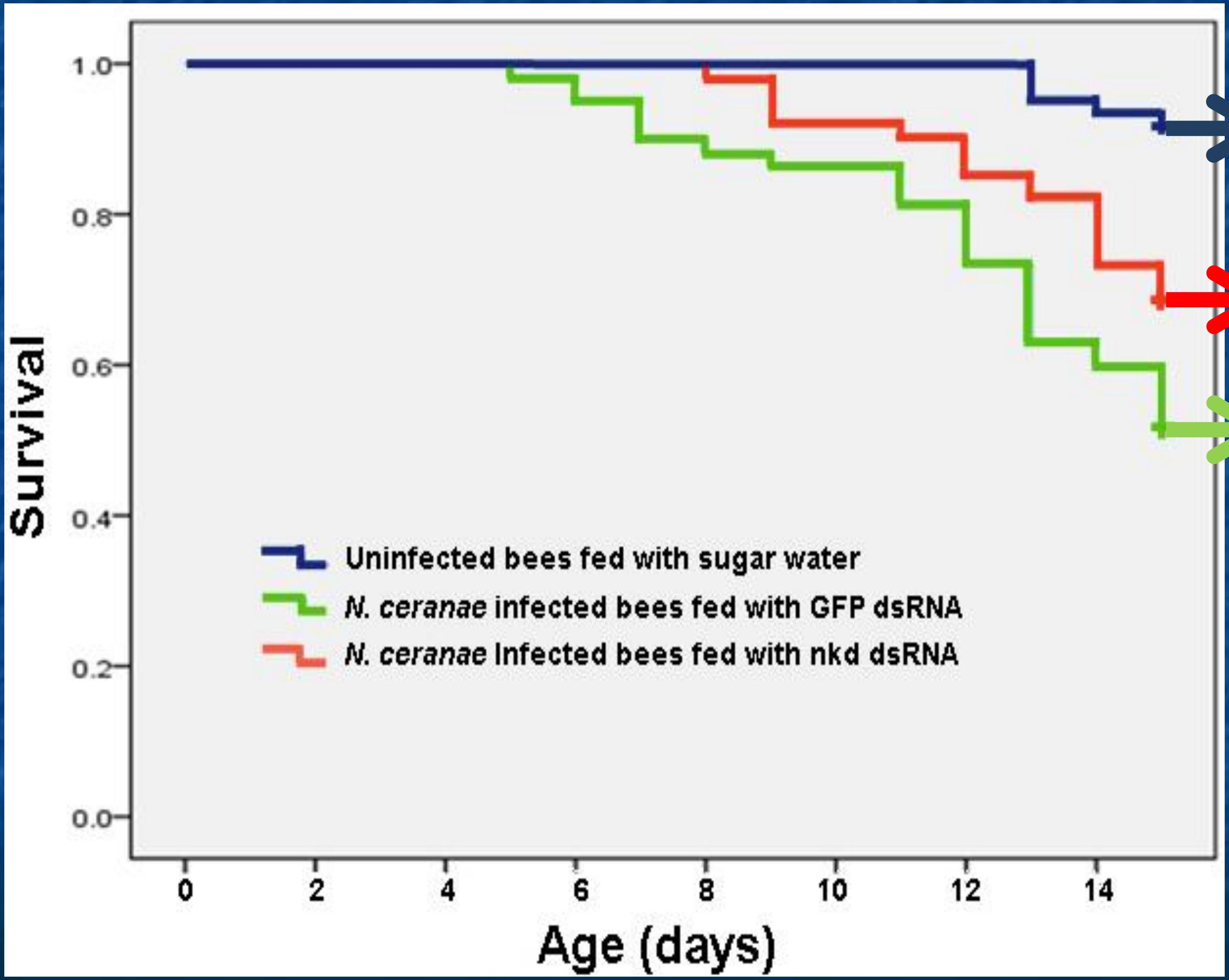
Li et al. (2016) Silencing honey bee (Apis mellifera) naked cuticle (nkd) improves host immune function and reduces Nosema ceranae infections. Applied and Environmental Microbiology. 82:6779-6787.

EFFECT OF *nkd* GENE SILENCING ON THE *N. ceranae* INFECTION LEVELS IN ADULT BEES



Li et al. (2016) Silencing honey bee (Apis mellifera) naked cuticle (nkd) improves host immune function and reduces Nosema ceranae infections. Applied and Environmental Microbiology. 82:6779-6787.

EFFECT OF *nkd* GENE SILENCING ON THE *LIFESPAN OF N. ceranae infected* HONEY BEES



Uninfected Bees

Nosema infected bees
With dsRNA treatment

Nosema infected bees
without dsRNA treatment

Li et al. (2016) Silencing honey bee (Apis mellifera) naked cuticle (nkd) improves host immune function and reduces Nosema ceranae infections. Applied and Environmental Microbiology. 82:6779-6787.

A NUTRITIONAL APPROACH

Group 1: pollen
Group 2: Pollen + Antibiotics
Group 3: neither pollen nor antibiotics
Group 4: Antibiotics

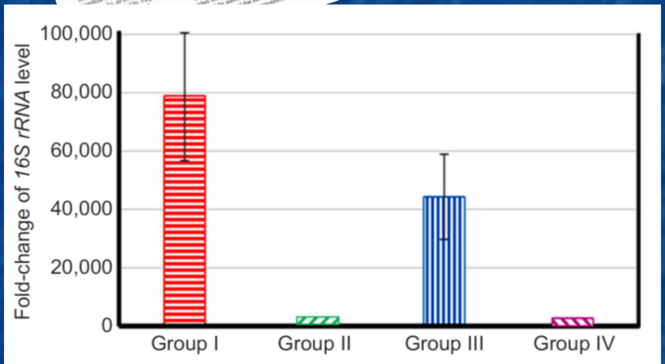


Fig. 2. Effect of antibiotics on the activity of honey bee gut bacteria.

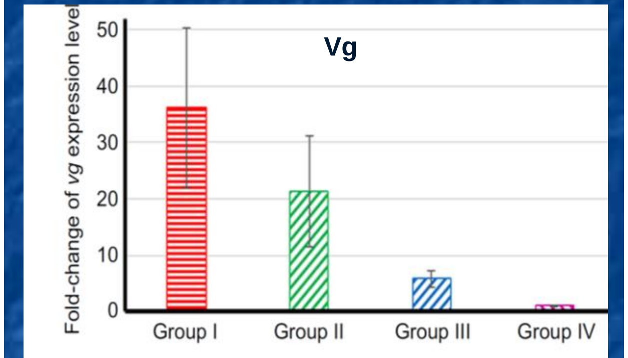


Fig. 4. Effect of pollen diet and antibiotics on the expression of *vg*

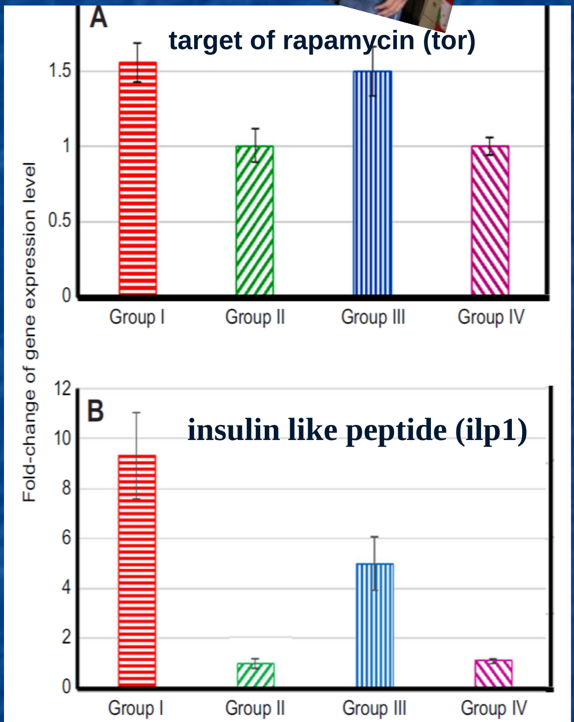
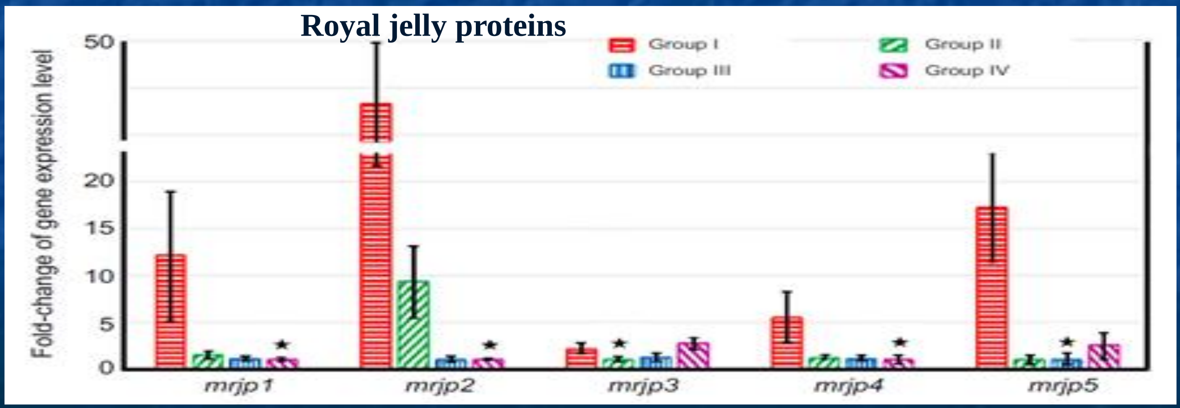


Fig. 3. Effect of pollen diet and antibiotics on the expression of *tor* and *ilp1* in honey bees. (A,B) The relative expression levels of *tor* (A) and *ilp1* (B).



Li, J. H., et al. 2019. Pollen reverses decreased lifespan, altered nutritional metabolism, and suppressed immunity in honey bees (Apis mellifera) treated with antibiotics. J Exp Biol. 222: jeb202077

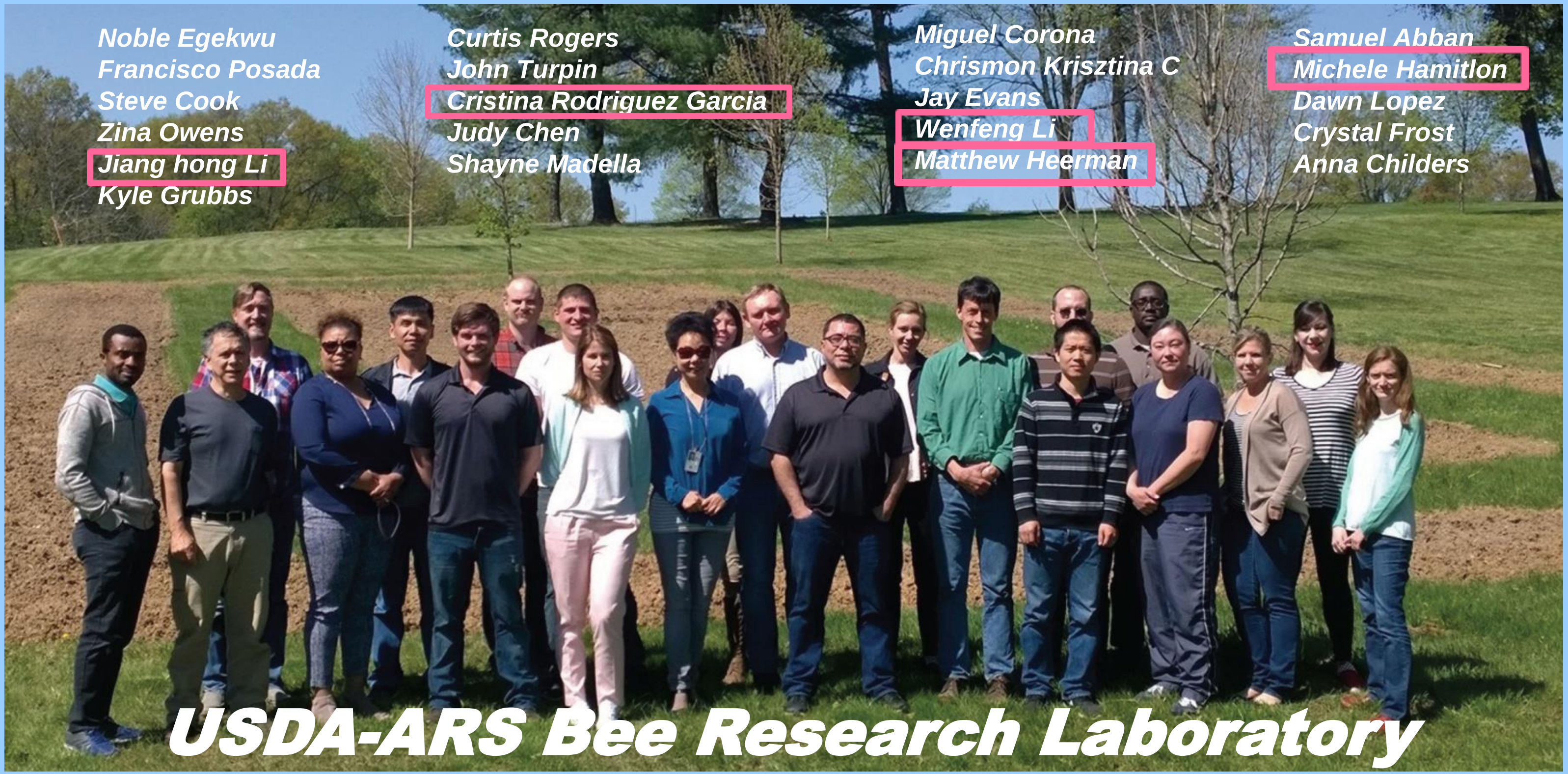
CONCLUSIONS

- Silencing both parasite/pathgen virulent factors and host immune suppressors could be an efficient way to improve honey bee immunity, suppress Nosema reproduction, and improve overall honey bee health.

- *RNAi holds great therapeutic potential for* honey bee disease treatment that merits further exploration.

- Pollen and gut microbes play essential role in promoting honey bee immunity and health.

ACKNOWLEDGEMENTS



Funding
USDA-ARS
USDA-NIFA Grant
(2014-67013-21784)

NIH-NIDDK
Weiping Chen
Renhui Li

Agri. & Agri-Food Canada
Stephen Pernal
Andony Melathopoulos

Penn State University
Christina M. Grozinger

Kentucky State University
Thomas Webster

Uni. Of Maryland
Dennis vanEngelsdorp[9]
Lisa D Sadzewicz

This is the end