Immunity, stress and sub-lethal effects of neonicotinoids

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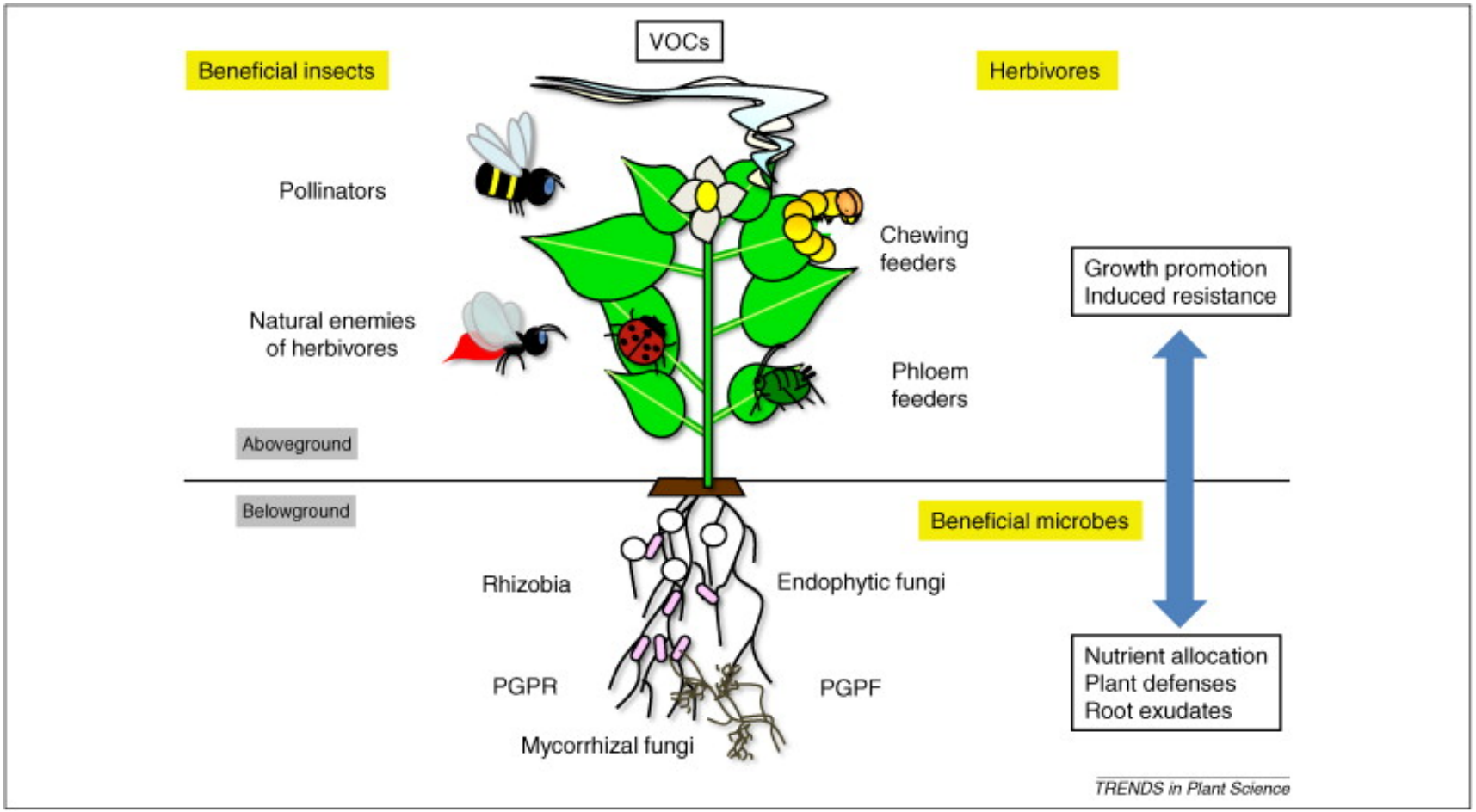
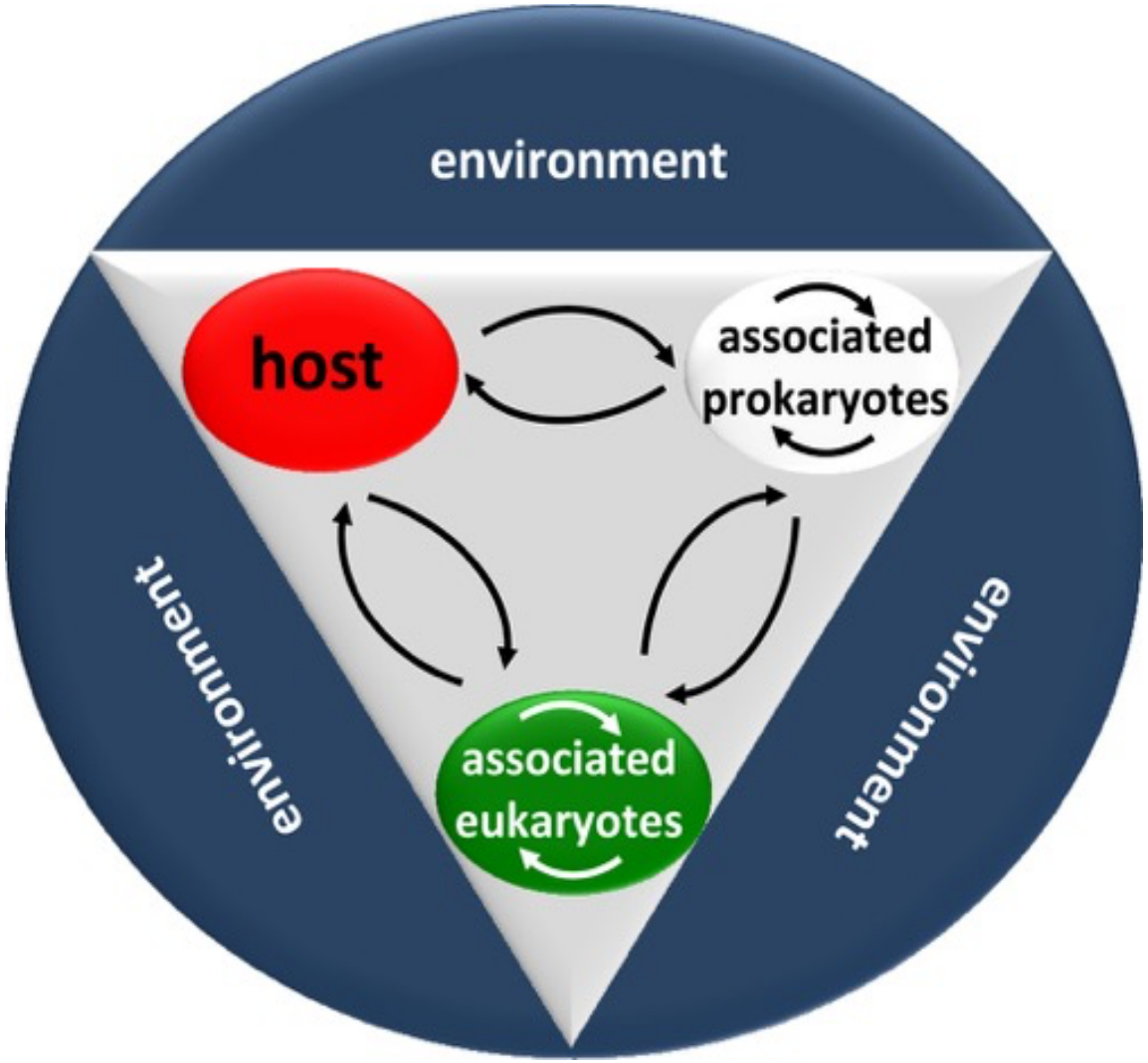
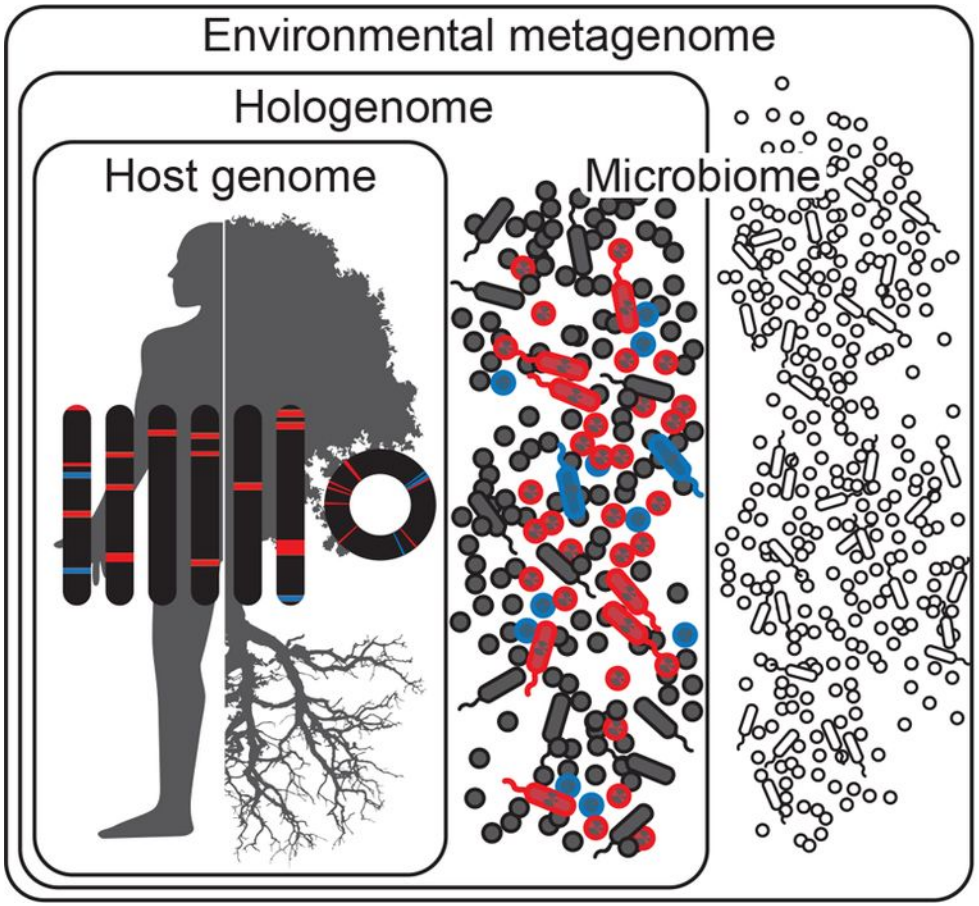
Multitrophic Interactions



Interactions at metaorganism level



Holobiont phenotype is controlled by the hologenome



Host and symbiont genes that alone and/or together affect a holobiont phenotype

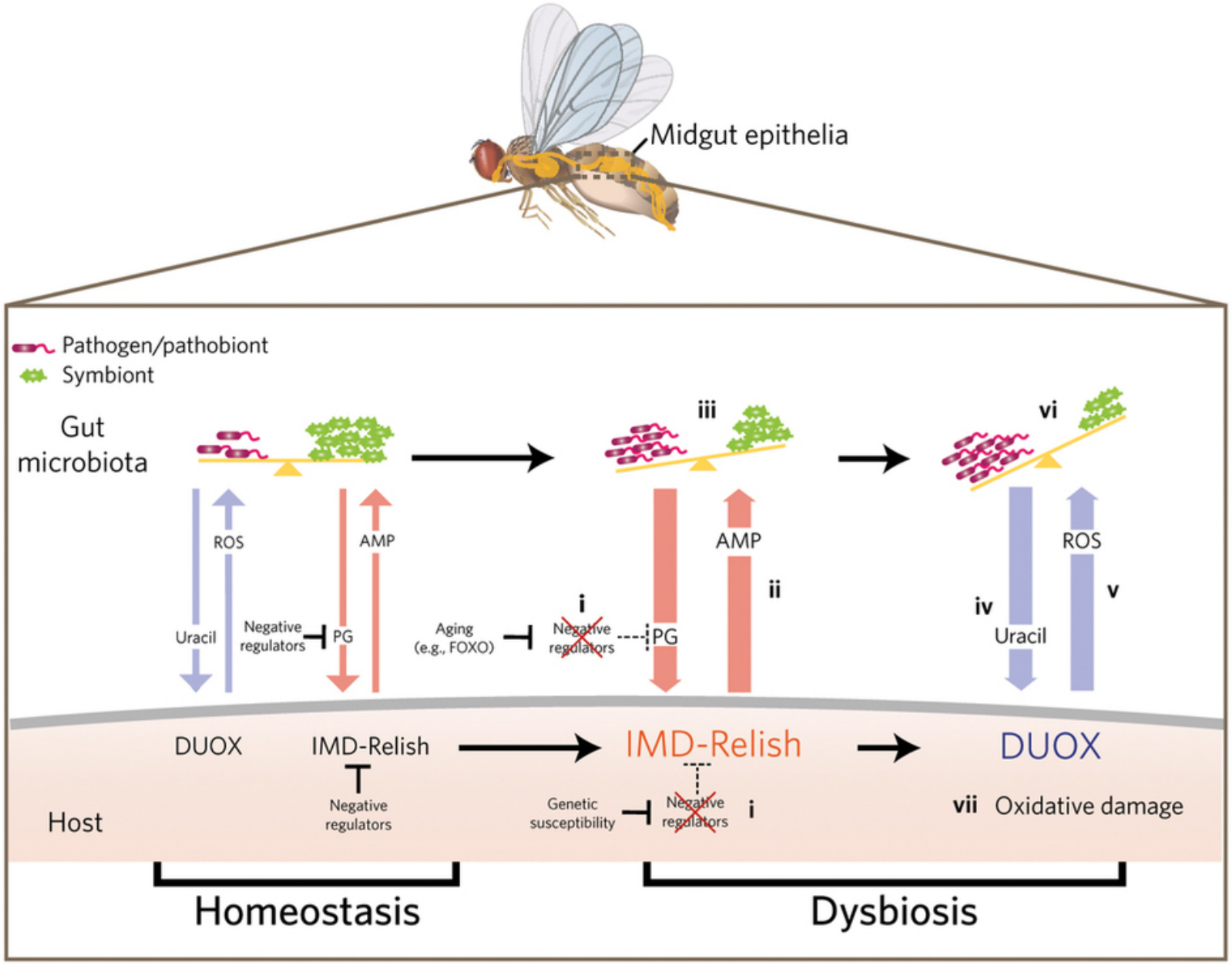
Coevolved host and symbiont genes that affect a holobiont phenotype

Host genes and symbionts that do not affect a holobiont phenotype

Environmental microbes that are not part of the holobiont

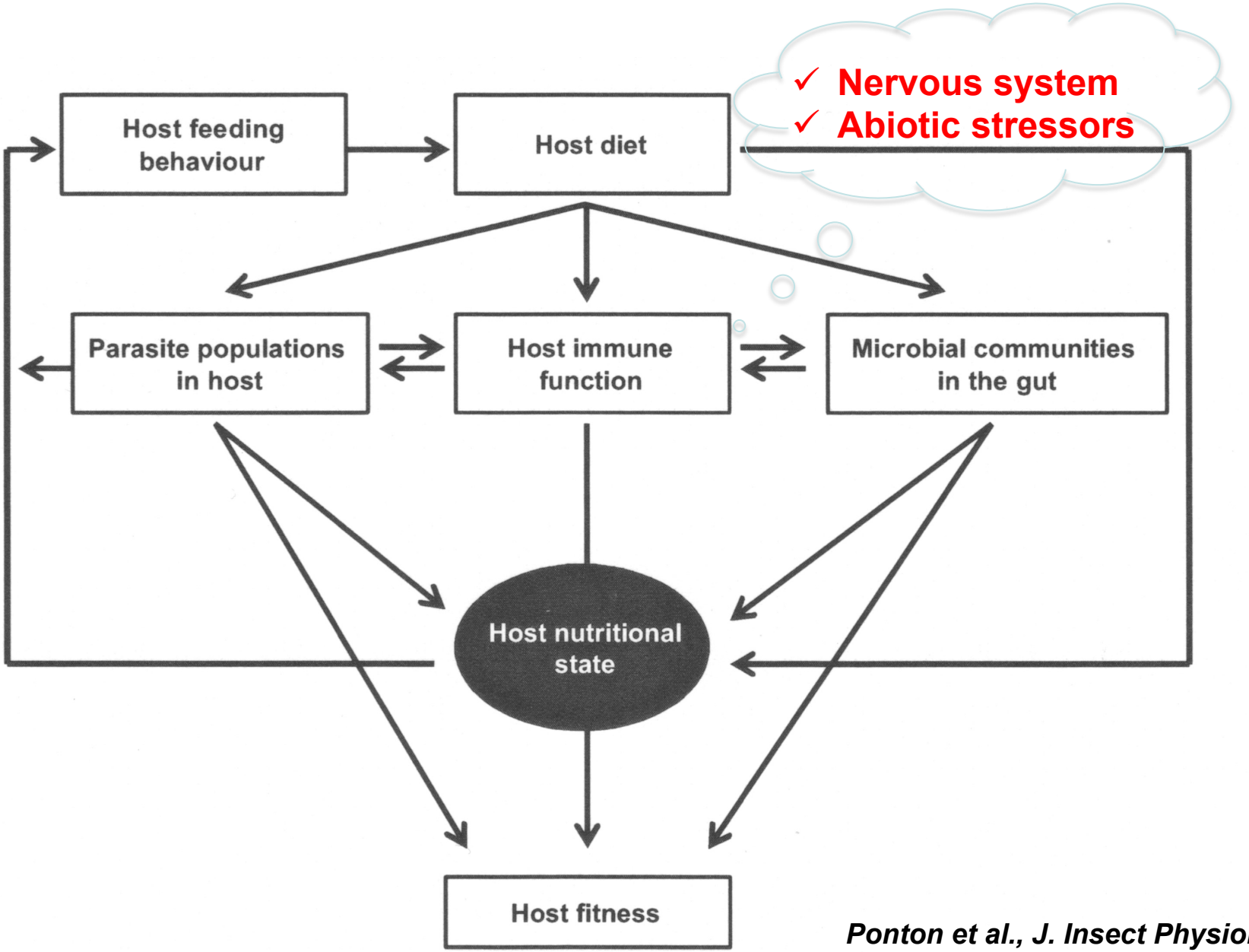
Kevin R. Theis et al. mSystems 2016;1:e00028-16

Gut Microbiota and Immunity



Lee & Hase, Nature Chemical Biology, 2014

Multifactorial regulation of immunity



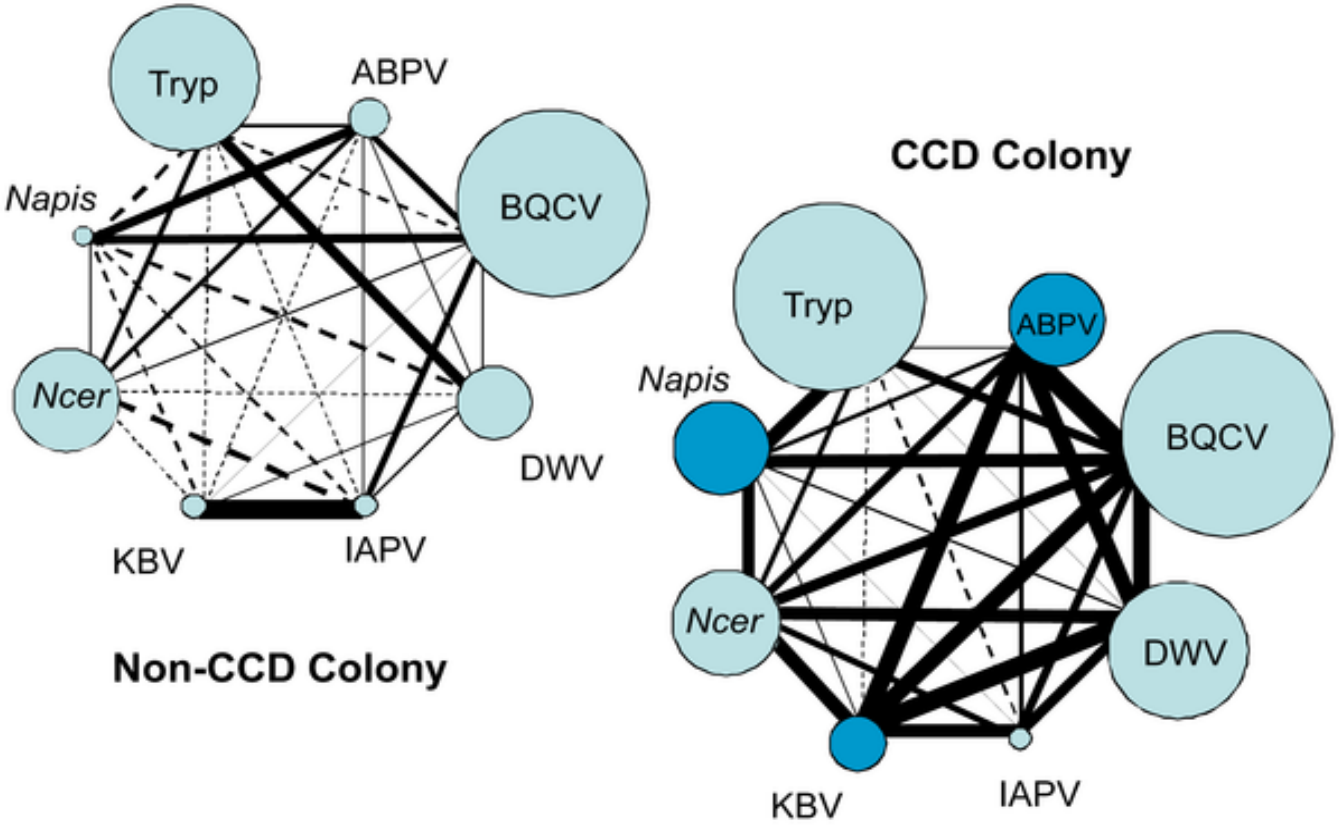
Ponton et al., J. Insect Physiol., 2013

Stress and Honeybee Immunity

SMARTBEES

EU – FP7

Pathogen loads are highly covariant in collapsing colonies



✓Increased susceptibility to a diverse set of pathogens

✓ Co-infections can act synergistically

Cornman et al. , 2012

PLOS ONE

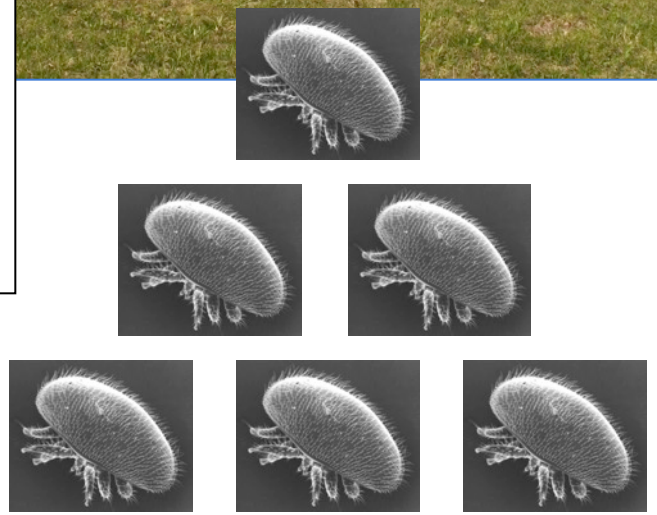
The induced collapse experiment

>20 km

1.6 km

Same environment
but no interactions

Observations on:
- colony strength
- mite infestation
- bee mortality
- pathogens

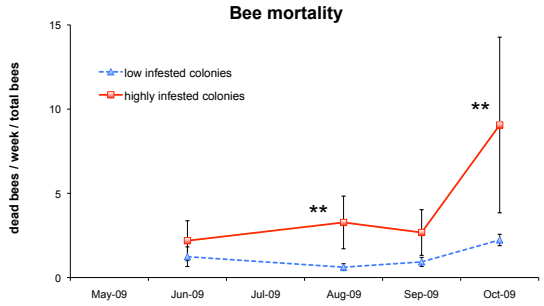


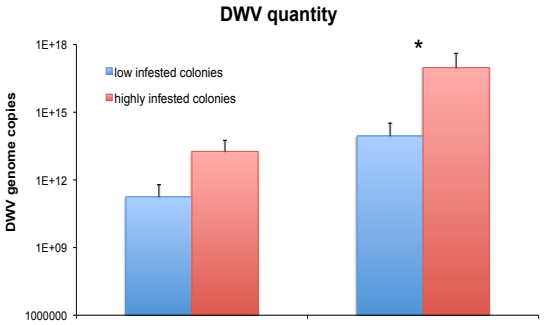
low infested colonies (LIC)

highly infested colonies (HIC)

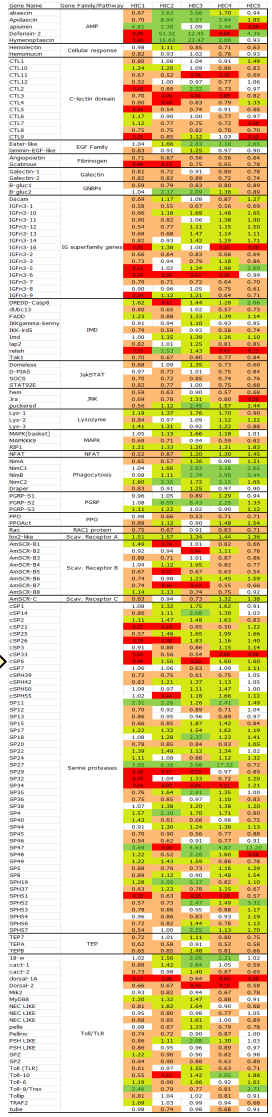
Expression of immune genes

Bees from HIC





RNA-seq



Real time RT-PCR of selected genes

Transcription of *dorsal-1A (NF-kB)* is highly down-regulated in HIC

Nazzi *et al.*, 2012

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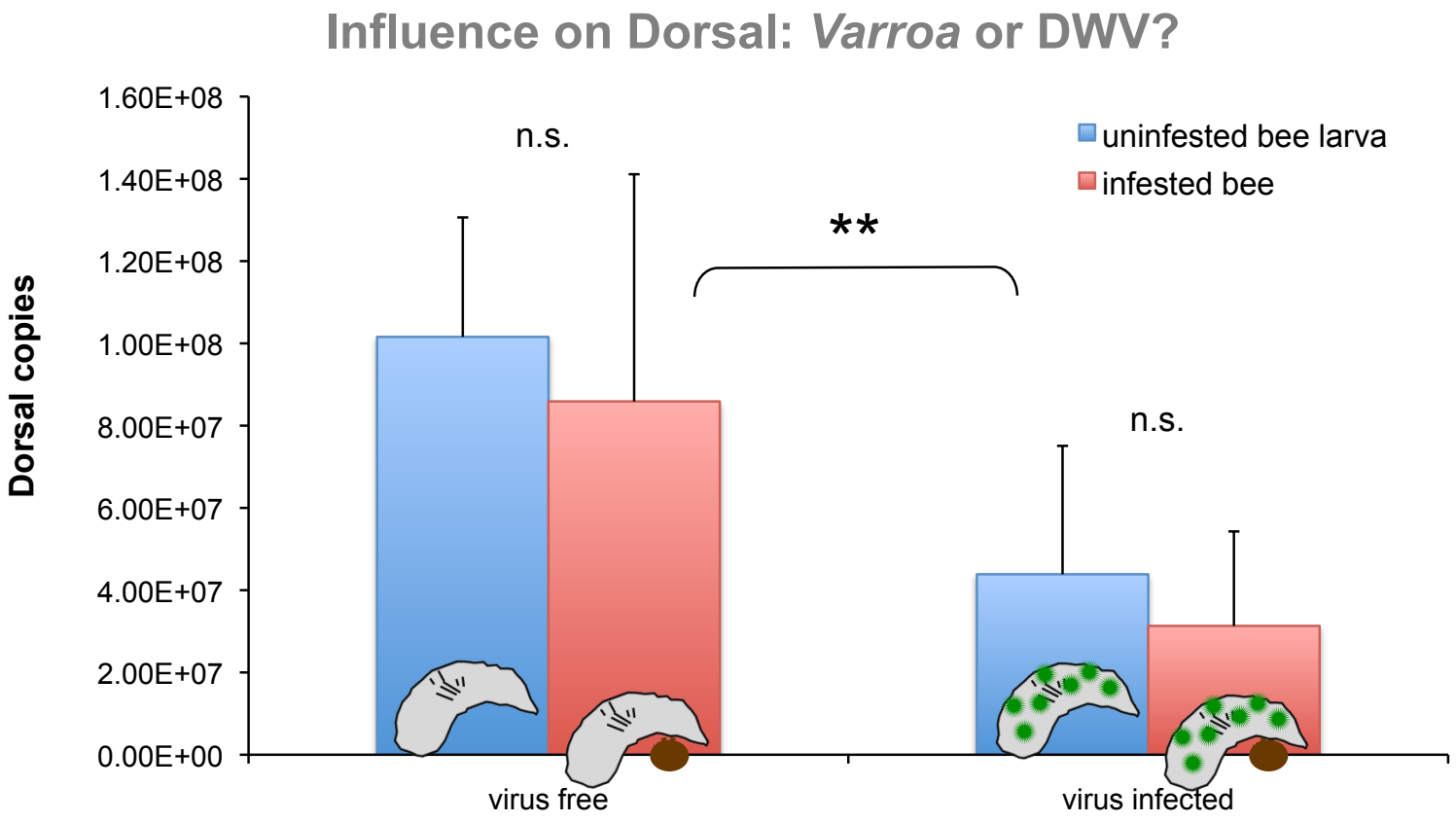
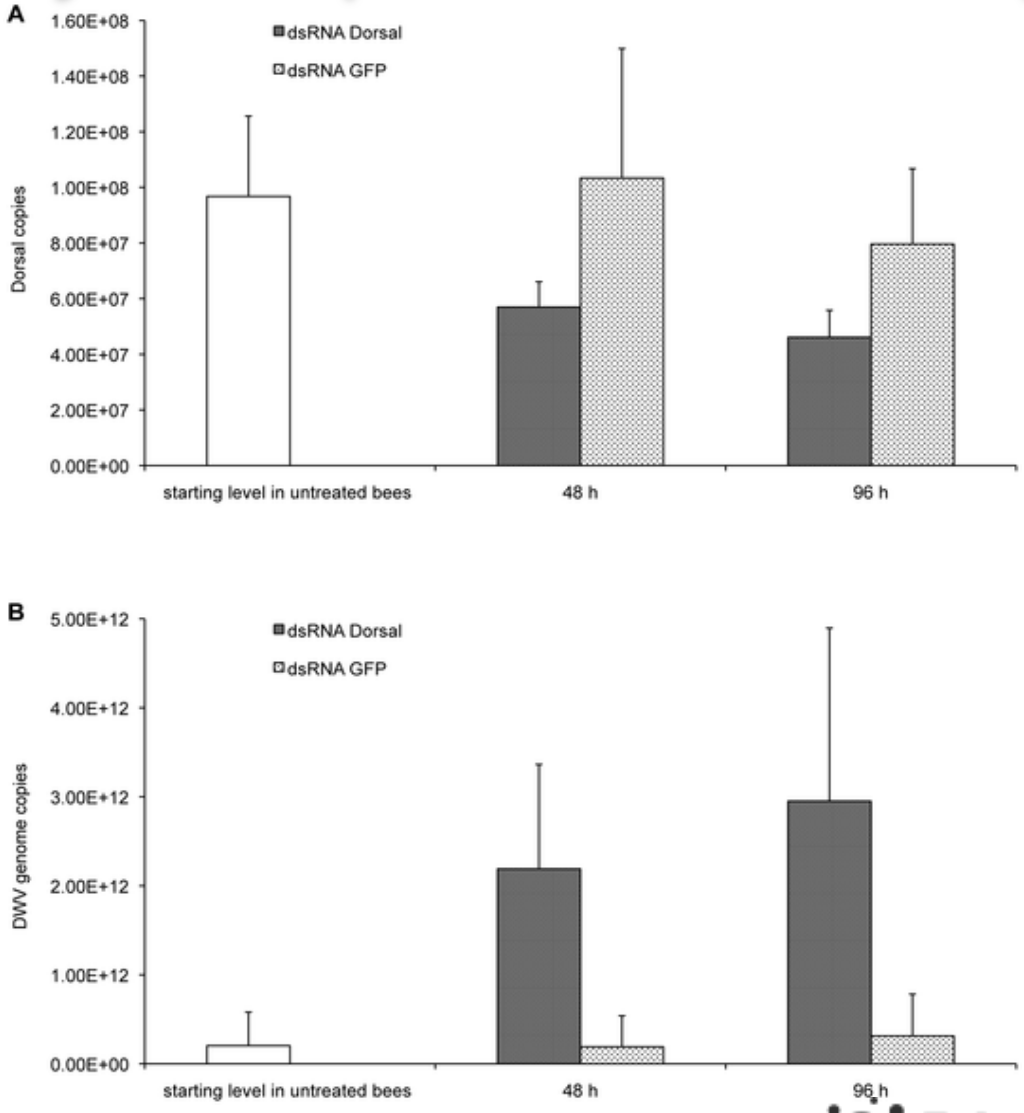
Dorsal expression is influenced by DWV



Nazzi *et al.*, 2012

PLOS | PATHOGENS

The down-regulation of the transcription factor dorsal-1A by RNAi promotes DWV replication



Nazzi et al., 2012

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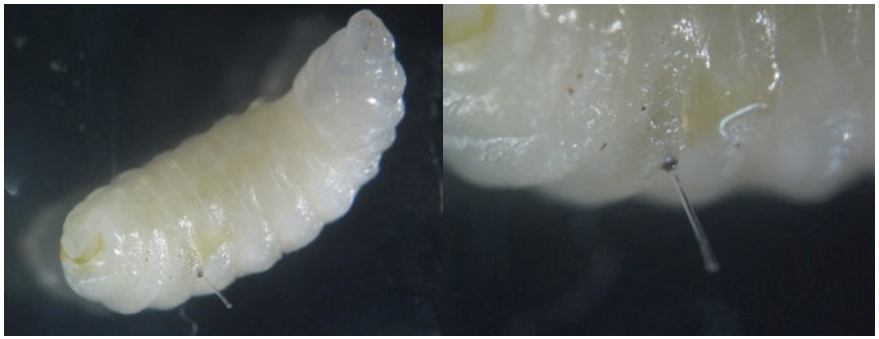
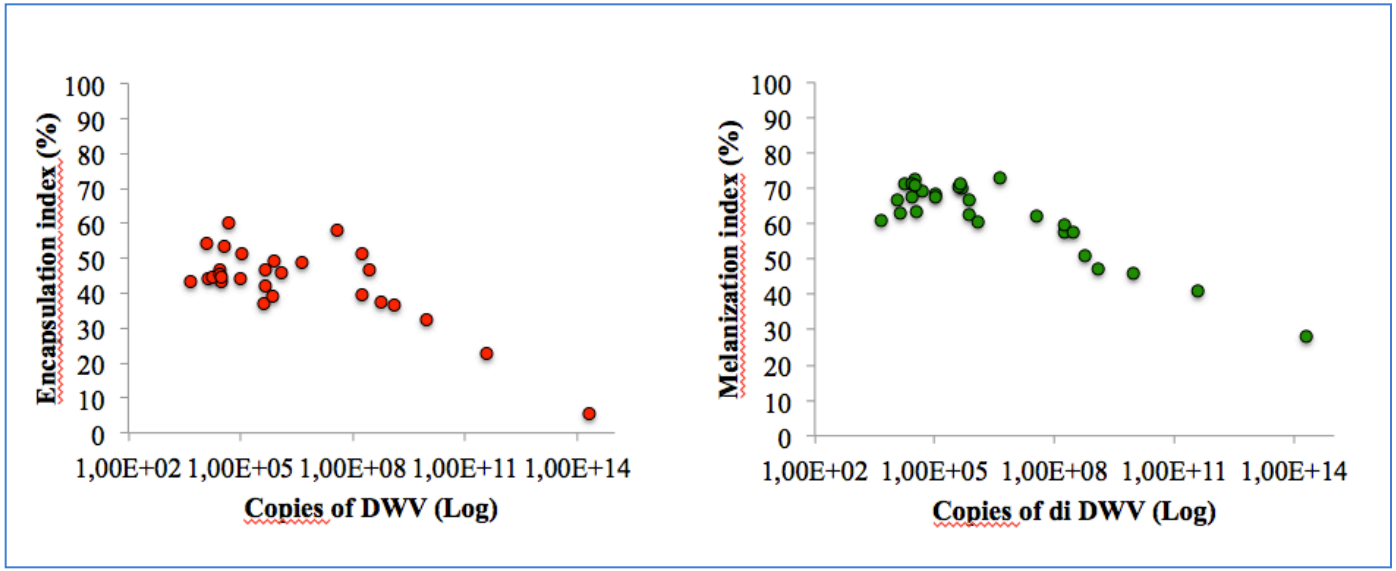


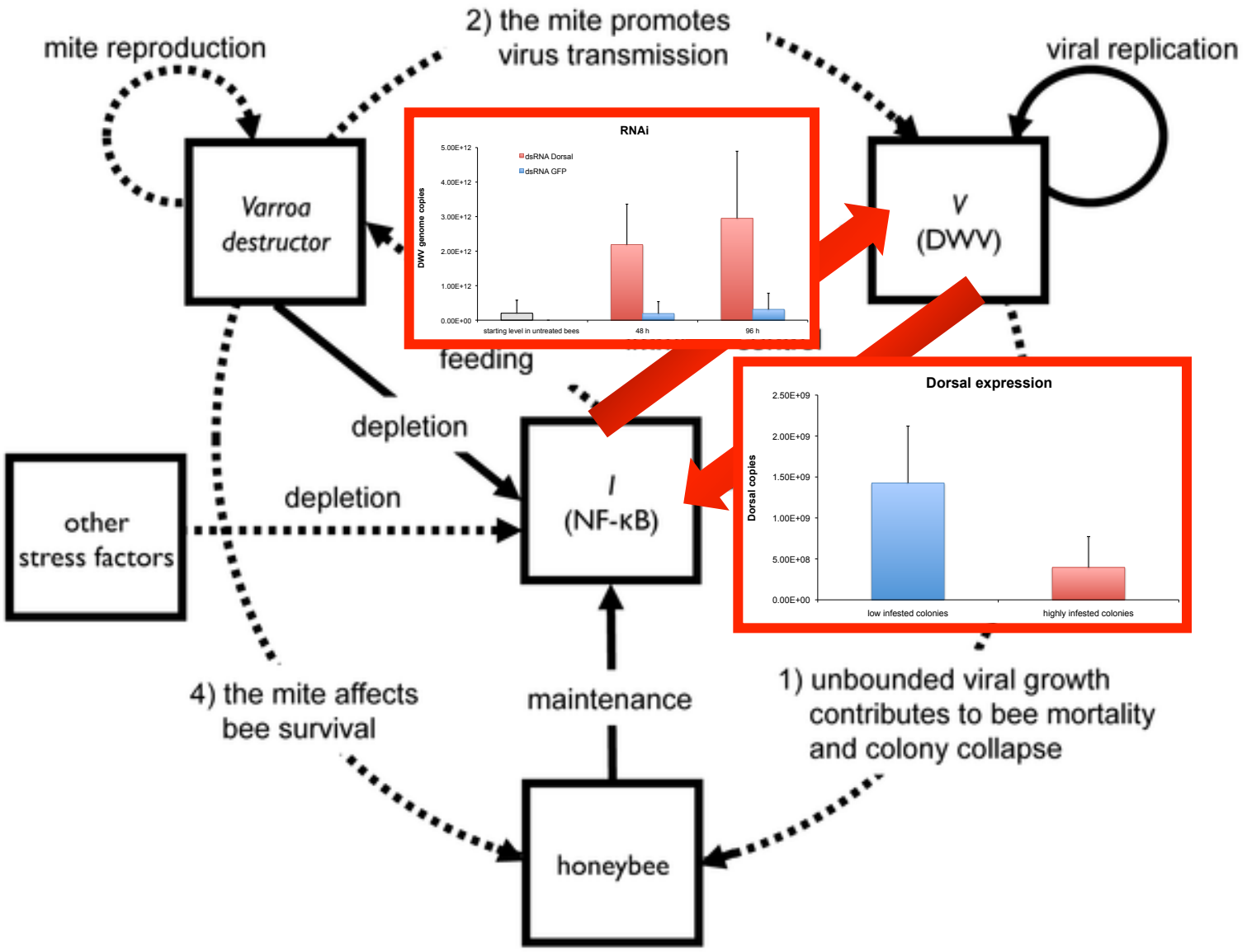
DWV titer positively correlates with honeybee immunosuppression

Nylon thread implantation

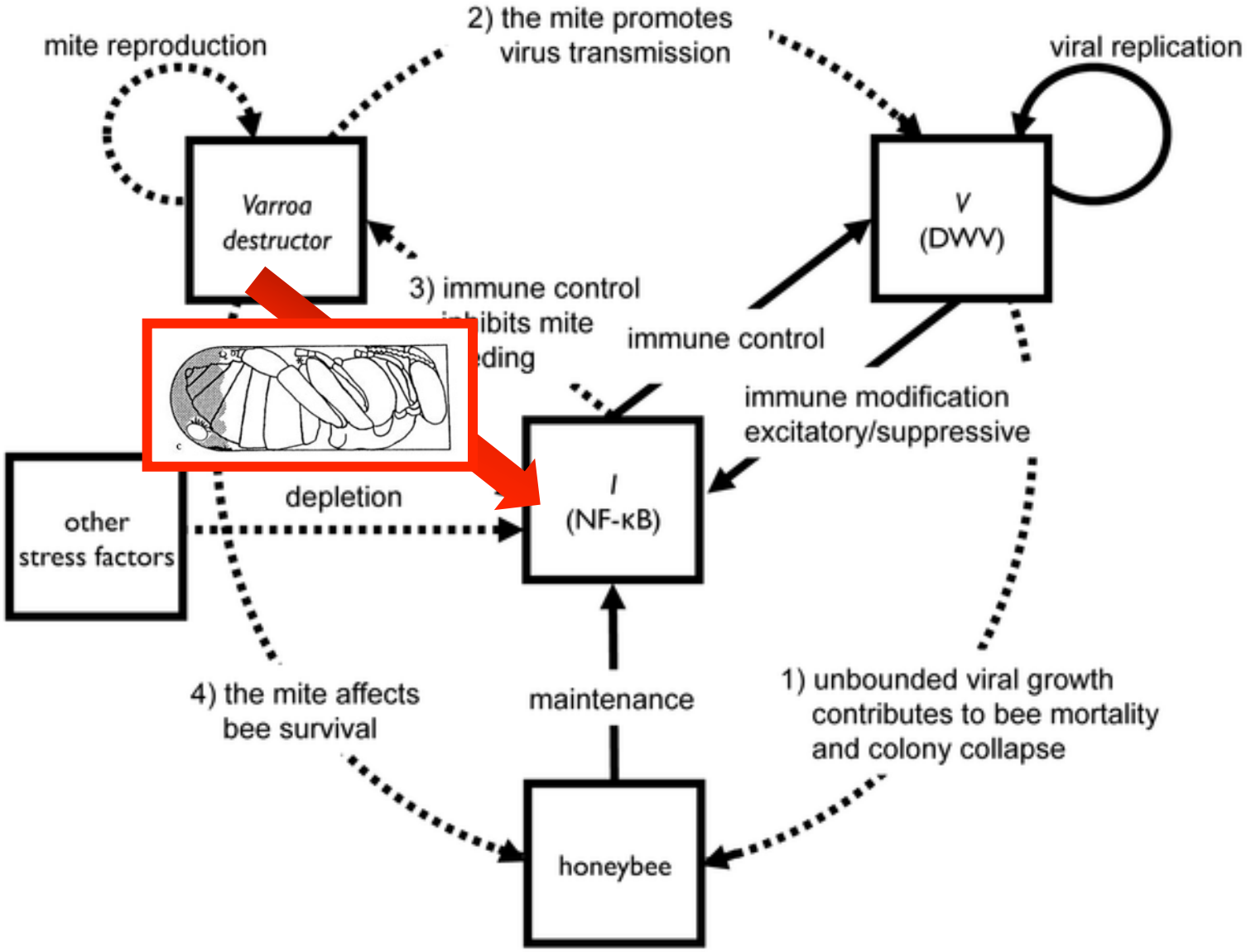


Di Prisco et al. PNAS 2016

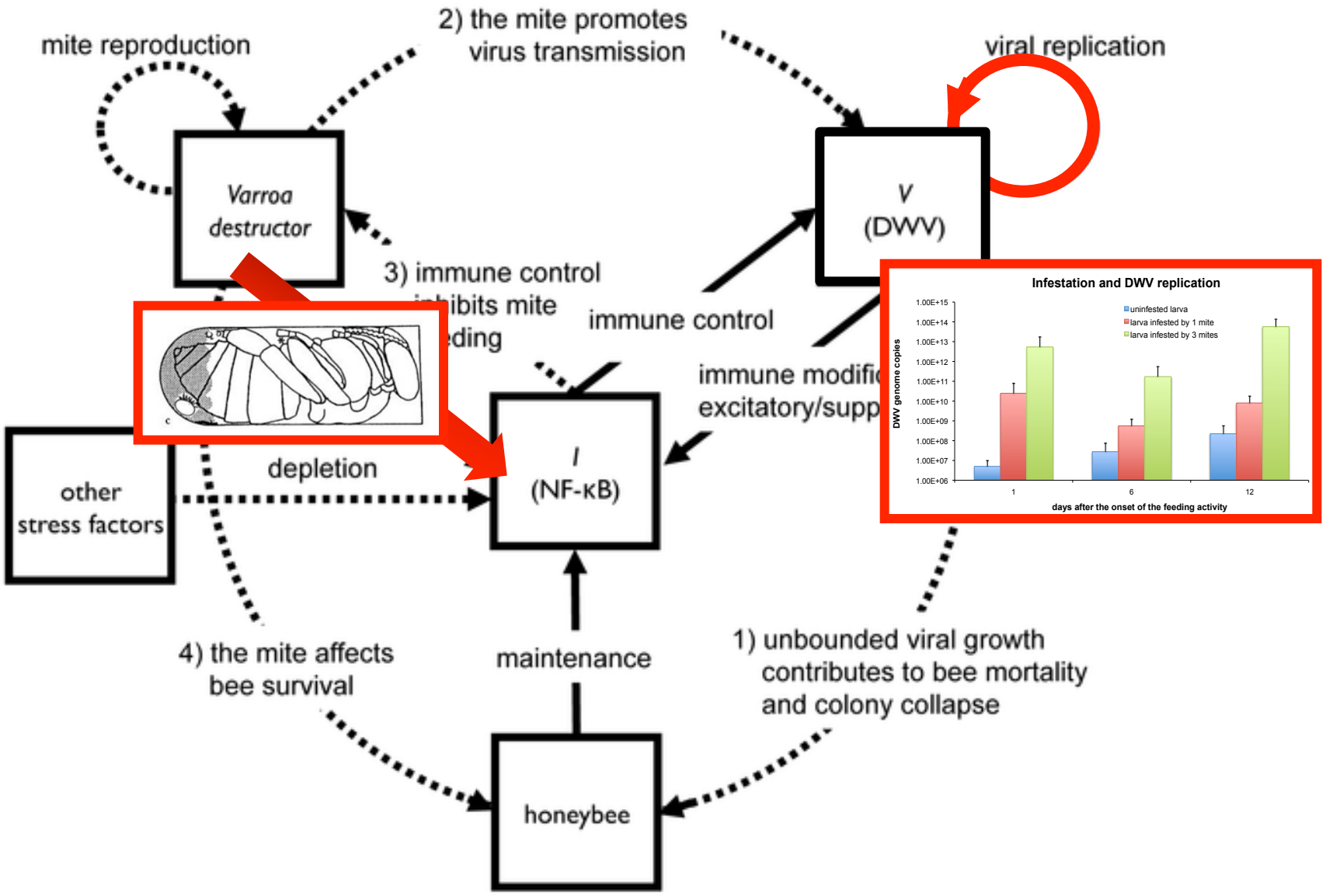
A delicate balance underpins covert DWV infections



Varroa triggers immune reactions associated with a severe metabolic stress…

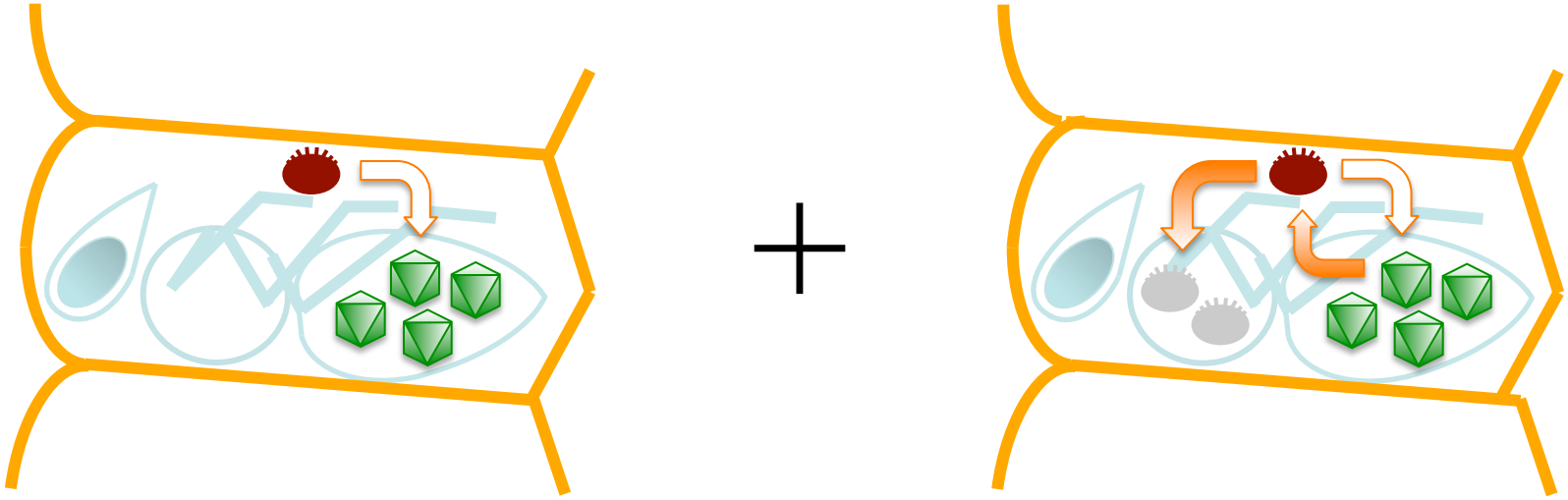


…which promote viral replication



Varroa acts as a vector and promotes DWV replication

Bee immunosuppression by DWV favours Varroa feeding and enhances mite's fitness



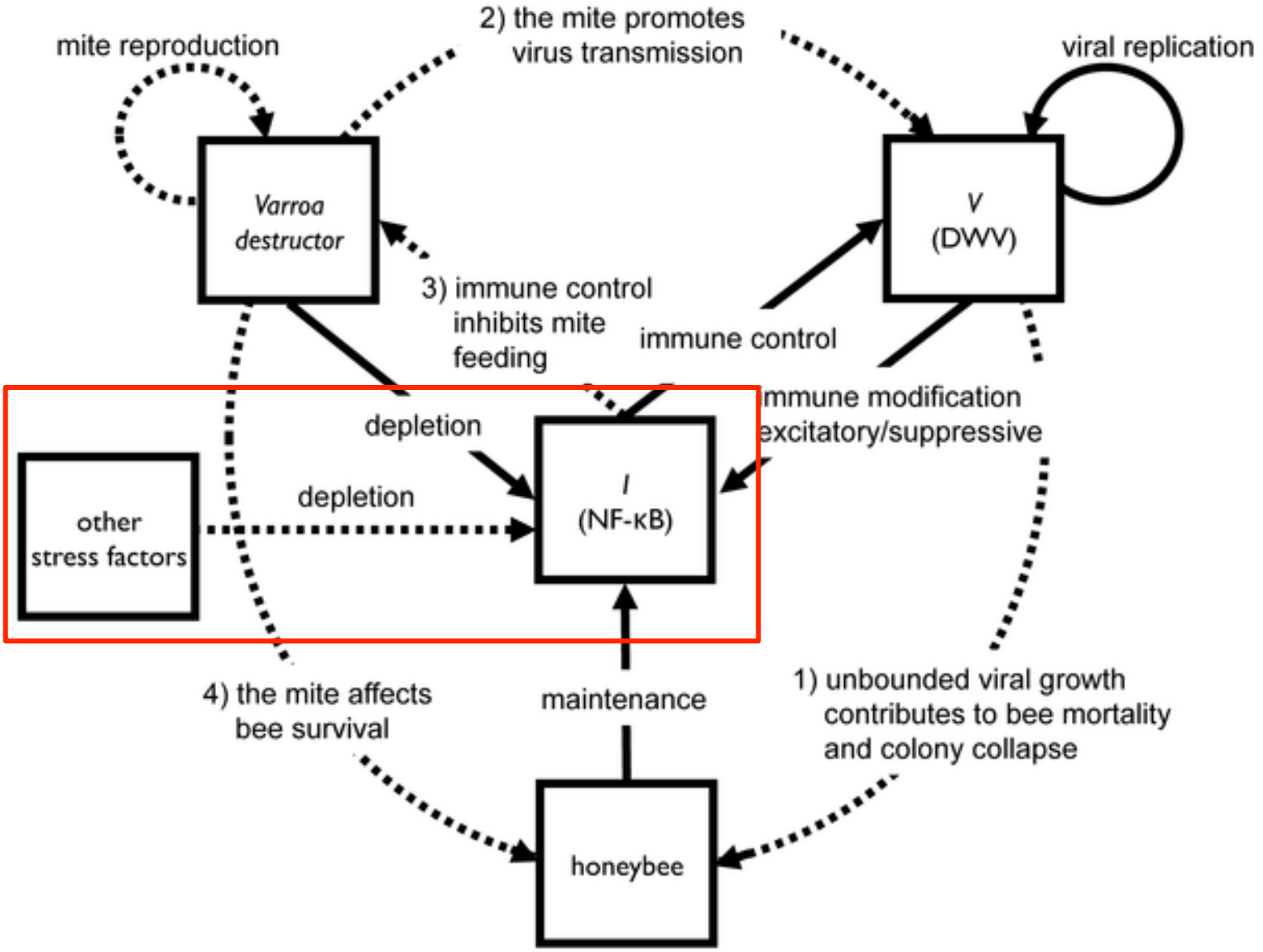
PNAS

A mutualistic symbiosis between a parasitic mite and a pathogenic virus undermines honey bee immunity and health

Gennaro Di Prisco[a,1], Desiderato Annoscia[b,1], Marina Margiotta[a], Rosalba Ferrara[a], Paola Varricchio[a], Virginia Zanni[b], Emilio Caprio[a], Francesco Nazzi[b,2], and Francesco Pennacchio[a,2]

[a]Dipartimento di Agraria, Laboratorio di Entomologia "E. Tremblay," Università degli Studi di Napoli "Federico II," 80055 Portici (NA), Italy; and [b]Dipartimento di Scienze AgroAlimentari Ambientali e Animali, Università degli Studi di Udine, 33100 Udine, Italy

Do stress factors acting on bee immunocompetence influence DWV replication?



Science of the Total Environment 408 (2010) 3775–3786

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

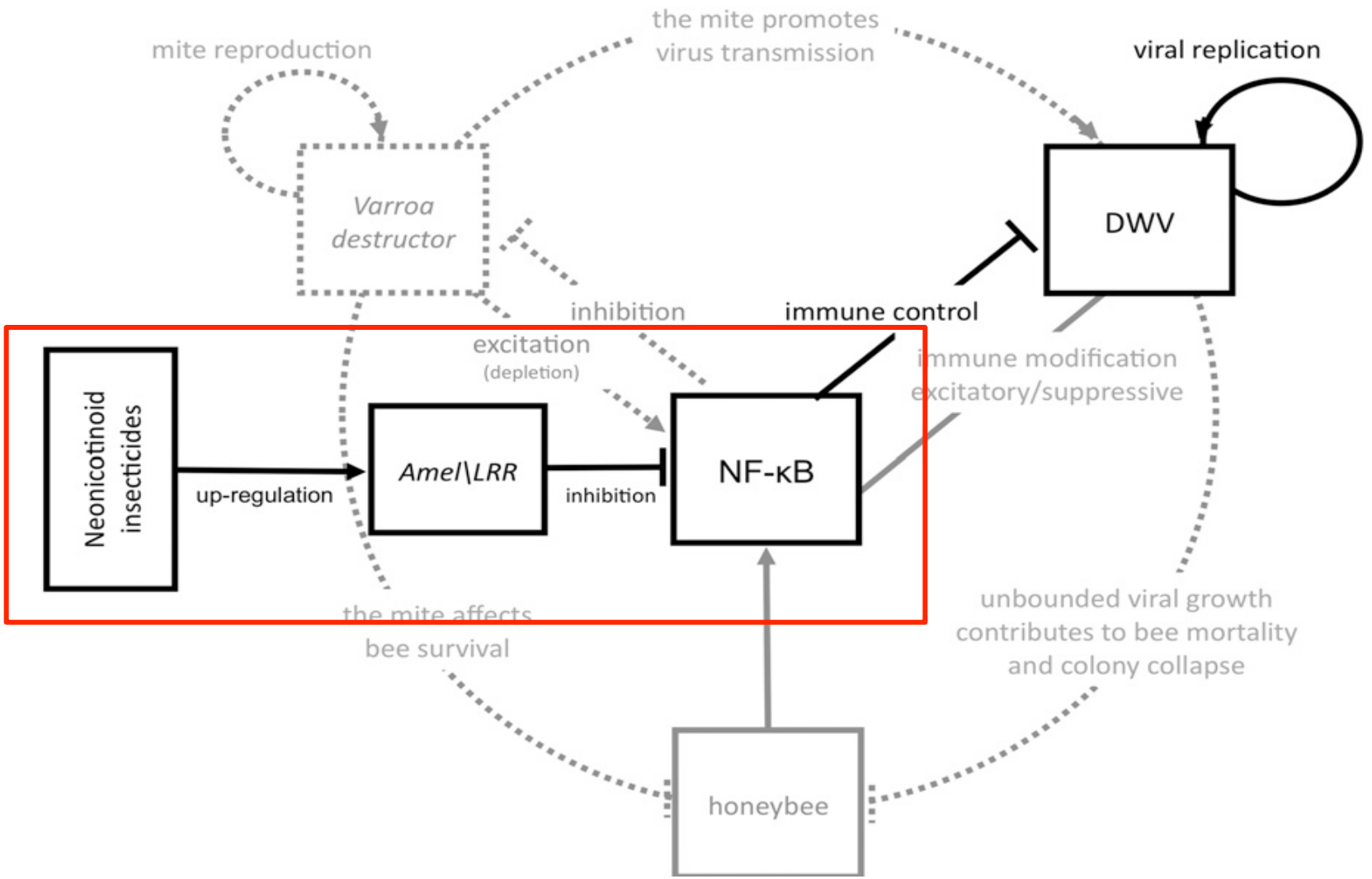
Transcriptomic and proteomic effects of a neonicotinoid insecticide mixture in the marine mussel (*Mytilus galloprovincialis*, Lam.)

Francesco Dondero [a,*,1], Alessandro Negri [a,1], Lara Boatti [a], Francesco Marsano [a], Flavio Mignone [b], Aldo Viarengo [a]

[a] Department of Environmental and Life Sciences, Università del Piemonte Orientale Amedeo Avogadro, Alessandria, Italy
[b] Department of Structural Chemistry, University of Milan, Milan, Italy

"Thiacloprid elicited the modulation of gene transcription and mRNA metabolic processes: three ribonucleoproteins, and two transcription factors (mflj00348 protein, also known as "caterpiller" in mammals) were identified. The latter sequences, in human cells, may modulate T-cell activation, decrease the transcription of genes that are normally up-regulated after T-cell stimulation and delays degradation of NFKBIA/IKBA"

Neonicotinoid impact on honey bee immunity



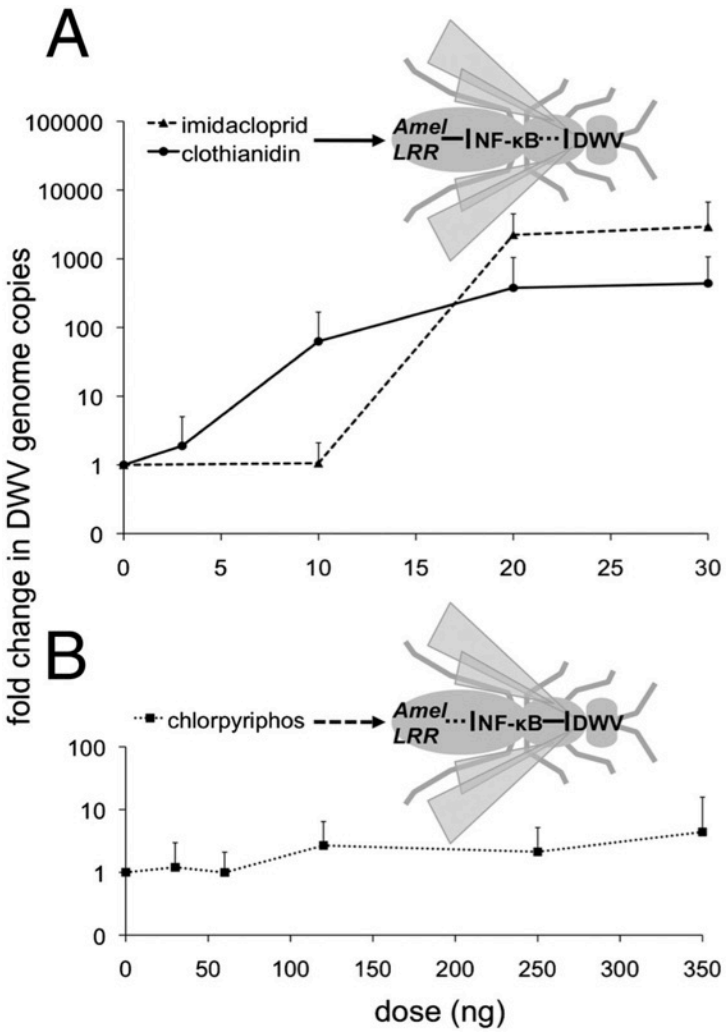
Di Prisco et al. 2013

PNAS

Effect of insecticides on DWV replication in honey bees bearing covert infections

Topical

insecticide treatment



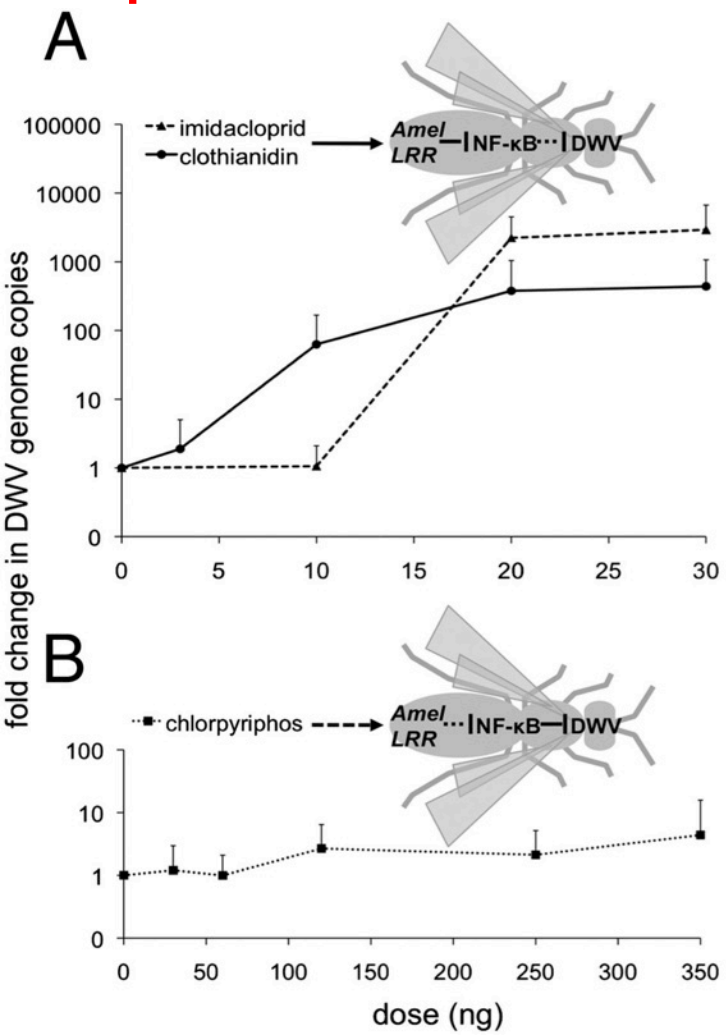
Di Prisco et al. 2013

PNAS

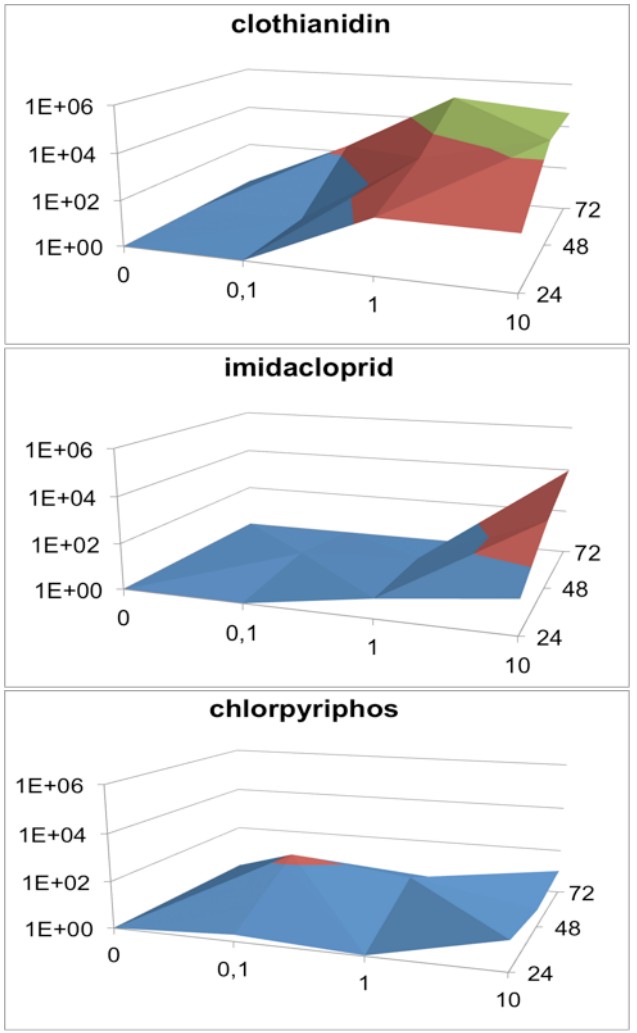
Effect of insecticides on DWV replication in honey bees bearing covert infections

insecticide treatment

Topical



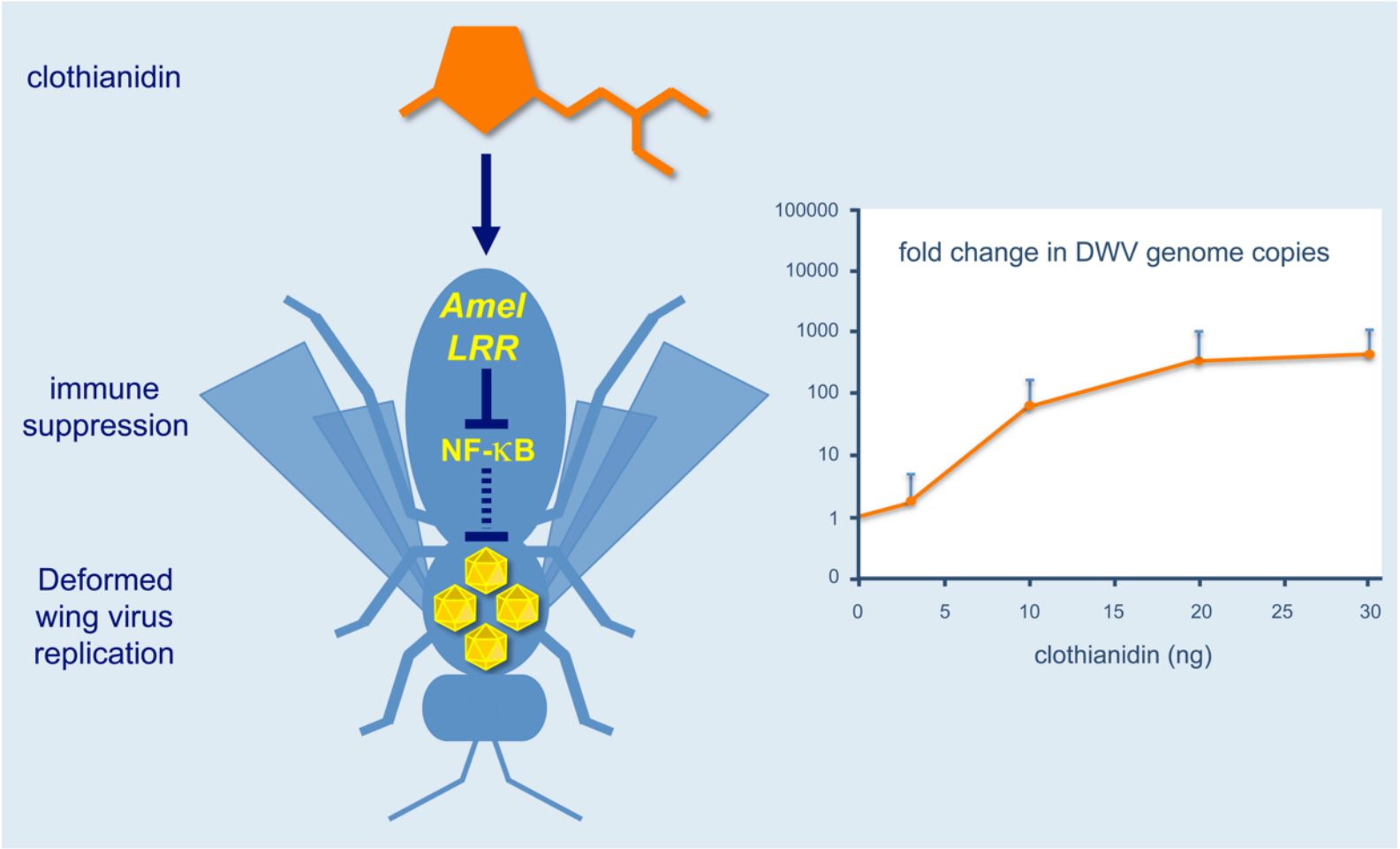
Oral



Di Prisco et al. 2013

PNAS

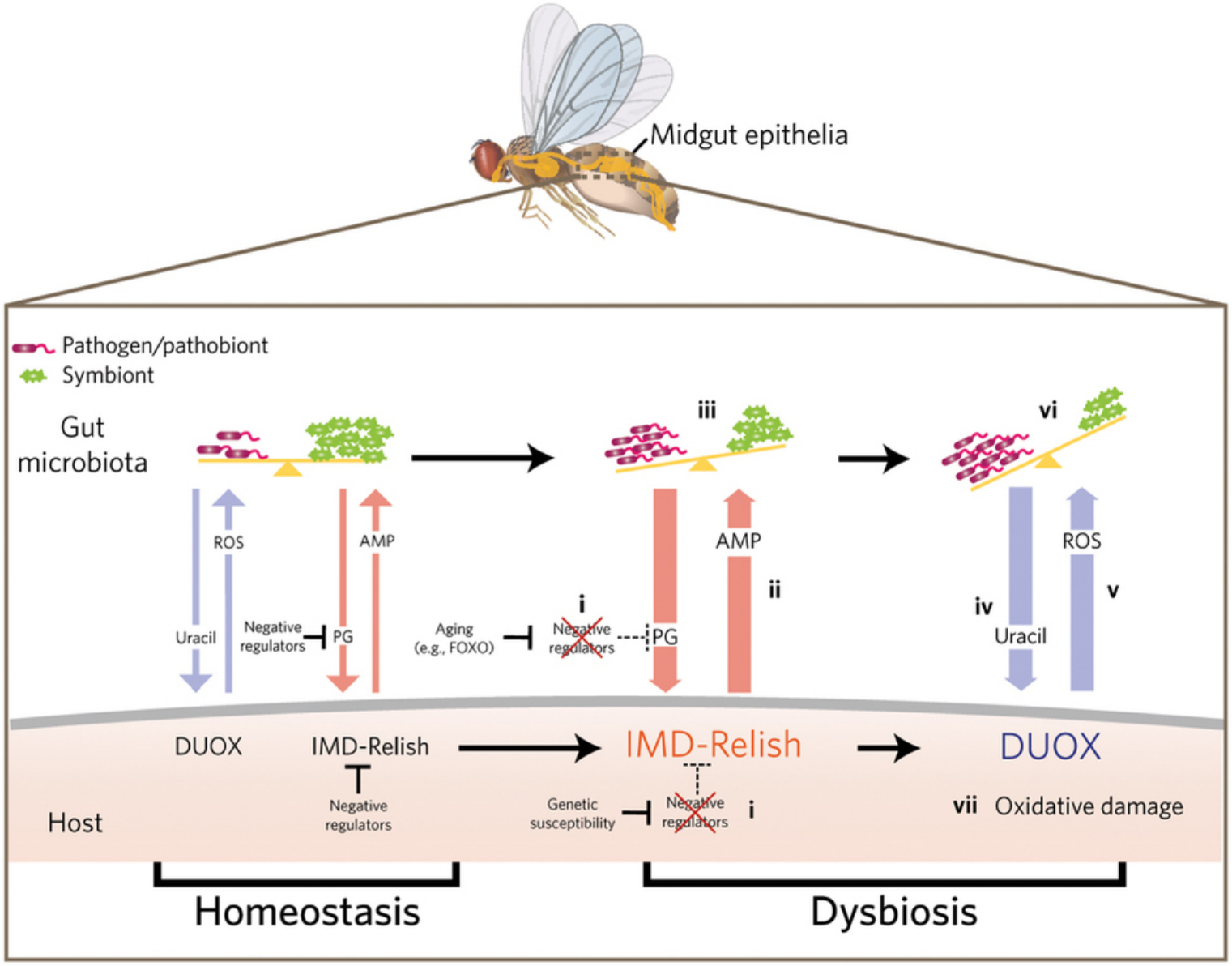
Neonicotinoids and honey bee antiviral immunity



Di Prisco et al. 2013

PNAS

Gut Microbiota and Immunity



Lee & Hase, Nature Chemical Biology, 2014

www.nature.com/scientificreports

OPEN

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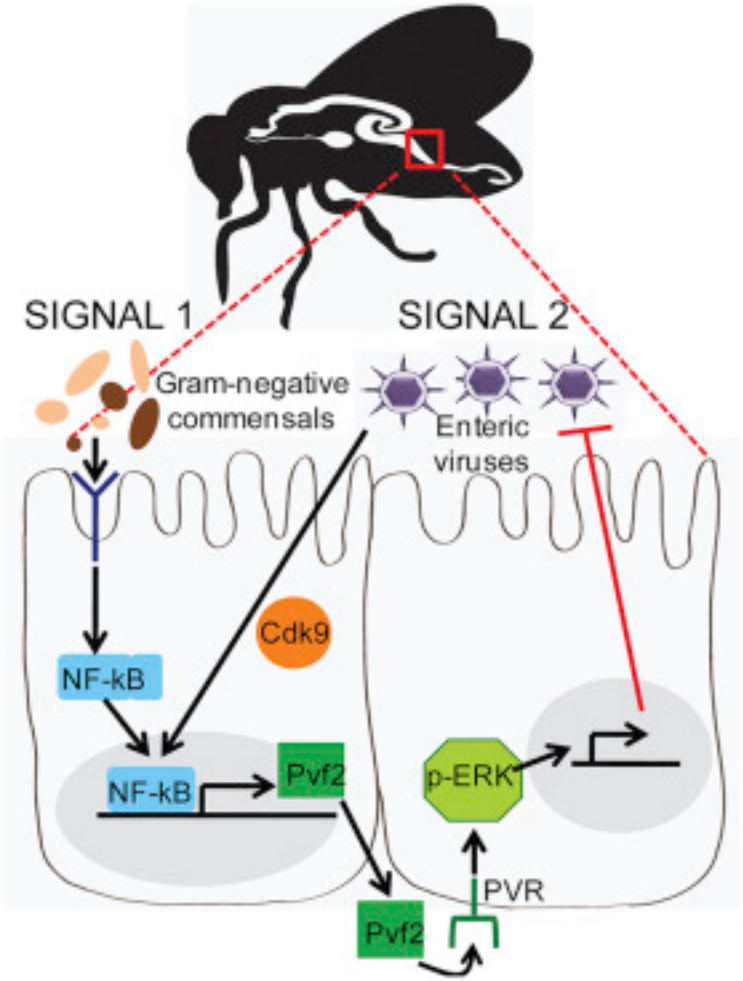
Accepted: 19 April 2017
Published online: 02 June 2017

Neonicotinoid-induced pathogen susceptibility is mitigated by *Lactobacillus plantarum* immune stimulation in a *Drosophila melanogaster* model

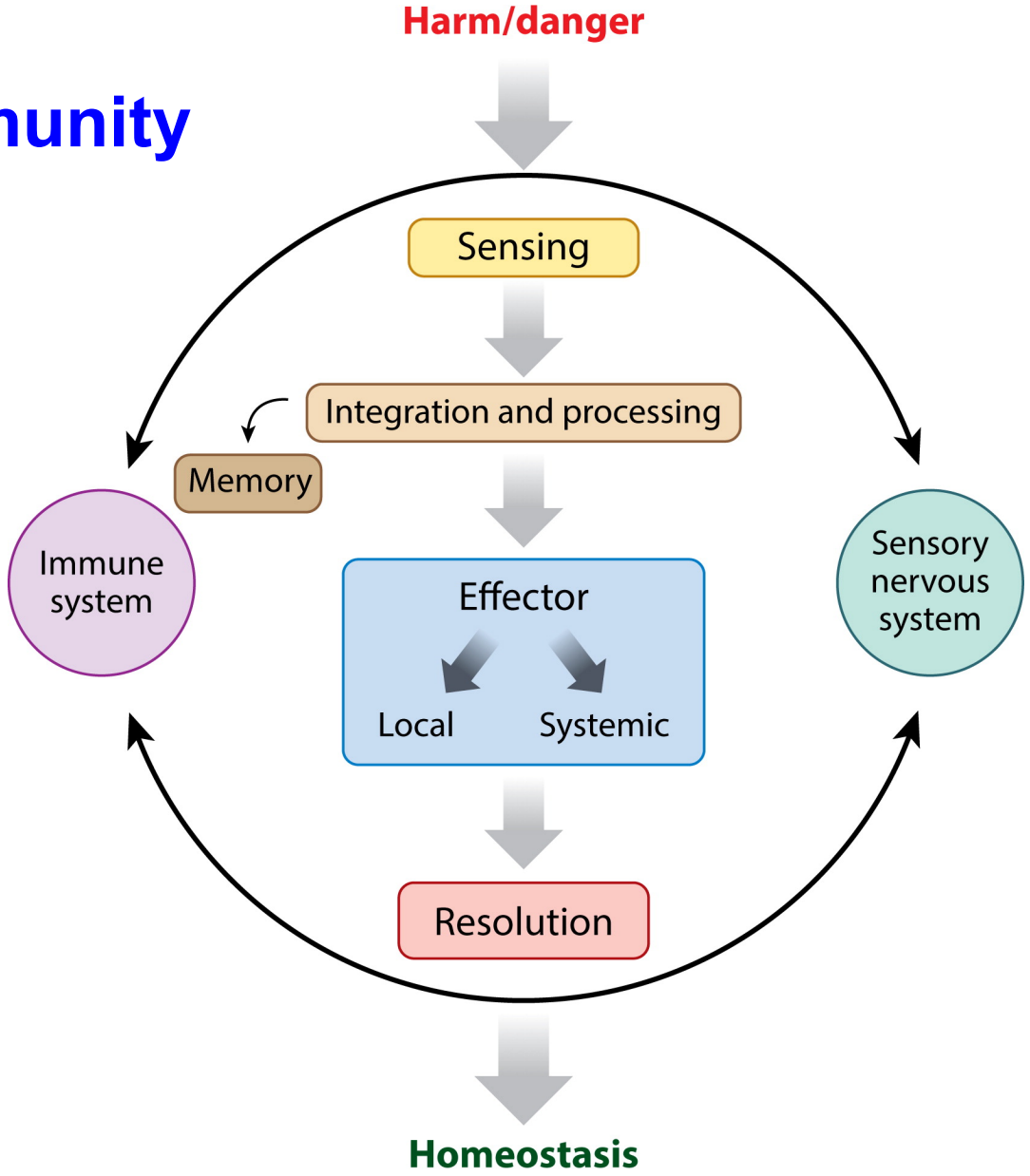
Brendan A. Daisley[1,2], Mark Trinder[1,2], Tim W. McDowell[3], Hylke Welle[1,2,4], Josh S. Dube[2], Sohrab N. Ali[2,5], Hon S. Leong[2,6], Mark W. Sumarah[3] & Gregor Reid[1,2,6]

Microbiota priming of antiviral immunity



Sansone et al., 2015, Cell Host & Microbe 18, 571–581

Neural control of immunity



Talbot S, et al. 2016.
Annu. Rev. Immunol. 34:421–47

www.nature.com/scientificreports

OPEN

The neonicotinoid insecticide Clothianidin adversely affects immune signaling in a human cell line

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Accepted: 18 September 2017
Published online: 18 October 2017

Gennaro Di Prisco, Marco Iannaccone, Flora Ianniello, Rosalba Ferrara, Emilio Caprio, Francesco Pennacchio & Rosanna Capparelli

Life Sciences 188 (2017) 10–16

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Life Sciences

journal homepage: www.elsevier.com/locate/lifescie

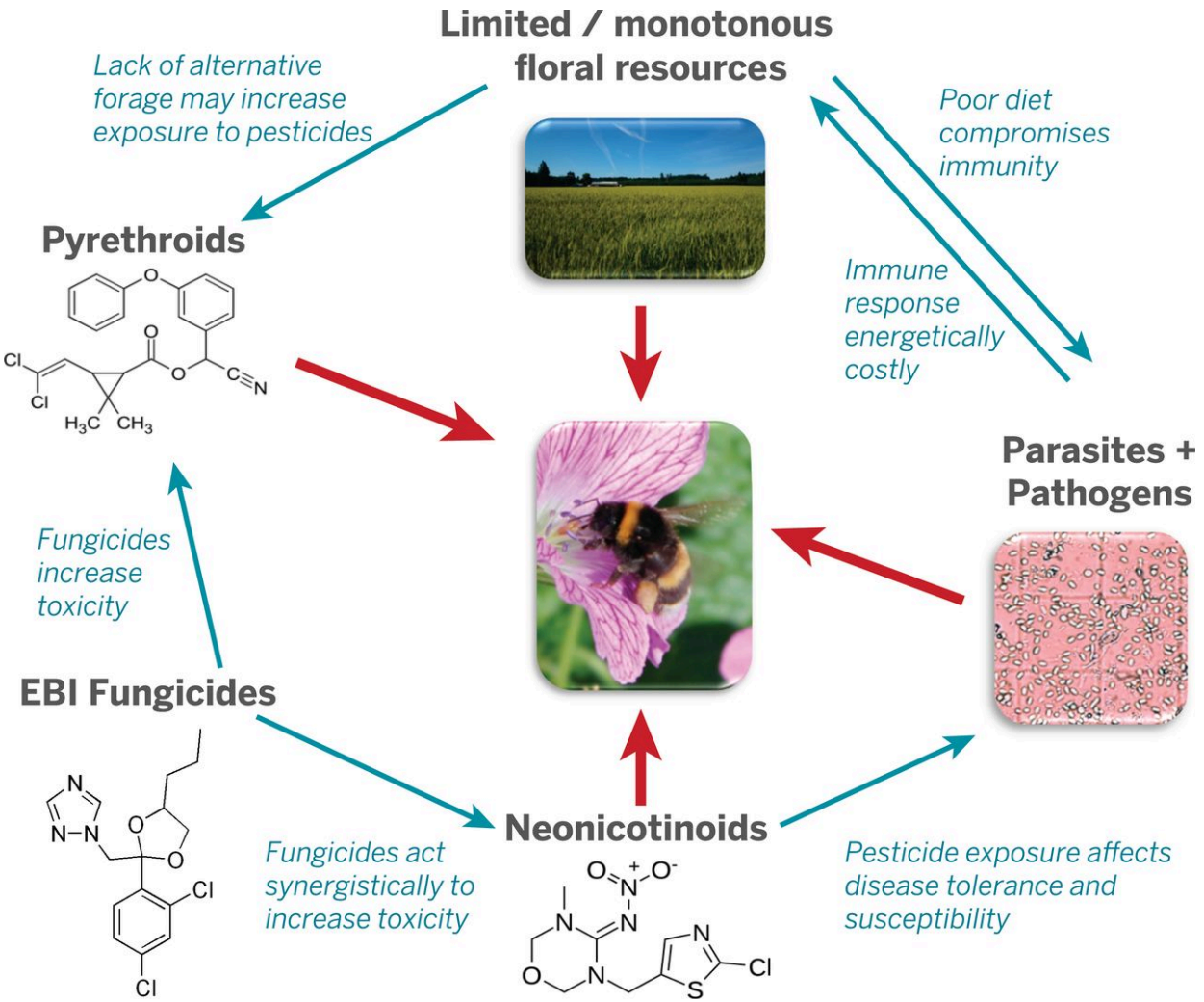
Specific immune responses in mice following subchronic exposure to acetamiprid

Soumaya Marzouki[a,1], Ines Bini Dhouib[b,c,1], Chaouki Benabdessalem[a], Raja Rekik[a], Raoudha Doghri[d], Ammar Maroueni[e], Zakaria Bellasfar[e], Saloua Fazaa[c], Jihene Bettaieb[a,f], Mohamed Ridha Barbouche[a,f], Melika Ben Ahmed[a,f,*]

Results: The ACE-treated mice showed a significant immunosuppression of the specific humoral response with a restorative effect of curcumin when administered with ACE. Similarly, ACE significantly decreased the level of splenocyte proliferation after either a non specific or a specific activation. Curcumin partially restores the antigen specific cellular immune response. Moreover, when administered alone, curcumin significantly inhibits the proliferative responses to the mitogen confirming its anti-mitogenic effect. Histological analysis showed alteration of spleens of mice exposed to ACE.

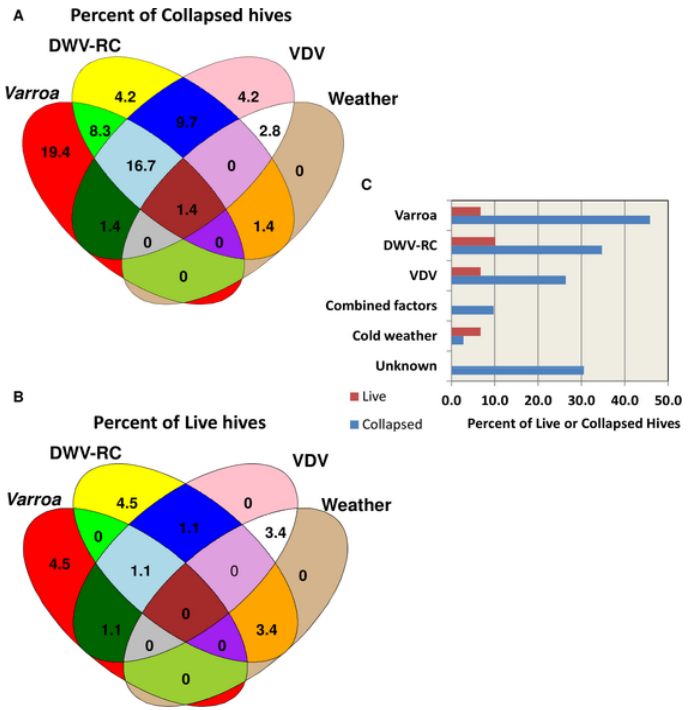
Significance: Altogether, our data indicated that ACE could potentially be harmful to the immune system.

Wild and managed bees are exposed to a number of interacting stressors



Goulson et al. Science 2015

Multifactorial induction of hive collapse



- ✓ Varroa infestation and DWV replication contribute to 70% of colony losses
- ✓ A single factor may not be sufficient to trigger colony losses
- ✓ A combination of stressors appears to impact hive health

Kielmanowicz et al., 2015

PLOS | PATHOGENS

Conclusions

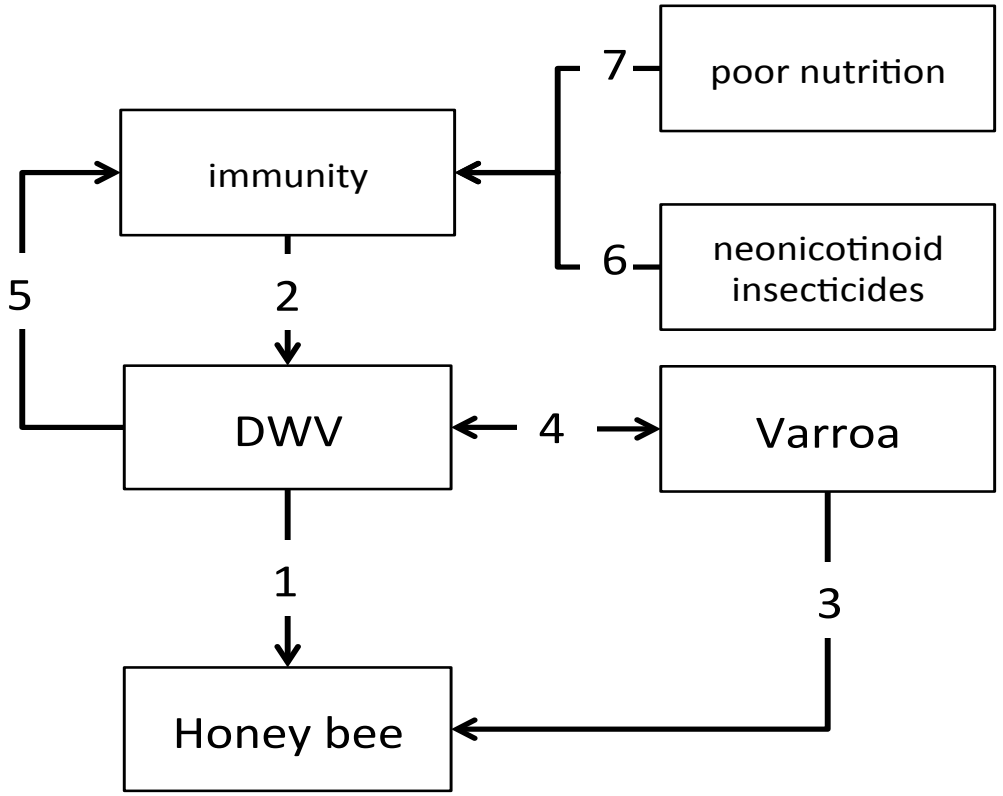
✓DWV mediates honeybee immunosuppression by targeting NF-kB signaling

✓*Varroa* mites promote DWV replication, exacerbate immunosuppression and enhance their fitness

✓ Neonicotinoids upregulate an inhibitor of NF-kB activation and triggers immunosuppression, which promotes DWV replication

✓Nutrition cross-modulates honey bee immune pathways

The “Sword of Damocles” paradigm



Nazzi and Pennacchio – Viruses, 2018

University of Napoli "Federico II"

Department of Agricultural Sciences

Thank you!