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Transgenerational effects on pest evolution

Transgenerational effects of insecticides - implications for rapid pest evolution in
agroecosystems

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Highlights

- Insecticide-induced effects can be transgenerationally inherited.
- Epigenetic modifications are heritable.
- Epigenetic modifications are responsive to insecticide-induced stress.
- Pesticide use may directly and indirectly drive the evolution of insect pests in agroecosystems via epigenetic processes.

Abstract

Although pesticides are a major selective force in driving the evolution of insect pests, the evolutionary processes that give rise to insecticide resistance remain poorly understood. Insecticide resistance has been widely observed to increase with frequent and intense insecticide exposure, but can be lost following the relaxation of insecticide use. One possible but rarely explored explanation is that insecticide resistance may be associated with epigenetic modifications, which influence the patterning of gene expression without changing underlying DNA sequence. Epigenetic modifications such as DNA methylation, histone modifications, and small RNAs have been observed to be heritable in arthropods, but their role in the context of rapid evolution of insecticide resistance remain poorly understood. Here, we discuss evidence supporting how: 1) insecticide-induced effects can be transgenerationally inherited, 2) epigenetic modifications are heritable, and 3) epigenetic modifications are responsive to pesticide and xenobiotic stress. Therefore, pesticides may drive the evolution of resistance via epigenetic processes. Moreover, insect pests primed by pesticides may be more tolerant of other stress, further enhancing their success in adapting to agroecosystems. Resolving the role of epigenetic modifications in the rapid evolution of insect pests has the potential to lead to new approaches for integrated pest management as well as improve our understanding of how anthropogenic

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36 stress may drive the evolution of insect pests.

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Introduction

The pesticide treadmill describes how agricultural insect pests evolve resistance in response to frequently used pesticides, rendering them ineffective. Pesticides are pervasive in agriculture, and are a major selective force driving the evolution of insect pests in agroecosystems [1]. Although insecticide resistance has been documented in a wide range of insect pests [2] and the genetic basis of major gene resistance has been mapped in key pests for select insecticides [3], the broader evolutionary processes that give rise to insecticide resistance remain poorly understood [4,5]. Farmers and entomologists have observed that insecticide resistance increases with the frequency of exposure to particular insecticides [6–8], but can be lost following the relaxation of insecticide use [9–11]. The rapid gain and loss of resistance appears to occur far more rapidly than expected based upon mutation rates [12,13], suggesting that insecticides themselves may increase the rate of mutation or cause physiological changes in pest organisms [5]. One possible explanation that has been relatively unexplored is that the evolution of insecticide resistance results from epigenetic modifications, which are heritable and influence gene expression without changing the underlying DNA sequence.

The evolution of insecticide resistance has been considered an evolutionary paradox [5], in that pest species which have experienced repeated genetic bottlenecks due to invasion and selection remain able to adapt very rapidly, despite limited genetic diversity. The same insect pests have evolved resistance to insecticides in all of the major classes [14], and are expected to evolve resistance to future chemistries [15]. Extreme genetic bottlenecks also do not appear to limit the likelihood that insecticide resistance evolves. For example, all Colorado potato beetle (*Leptinotarsa decemlineata* Say) populations in Europe are descended from the introduction of a

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single female, or single mtDNA haplotype [16]. Despite this strong historic bottleneck, *L. decemlineata* populations in Eurasia have evolved resistance to a wide range of insecticides in Europe, the Middle East, and East Asia [6,17,18]. There is a seeming inevitability of insecticide resistance developing in pests, where new phenotypes arise following environmental stress at rates that may not be explained by natural selection. Indeed, Skinner et al. [19] argued how epigenetic processes fit within a neo-Lamarckian framework, because environmental epigenetic patterning can influence transgenerational transmission of phenotypic variation. By influencing epigenetic modifications, xenobiotic and environmental stressors can directly influence the phenotypic responses of organisms to their environment.

Epigenetics is the field of study that examines how environmental factors influence heritable changes in gene expression. There are several epigenetic mechanisms that are heritable and could underlie transgenerational effects of insecticides: DNA methylation [20], histone modifications [21], and heritable noncoding RNA [22]. Here, we discuss evidence supporting how 1) insecticide-induced effects can be transgenerationally inherited, 2) epigenetic modifications are heritable, and 3) epigenetic modifications are responsive to insecticide-induced stress. We draw on other model systems from a diverse body of literature, including genetics, epigenetics, and toxicology to identify gaps in our understanding around the evolution of insecticide resistance in insect pests. We close with a discussion of the implications of epigenetic processes for insect fitness in intensively-managed agroecosystems.

Insecticide-induced hormetic effects can be heritable

Insecticides not only select for insecticide resistance and point mutations at target sites, but they can also affect physiological and life-history traits [23]. In particular, exposure to

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sublethal dosages of insecticides can incur stress and lead to increased phenotypic variation [24]. Stress responses can lead to hormesis, a well-known phenomenon from toxicological literature, where small dosages can stimulate biological functions whereas large dosages are detrimental or lethal [24]. Hormetic responses include activation of stress response pathways in a variety of taxa from microbes, plants, and animals. They are not related to any special class of compounds, as hormetic effects have been reported for over 240 different chemical classes [23]. Sublethal exposure to insecticides can induce hormetic effects and lead to variety of positive life history effects, such as mating success [25], fecundity [26], and body size [27]. By positively influencing traits associated with fitness, hormetic effects may play an important role in pest evolution.

There is evidence that individuals exposed to stressful conditions, either abiotic or biotic, can prime gene expression in their offspring to be able to better tolerate stress [28,29]. Insecticides have been shown to induce transgenerational insecticide induced hormetic effects, but thus far the results have been difficult to interpret. For example, *Myzus persicae* aphids treated with sublethal levels of imidacloprid produce offspring that survive longer when exposed to food/water stress, but tolerance to insecticide stress is unchanged [30]. Similarly, although sublethal levels of precocene (an antagonist to Juvenile hormone) stimulate reproduction in *M. persicae*, the results are not passed on to subsequent generations [31*]. Although chemical-induced hormesis has been reported from many groups and these changes have also been reported to be inherited [23] the genetic, epigenetic, and toxicological basis of hormesis is still poorly understood [5,32].

Epigenetic modification and transgenerational inheritance

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Epigenetic modifications have been shown to be heritable [20]. DNA methylation, the addition of a methyl group to the 5 carbon position of cytosine a nucleotide (usually the cytosine in CpG dinucleotides), is a well-documented mechanism of epigenetic inheritance that can influence phenotypic variation (Table 1), and is found in most, if not all, orders of insects [32]. Methylation in insects is largely found within coding regions, and is closely linked with gene expression and alternative splicing - where a single gene can generate a diversity of gene transcripts of differing length, based on which exons are translated [33]. Methylation can occur at any location in the genome, but the effects of DNA methylation vary based on its location in the genome (Figure 1): A) changes in DNA methylation at the promoter region can influence gene expression in downstream genomic regions [34], B) methylation suppresses gene expression of transposable elements (TEs, which are mobile genetic elements responsible for the majority of mutations in many genomes) and prevent TE mobilization [35], and C) Gene body methylation can increase gene expression [32], as well as an increase in the number of alternative splice variants [36]. Changes in methylation patterns in arthropods can be associated with changes in levels of resistance to insecticides. *Myzus persicae*, can gain insecticide resistance through the duplication of esterase genes and subsequent overexpression of esterases [37]. After suspending insecticide exposure, extra copies of esterase genes can be methylated, leading to a loss of resistance. It is possible that these aphid populations could quickly become resistant again following demethylation of these amplified genes.

Histone modifications include additions of acetyl or methyl groups on the histone proteins around which nuclear DNA is wrapped, which can influence gene regulation and expression [38]. The full effects of these modifications are not well known, especially in arthropods. However, it does appear that some histone modifications are able to be transmitted

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transgenerationally [39]. Different noncoding RNA (ncRNA) [22] can be inherited through either the male or female gametes, though most current research does not incorporate analysis of heritable RNA. Certain types of small RNA can direct and maintain DNA methylation and histone modification, and therefore affect chromatin structure [40]. DNA methylation, histone modifications, and ncRNAs form a constellation of interacting effects that result in a phenotypic response [41]. To fully understand how epigenetic modifications influence transgenerational phenotypic inheritance, it would be optimal to assess all three mechanisms simultaneously through concurrent small RNA-seq, bisulfate-treated DNA-seq, and histone modification assays, in as many tissues and individuals as possible. Ideally, multiple generations would be sequenced, to determine if changes in epigenetics and gene expression differ consistently between treatments. Because the cost of sequencing is the major limiting factor for these studies, projected lower sequencing costs in the future should enable these types of studies.

Epigenetic modifications are responsive to xenobiotic stress

Exposure to insecticides and other xenobiotic compounds can alter DNA methylation status in arthropods, and these epigenetic changes can persist for at least several generations [20,42,43]. Table 1 lists a number of examples of stress leading to epigenetic changes in arthropods. Studies focusing on insects are few in number, so our scope is broadened to include examples from aquatic ecotoxicology literature, which includes a number of non-insect arthropods. Oppold (2015) found that exposure of mosquitoes to a fungicide leads to heritable changes in methylation and decreases in sensitivity to imidacloprid, an insecticide. Methylated cytosines also spontaneously deaminate, becoming thymines, at a higher rate than non-methylated cytosines, which can lead to higher mutation rates in methylated regions [44]. If

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genes that are associated with resistance are methylated, which leads to increased expression and increased mutation rate, then genes that are most upregulated in response to insecticide resistance may also be the most likely to experience spontaneous deamination.

Both the role of histone modifications and small RNA in modifying epigenetic responses to toxins are less understood than DNA methylation in arthropods, though it has been shown that methylation and histone modifications tend to be co-located in the genome [38]. Kishimoto et al. [45*] showed that parental hormetic responses to oxidative stress can be epigenetically transmitted to descendants via histone modifications. A wide range of environmental chemicals, such as heavy metals, air pollutants, dioxins, and endocrine disruptors, can alter histone modifications [46], but it is unknown whether these changes are heritable. We have not found any studies on arthropods examining if insecticides can induce transgenerational small RNAs responses. Small RNAs have been found to interact with histone modifications [47], so changes in small RNAs may be implicated in the transgenerational inheritance of stress phenotypes as well.

Implications for transgenerational effects on insect fitness in agroecosystems

We hypothesize that pesticide use can directly and indirectly drive the evolution of insect pests in agroecosystems via epigenetic processes (Figure 2). Pesticides may directly stimulate the expression of advantageous phenotypes, which may be underwritten by epigenetic modifications. Continued insecticide use on populations developing resistance would thus operate as ‘natural selection’ and selectively increase the frequency of insect phenotypes that are adaptive to pesticides. Indirectly, pesticide use may maintain stressful environments that hormetically prime insect pests to become more tolerant of stressful conditions. For instance, sublethal exposure to

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insecticides can influence adult body size of the *L. decemlineata* [23], which may allow insect pests to be better able to tolerate overwintering conditions [48]. Insecticides can also increase female fecundity [49] or propensity to mate [25], which can increase population size.

The phenotypic traits of insect pests that allow them to thrive under insecticide exposure may also facilitate global invasions. For example, *L. decemlineata* is a globally-invasive pest that is expanding its range northwards into the Arctic Circle [48]. Insecticide exposure appears to stimulate the beetle to invest more in fat bodies and have a higher metabolic rate than control beetles [50]. While the higher metabolic rate and larger fat bodies may enable beetles to better detoxify chemicals, higher fat body reserves enable small individuals to overwinter successfully [51,52]. For example, sublethal applications of the pyrethroid deltamethrin on resistant *L. decemlineata* populations can have stimulatory effects rendering exposed individuals larger which is also inherited to the next generation (Lindström, unpublished data).

To date, most of the research examining the role of pesticides or xenobiotics in epigenetic change come from the field of aquatic toxicology [53**], where environmental exposure to toxins can be highly variable and difficult to predict. In contrast, pesticide use in agroecosystems is intentionally part of an active pest management system, where insect responses to stresses can cause positive feedbacks on subsequent management decisions. Agroecosystems are also highly controlled systems, which allows for greater experimental control for field and landscape level studies. Along these lines, it would be important to know how epigenetic responses to the same insecticides may vary among individuals, populations, and species. Such information would help provide insight on whether epigenetic responses can be broadly predictable across individuals and species, and possibly, how pesticide resistance may be better managed. A combination of new genomic tools, epigenetic assays, and computationally-intensive approaches may allow us to

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better understand to what extent epigenetic responses within insects help drive the pesticide treadmill.

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References

1. Food and Agriculture Organization of the United Nations: *FAOSTAT Statistics Database*. 2014.
2. Insecticide Resistance Action Committee: **Arthropod Pesticide Resistance Database** <http://www.irac-online.org>. Accessed September 15, 2017.
3. Ffrench-Constant RH: **Insecticide resistance comes of age**. *Genome Biol.* 2014, **15**:106.
4. Ffrench-Constant RH: **The molecular genetics of insecticide resistance**. *Genetics* 2013, **194**:807–15.
5. Gressel J: **Low pesticide rates may hasten the evolution of resistance by increasing mutation frequencies**. *Pest Manag. Sci.* 2011, **67**:253–257.
6. Tang L De, Qiu BL, Cuthbertson AGS, Ren SX: **Status of insecticide resistance and selection for imidacloprid resistance in the ladybird beetle *Propylaea japonica* (Thunberg)**. *Pestic. Biochem. Physiol.* 2015, **123**:87–92.

- 221 7. Malekmohammadi M: **Resistance of Colorado potato beetle (*Leptinotarsa decemlineata***
 222 **Say) to commonly used insecticides in Iran.** *J. Asia. Pac. Entomol.* 2014, **17**:213–220.
- 223 8. Zhou C, Liu Y, Yu W, Deng Z, Gao M, Liu F, Mu W: **Monitoring resistance of field**
 224 **populations of diamondback moth *Plutella xylostella* L. (Lepidoptera:**
 225 **Yponomeutidae) to five insecticides in South China: A ten-year case study.** *Crop*
 226 *Prot.* 2011, **30**:272–278.
- 227 9. Yang Y, Dong B, Xu H, Zheng X, Tian J, Heong K, Lu Z: **Decrease of insecticide**
 228 **resistance over generations without exposure to insecticides in *Nilaparvata lugens***
 229 **(Hemipteran: Delphacidae).** *J. Econ. Entomol.* 2014, **107**:1618–1625.
- 230 10. Foster SP, Denholm I, Devonshire AL: **The ups and downs of insecticide resistance in**
 231 **peach-potato aphids (*Myzus persicae*) in the UK.** *Crop Prot.* 2000, **19**:873–879.
- 232 11. Ffrench-Constant RH, Devonshire AL, White RP: **Spontaneous loss and reselection of**
 233 **resistance in extremely resistant *Myzus persicae* (Sulzer).** *Pestic. Biochem. Physiol.*
 234 1988, **30**:1–10.
- 235 12. Drake JW, Charlesworth B, Charlesworth D, Crow JF: **Rates of spontaneous mutation.**
 236 *Genetics* 1998, **148**:1667–1686.
- 237 13. Jablonka E, Raz G: **Transgenerational epigenetic inheritance: prevalence,**
 238 **mechanisms, and implications for the study of heredity and evolution.** *Q. Rev. Biol.*
 239 2009, **84**:131–176.
- 240 14. Sparks TC, Nauen R: **IRAC: Mode of action classification and insecticide resistance**
 241 **management.** *Pestic. Biochem. Physiol.* 2015, **121**:122–128.
- 242 15. fFrench-Constant RH: **Which came first: insecticides or resistance?** *Trends Genet.*
 243 2007, **23**:1–3.

- 244 16. Grapputo A, Boman S, Lindström L, Lyytinen A, Mappes J: **The voyage of an invasive**
 245 **species across continents: genetic diversity of North American and European**
 246 **Colorado potato beetle populations.** *Mol. Ecol.* 2005, **14**:4207–19.
- 247 17. Stankovic S, Zabel A, Kostic M, Manojlovic B, Rajkovic S: **Colorado potato beetle**
 248 **[*Leptinotarsa decemlineata* (Say)] resistance to organophosphates and carbamates in**
 249 **Serbia.** *J. Pest Sci. (2004).* 2004, **77**:11–15.
- 250 18. Jiang W, Wang Z, Xiong M, Lu W: **Insecticide resistance status of Colorado potato**
 251 **beetle (Coleoptera□: Chrysomelidae) adults in Northern Xinjiang Uygur**
 252 **Autonomous Region.** *J. Econ. Entomol.* 2017, **103**:1365–1371.
- 253 19. Skinner MK: **Environmental epigenetics and a unified theory of the molecular aspects**
 254 **of evolution: A neo-Lamarckian concept that facilitates neo-Darwinian evolution.**
 255 *Genome Biol. Evol.* 2015, **7**:1296–1302.
- 256 20. Vandegheuchte MB, Lemièrre F, Vanhaecke L, Vanden Berghe W, Janssen CR: **Direct**
 257 **and transgenerational impact on *Daphnia magna* of chemicals with a known effect on**
 258 **DNA methylation.** *Comp. Biochem. Physiol. C. Toxicol. Pharmacol.* 2010, **151**:278–85.
- 259 21. Niu Y, DesMarais TL, Tong Z, Yao Y, Costa M: **Oxidative stress alters global histone**
 260 **modification and DNA methylation.** *Free Radic. Biol. Med.* 2015, **82**:22–8.
- 261 22. Liebers R, Rassoulzadegan M, Lyko F: **Epigenetic regulation by heritable RNA.** *PLoS*
 262 *Genet.* 2014, **10**:e1004296.
- 263 23. Calabrese EJ, Blain RB: **The hormesis database: The occurrence of hormetic dose**
 264 **responses in the toxicological literature.** *Regul. Toxicol. Pharmacol.* 2011, **61**:73–81.
- 265 24. Calabrese EJ, Mattson MP: **Hormesis provides a generalized quantitative estimate of**
 266 **biological plasticity.** *J. Cell Commun. Signal.* 2011, **5**:25–38.

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25. Haddi K, Mendes M V., Barcellos MS, Lino-Neto J, Freitas HL, Guedes RNC, Oliveira EE, Narciso R, Guedes C, Oliveira EE: **Sexual success after stress? Imidacloprid-induce hormesis in males of the neotropical stink bug *Euschistus heros*. *PLoS One* 2016, **11**:e0156616.**
26. Ayyanath MM, Scott-Dupree CD, Cutler GC: **Effect of low doses of precocene on reproduction and gene expression in green peach aphid. *Chemosphere* 2015, **128**:245–251.**
27. Stanley JK, Perkins EJ, Habib T, Sims JG, Chappell P, Escalon BL, Wilbanks M, Garcia-Reyero N: **The good, the bad, and the toxic: approaching hormesis in *Daphnia magna* exposed to an energetic compound. *Environ. Sci. Technol.* 2013, **47**:9424–9433.**
28. Freitak D, Knorr E, Vogel H, Vilcinskas A: **Gender-and stressor-specific microRNA expression in *Tribolium castaneum*. *Biol. Lett.* 2012, **8**:860–863.**
29. Tidbury HJ, Pedersen AB, Boots M: **Within and transgenerational immune priming in an insect to a DNA virus. *Proceedings. Biol. Sci.* 2011, **278**:871–6.**
30. Rix RR, Ayyanath MM, Christopher Cutler G: **Sublethal concentrations of imidacloprid increase reproduction, alter expression of detoxification genes, and prime *Myzus persicae* for subsequent stress. *J. Pest Sci.* 2016, **89**:1–9.**
- *31. Ayyanath M-M, Cutler GC, Scott-Dupree CD, Prithiviraj B, Kandasamy S, Prithiviraj K: **Gene expression during imidacloprid-induced hormesis in green peach aphid. *Dose. Response.* 2014, **12**:480–97.**
- This study shows heritable changes in methylation following imidacloprid exposure in an arthropod pest.
32. Glastad KM, Hunt BG, Yi S V, Goodisman MAD: **DNA methylation in insects: on the**

- brink of the epigenomic era. *Insect Mol. Biol.* 2011, **20**:553–65.
33. Flores K, Wolschin F, Corneveaux JJ, Allen AN, Huentelman MJ, Amdam G V: **Genome-wide association between DNA methylation and alternative splicing in an invertebrate.** *BMC Genomics* 2012, **13**:480.
34. Hunt BG, Glastad KM, Yi S V, Goodisman MAD: **The function of intragenic DNA methylation: insights from insect epigenomes.** *Integr. Comp. Biol.* 2013, **53**:319–28.
35. Fablet M, Vieira C: **Evolvability, epigenetics and transposable elements.** *Biomol. Concepts* 2011, **2**:333–41.
36. Field LM, Devonshire AL, Ffrench-Constant RH, Forde BG: **Changes in DNA methylation are associated with loss of insecticide resistance in the peach-potato aphid *Myzus persicae* (Sulz.).** *FEBS Lett.* 1989, **243**:323–327.
37. Hunt BG, Glastad KM, Yi S V, Goodisman MAD: **Patterning and regulatory associations of DNA methylation are mirrored by histone modifications in insects.** *Genome Biol. Evol.* 2013, **5**:591–8.
38. Szyf M: **Nongenetic inheritance and transgenerational epigenetics.** *Trends Mol. Med.* 2015, **21**:134–144.
39. Holoch D, Moazed D: **RNA-mediated epigenetic regulation of gene expression.** *Nat. Rev. Genet.* 2015, **16**:71–84.
40. Peschansky VJ, Wahlestedt C: **Non-coding RNAs as direct and indirect modulators of epigenetic regulation.** *Epigenetics* 2014, **9**:3–12.
41. Vandegehuchte MB, Kyndt T, Vanholme B, Haegeman A, Gheysen G, Janssen CR: **Occurrence of DNA methylation in *Daphnia magna* and influence of multigeneration Cd exposure.** *Environ. Int.* 2009, **35**:700–6.

Transgenerational effects on pest evolution

42. Vandegehuchte MB, De Coninck D, Vandenbrouck T, De Coen WM, Janssen CR: **Gene transcription profiles, global DNA methylation and potential transgenerational epigenetic effects related to Zn exposure history in *Daphnia magna*.** *Environ. Pollut.* 2010, **158**:3323–9.
  43. Poulos RC, Olivier J, Wong JWH: **The interaction between cytosine methylation and processes of DNA replication and repair shape the mutational landscape of cancer genomes.** *Nucleic Acids Res.* 2017, **45**:7786–7795.
  44. Baccarelli A, Bollati V: **Epigenetics and environmental chemicals.** *Curr. Opin. Pediatr.* 2009, **21**:243–51.
  - *45. Kishimoto S, Uno M, Okabe E, Nono M, Nishida E: **Environmental stresses induce transgenerationally inheritable survival advantages via germline-to-soma communication in *Caenorhabditis elegans*.** *Nat. Commun.* 2017, **8**:14031.
- This study, in *C.elegans*, shows how stress resistance is transmitted to subsequent generations via epigenetic alterations.
46. Rechavi O, Lev I: **Principles of transgenerational small RNA inheritance in *Caenorhabditis elegans*.** *Curr. Biol.* 2017, **27**:R720–R730.
  47. Piironen S, Ketola T, Lyytinen A, Lindström L: **Energy use, diapause behaviour and northern range expansion potential in the invasive Colorado potato beetle.** *Funct. Ecol.* 2011, **25**:527–536.
  48. Alyokhin A, Guillemette R, Choban R: **Stimulatory and suppressive effects of novaluron on the Colorado potato beetle reproduction.** *J. Econ. Entomol.* 2009, **102**:2078–2083.
  49. Piironen S, Boman S, Lyytinen A, Mappes J, Lindström L: **Sublethal effects of**

- 338 **deltamethrin exposure of parental generations on physiological traits and**
 339 **overwintering in *Leptinotarsa decemlineata*. *J. Appl. Entomol.* 2014, **138**:149–158.**
- 340 50. Piironen S, Lyytinen A, Lindström L: **Stress for invasion success? Temperature stress**
 341 **of preceding generations modifies the response to insecticide stress in an invasive**
 342 **pest insect. *Evol. Appl.* 2013, **6**:313–23.**
- 343 51. Lehmann P, Lyytinen A, Piironen S, Lindström L: **Northward range expansion**
 344 **requires synchronization of both overwintering behaviour and physiology with**
 345 **photoperiod in the invasive Colorado potato beetle (*Leptinotarsa decemlineata*).**
 346 *Oecologia* 2014, **176**.
- 347 52. Brander SM, Biales AD, Cannon RE: **The role of epigenomics in aquatic toxicology.**
 348 *Environ. Toxicol. Chem.* 2017, **36**:2565–2573.
- 349 **53. Oppold A, Kreß A, Bussche J Vanden, Diogo JB, Kuch U, Oehlmann J, Vandegehuchte
 350 MB, Müller R: **Epigenetic alterations and decreasing insecticide sensitivity of the**
 351 **Asian tiger mosquito *Aedes albopictus*. *Ecotoxicol. Environ. Saf.* 2015, **122**:45–53.**
- 352 Oppold *et al.* demonstrate that exposure to a toxic compound can affect epigenetic state for
 353 several generations, and that there is a phenotypic effect (decreased susceptibility to
 354 imidacloprid) associated with these methylation alterations.
- 355
- 356 54. Norouzitallab P, Baruah K, Vandegehuchte M, Van Stappen G, Catania F, Vanden
 357 Bussche J, Vanhaecke L, Sorgeloos P, Bossier P: **Environmental heat stress induces**
 358 **epigenetic transgenerational inheritance of robustness in parthenogenetic *Artemia***
 359 **model. *FASEB J.* 2014, **28**:3552–63.**
- 360 55. Vandegehuchte MB, Lemièrre F, Janssen CR: **Quantitative DNA-methylation in**
 361 ***Daphnia magna* and effects of multigeneration Zn exposure. *Comp. Biochem. Physiol.***
 362 ***C. Toxicol. Pharmacol.* 2009, **150**:343–8.**

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- 363 **56. Asselman J, De Coninck DI, Beert E, Janssen CR, Orsini L, Pfrender ME, Decaestecker
 364 E, De Schamphelaere KA: **Bisulfite sequencing with *Daphnia* highlights a role for**
 365 **epigenetics in regulating stress response to *Microcystis* through preferential**
 366 **differential methylation of serine and threonine amino acids.** *Environ. Sci. Technol.*
 367 2017, **51**:924–931.

368 This study describes how stress-induced methylation patterns can be associated with certain
 369 codon and genes with certain functions relevant to a stress response.
 370

- 371 57. Kumar S, Kim Y: **An endoparasitoid wasp influences host DNA methylation.** *Sci. Rep.*
 372 2017, **7**:43287.
- 373 58. Seong K-H, Li D, Shimizu H, Nakamura R, Ishii S: **Inheritance of stress-induced, ATF-**
 374 **2-Dependent Epigenetic Change.** *Cell* 2011, **145**:1049–1061.

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378

379 Table 1. Examples of epigenetic alterations following exposure to anthropogenic and “natural”,
 380 (non-anthropogenic) stress.

	Species	Treatment	Phenotypic Effects	DNA Methylation	Histone Modifications	Transgenerational effect	Reference
anthropogenic stressors	<i>Daphnia magna</i>	vinclozolin (fungicide)	body size	reduced methylation	n/a	N	[20]
	<i>Daphnia magna</i>	5-azacytidine (demethylating agents)	reproduction, body size	reduced methylation	n/a	Y	[20]
	<i>Myzus persicae</i> (Green Peach Aphid)	imidacloprid (insecticide)	changes in gene expression, including heat shock protein	increased, decreased, or no change based on concentration	n/a	Y	[31*]
	<i>Aedes albopictus</i> (Asian Tiger Mosquito)	genistein (phytohormone)	decrease in sensitivity to imidacloprid	cautious decrease	n/a	Y	[54]
	<i>Aedes albopictus</i> (Asian Tiger Mosquito)	vinclozolin (fungicide)	decrease in sensitivity to imidacloprid	cautious increase	n/a	Y	[54]
"natural" stressors	<i>Artemia</i> sp. (brine shrimp)	heat stress	increased Hsp70 production, heat tolerance, and resistance vs. pathogens	changes in methylation	histones H3 and H4 acetylation	Y	[55]
	<i>Daphnia magna</i>	zinc	changes in gene expression	reduced methylation	n/a	Y	[56*]
	<i>Daphnia magna</i>	toxic cyanobacterium <i>Microcystis aeruginosa</i>	n/a	differential methylation primarily in exonic regions, enriched for serine/threonine amino acid codons and genes related to protein synthesis, transport and degradation, in genes susceptible to alternative splicing in response to <i>Microcystis</i> stress	n/a	N	[57]
	<i>Plutella xylostella</i> (Diamondback Moth)	endoparasitoid	altered gene expression	reduced methylation	n/a	N	[58]

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	<i>Drosophila melanogaster</i> (Fruit Fly)	Heat shock or osmotic stress	n/a	n/a	heterochromatin disruption	Y	[59]

Figure Legends.

Figure 1. Examples of how changes in methylation status of in different gene regions can effect gene expression. Compared to the “normal” unmethylated region, A) has promoter methylation, leading to decreased gene expression; B) exhibits methylation in transposable element regions, leading to those elements not being expressed, and C) shows gene body methylation as found in arthropods, leading to increased gene expression as well as an increased variety of splice variants in those transcripts.

Figure 2. How exposure to a stressor may lead to heritable epigenetic changes that could lead to stress-resistant phenotype in an invasive agricultural insect pests.

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