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1 **Transposable elements and the evolution of insects**

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13

14 **Abstract**

15 Insects are major contributors to our understanding of the interaction between transposable
16 elements (TEs) and their hosts, owing to seminal discoveries, as well as to the growing number of
17 sequenced insect genomes, population genomics and functional studies. Insect TE landscapes are
18 highly variable both within and across insect orders, although phylogenetic relatedness appears to
19 correlate with similarity in insect TE content. This correlation is unlikely to be solely due to
20 inheritance of TEs from shared ancestors and may partly reflect preferential horizontal transfer of
21 TEs between closely related species. The influence of insect traits on TE landscapes remains however
22 unclear. Recent findings indicate that in addition to being involved in insect adaptations and aging,
23 TEs are seemingly at the cornerstone of insect antiviral immunity. Thus, TEs are emerging as essential
24 insect symbionts, which may have deleterious or beneficial consequences on their hosts depending
25 on context.

26

27 **Keywords**

28 Transposable elements, adaptation, antiviral immunity, aging, evolution, horizontal transfer

29 Introduction

30 Transposable elements (TEs) are pieces of DNA able to move from one genomic locus to another,
31 often duplicating themselves in the process (13). The large diversity of TE types is classified in two
32 classes: retrotransposons (Class-I TEs), which move through a replicative process involving reverse
33 transcription of the TE mRNA, and DNA transposons (Class-II TEs), which mobilize through replicative
34 or non-replicative transposition of DNA copies (24, 144). TEs are found in the genomes of virtually all
35 organisms, often in very large amounts. The structure of TEs, their mobility and repeated nature have
36 profoundly shaped the evolution of their hosts (22, 39, 63, 123).

37 TEs were discovered in the 1940s by Barbara McClintock, who showed that some genetic elements
38 could move in the maize genome. This activity would induce chromosome breaks and sometimes
39 modify the expression of neighboring genes with visible changes in maize kernel color (92). These
40 initial studies have been mostly ignored for over three decades until they were finally rewarded by
41 the Nobel prize of Physiology or Medicine (in 1983). TEs then became increasingly considered as
42 important drivers of evolution, notably owing to major discoveries made in insects, mainly in
43 *Drosophila* flies (8). Examples include the hybrid dysgenesis phenomenon, whereby F1 hybrids
44 between males harboring *P* elements (class-II TEs) and females lacking them showed several defects
45 such as gonadal atrophy and sterility (17, 70, 72). The molecular underpinnings of hybrid dysgenesis
46 were only deciphered in 2008 through the discovery of the PIWI-associated RNAs (piRNAs)-mediated
47 control of TEs (15). In the meantime, molecular cloning and extensive studies of the *P* element led to
48 the development of this TE as one of the most widely used germline transformation tools in
49 *Drosophila* (87, 125). Other TE-based transformation systems were developed for non-*Drosophila*
50 species, including the one using *Piggybac*, a TE from the cabbage looper moth (*Trichoplusia ni*) that
51 was discovered because of its ability to jump into a baculovirus (41, 56).

52 Surveys of the distribution of *P* elements in wild and laboratory strains of various *Drosophila* species
53 also revealed that horizontal transfer (HT) of genetic material (here TEs) was not restricted to
54 bacteria but that it could occur in eukaryotes (27, 45). Other landmark TE discoveries made in
55 *Drosophila* include the so-called *P* neogenes derived from stationary *P* element copies, which led to
56 the realization that TE protein domains can be co-opted to fulfill cellular functions (95, 102, 108).
57 Perhaps even more surprising, the finding that the classical telomeres had been replaced in
58 *Drosophila* flies with *HetA/TART/TAHRE* retrotransposons, which only transpose at chromosome
59 ends, revealed that *bona fide* TEs could be beneficial to their host (9, 101). Finally, seminal studies
60 mapped the genetic basis of insecticide resistance in the tobacco budworm (*Heliothis virescens*) and

61 *D. melanogaster* to TE-driven mutations, which contributed to set TEs as powerful facilitators of
62 genome evolution and host adaptation (26, 43, 98, 116).

63 These case-studies along with more recent multi-species, genome-wide surveys allow painting a
64 general picture of the composition, evolution and potential roles of TEs in insects, which is the topic
65 of this review. We first expose emerging macroevolutionary trends that underlie insect TE genomic
66 landscapes. We then discuss how the latest major discoveries on the impact of TEs in insect
67 adaptation, antiviral immunity and aging are continuously changing the way we view these genomic
68 symbionts.

69

70 **1 - Evolution of TEs within and across insect orders**

71 **1 - 1 Diversity and abundance of insect TEs**

72 The first comprehensive characterizations of TE abundance, diversity, age and genome distribution in
73 an insect were made possible thanks to analyses of the *D. melanogaster* genome (5, 7, 66, 69). These
74 studies illustrated how estimates of TE abundance and diversity heavily depend on the completeness
75 and quality of assembled genomes as well as on the methods used to annotate TEs. TE content
76 ranged from 2% of the *D. melanogaster* genome in early studies of euchromatic regions relying only
77 on similarity-based approaches, to about 15 % when heterochromatic regions were included and
78 combined *de novo* annotation pipelines were developed. The *D. melanogaster* TE landscape is
79 dominated by LTR-retrotransposons, which make up 10% of the genome, with non-LTR
80 retrotransposons and DNA transposons altogether occupying ~5% of the genome. The TE distribution
81 along *D. melanogaster* chromosomes is non-random, with a much lower density in euchromatic
82 regions where TEs generally occur as single full-length copies, than in pericentromeric
83 heterochromatin where TEs are arranged in dense islands of nested and often rearranged copies.
84 Bergman et al. (7) proposed that expression of such TE islands would produce transcripts made of
85 chimeric TEs which could be involved in suppressing the activity of multiple TE families. The
86 hypothesis was later confirmed with the discovery of dozens of pericentromeric TE-rich regions
87 called piRNA clusters acting as TE traps, the expression of which initiates piRNA-mediated TE
88 suppression (15, 150). Early studies based on between-copy genetic distances within TE families
89 found that most euchromatic TE copies resulted from very recent transposition events (14, 69). Their
90 recent origin is in agreement with subsequent studies showing that >80% of polymorphic TE copies
91 segregate at low (<0.2) frequency in *D. melanogaster* populations (75).

92 The analysis of other genomes quickly revealed that characteristics of fly TEs were not necessarily
93 representative of those found in other insects and that TE landscapes were highly dynamic in this
94 group (90). For example, although the overall content of classified TEs in the mosquito *Anopheles*
95 *gambiae* (about 13%) was close to that of *D. melanogaster*, LTR retrotransposons occupy about the
96 same amount of genomic space as non-LTR retrotransposons and DNA transposons in this species
97 (61, 96). Genome sequencing of another mosquito (*Aedes aegypti*), a Coleoptera (*Tribolium*
98 *castaneum*) and a Lepidoptera (*Bombyx mori*) further revealed that TE content varies substantially in
99 insects (from 6% in *T. castaneum* to 48% in *A. aegypti*) and that both DNA transposons and non-LTR
100 retrotransposons can be the dominant TEs in other species (97, 100, 139). The decrease in
101 sequencing costs was then accompanied by a rapid augmentation of the number of genome papers
102 with detailed sections on TE annotation (e.g. 19, 21, 23, 42, 44). One study reported that the
103 antarctic midge (*Belgica antarctica*) had both the smallest genome and the lowest TE content among
104 arthropods (71). It is now common to see papers reporting comparative analyses of multiple insect
105 genomes with efforts dedicated to surveying the evolution of TE contents across genomes (e.g. 1, 6,
106 15, 21, 28, 37, 45), as well as studies specifically dedicated to comparisons of TE contents at scales
107 ranging from insect genus to whole arthropods (55, 105, 110, 114, 148). We ourselves performed an
108 automated TE annotation on 195 publicly available insect genomes (103) (Figure 1).

109 A recent study also reported automated *de novo* TE-annotation and comparison of 73 arthropod
110 genomes (including 62 insects) (105). An interesting outcome of this analysis, as well as ours (Figure
111 1), is that the nature of a large fraction of the repetitive content of most insect genomes (11% in *D.*
112 *simulans* up to 93% in *Ephemera danica*; mean 56%, (105)) cannot be assessed using automated
113 procedures. Thus, interpretations on variation in TE content in insects must be taken with caution.
114 Bearing this limitation in mind, broad-scale TE landscape analyses reveal a high diversity of TEs in
115 insects, with most known TE superfamilies present in most insect species (105, 148). They also unveil
116 some degree of homogeneity in TE composition among insect groups spanning diverse taxonomic
117 levels (105). For example, in six tsetse fly species (*Glossina* spp), the genome proportion occupied by
118 DNA transposons (12.8-14.7%), LTR (0.4-0.8%) and non-LTR (5.8-2.9%) retrotransposons has
119 remained stable over 25 million years (2). In three Hemipteran species having diverged >200 million
120 years ago (*Cimex lectularius*, *Halyomorpha halys* and *Oncopeltus fasciatus*), genome proportions of
121 TE classes differ between species but non-LTR retrotransposons (7-14%) are always in higher
122 amounts than DNA transposons (1.3-4%) and LTR retrotransposons (0.6-1.4%). The situation is similar
123 in four lepidopteran species which diverged >100 million years ago (*Helicoverpa armigera*, *Bombyx*
124 *mori*, *Danaus plexippus*, *Heliconius melpomene*), in which non-LTR retrotransposons (4.2-20.4%) are
125 also always in higher amount than DNA transposons (0.9-3.1%) and LTR retrotransposons (0.3-0.7%).

126 While homogeneity in TE composition exists in some cases, pronounced differences have been found
127 in other cases. In hemipterans for example, SINEs and DNA transposons of the pea aphid
128 (*Acyrtosiphon pisum*) occupy the largest genome fraction (7.1% and 8.6%, respectively) while they
129 are either present in low amount (mean=1.2% and 2.3%, respectively) and/or occupy the lowest
130 genome fraction in the other six surveyed species (105). In coleopterans, DNA transposons occupy a
131 much larger genome fraction than retrotransposons in *T. castaneum* and *Anoplophora glabripennis*
132 while they are in minority compared to retrotransposons in *Agrilus plannipennis* and *Leptinotarsa*
133 *decemlineata* (105). Large differences in TE landscapes also exist at the genus level. Among 16
134 *Heliconius* butterfly species, TE composition may be similar at the level of TE class (DNA transposons
135 versus retrotransposons), but may differ drastically within each TE Class (110). For example, LTR
136 retrotransposons are almost absent in *H. doris* and *H. burneyi* but they make up 2 to 6% of the
137 genome of the other 14 species. Similarly, eight *Heliconius* species have a genome proportion of
138 SINEs <1% while SINEs make up 2 to 6% of the genome of the remaining eight species.

139 **1 – 2 The influence of vertical and horizontal transmission on insect TE landscapes**

140 The TE content of a genome is an equilibrium between the rate of TE acquisition, the replication
141 dynamics of TEs within the genome and the rate of TE loss by degradation/deletion. TEs are acquired
142 from ancestors (vertical inheritance) and potentially from other organisms (HT). TE replication
143 dynamics reflect rates of TE insertions (TE activity), which may be suppressed by host factors, as well
144 as the fate of these insertions under the influence of natural selection and genetic drift (73, 79, 115,
145 135). While the relative importance of the factors and processes shaping TE landscapes is not well
146 understood, insects are one of the groups in which they have been the most intensely studied so far
147 (see also (129) for a study in nematodes).

148 Multiple large-scale studies indicate a positive correlation between phylogenetic relatedness and
149 similarity of TE landscapes in insects (see above and refs. (105, 148)), although this correlation is not
150 formally tested. Variation in genome size also shows a strong phylogenetic signal and is positively
151 correlated to TE content both at the scale of arthropods (102, 146) and within insect orders: in
152 *Drosophila* species (40, 122), wood-white butterflies (130) and fireflies (84). This observation is
153 somewhat expected given that TEs, like any other genome component, are inherited from parents to
154 descendants. Yet in several pairs of closely related species showing relatively similar TE landscapes,
155 such as *D. melanogaster* and *D. simulans*, most TE copies have originated from transposition events
156 that are much more recent than the species split (14, 105). Their recent origin is further supported by
157 the fact that TE insertions in *D. melanogaster* are generally polymorphic within the species (75). As a

158 result, relatively few TE copies may be inherited over millions of years in a context of ongoing TE
159 activity, and species would be expected to diverge quickly with respect to their TE content.

160 On the other hand, a systematic survey of HT of TEs (HTT) between *D. melanogaster*, *D. simulans* and
161 *D. yakuba*, which diverged 11 million years ago, revealed that at least one third of the TE families in
162 these three species have been acquired through HTT, with an overall HTT rate of 0.035 events per TE
163 family per million years (4). It was also found that the number of HTT was higher between closely
164 related species than between distantly related ones, with twice as many events between *D.*
165 *melanogaster* and *D. simulans* as between any of these species and *D. yakuba* (4). A similar study
166 extended to 195 insect genomes inferred no fewer than 2248 HTT events between species having
167 diverged >40 million years ago (103). In addition to showing that HTT is not infrequent and has had a
168 strong impact on genome evolution in insects, with on average 2% of insect genome content deriving
169 from horizontally transferred TEs (and up to 25%), this study confirmed the role of phylogenetic
170 relatedness in favoring HTT. Preferential HTT between related species may thus explain the
171 phylogenetic signal in insect TE landscape variation in conjunction to inheritance from shared
172 ancestors.

173 In addition to phylogeny, geography was found to partly explain the distribution of HTT along the
174 insect tree. More HTT was detected between species originating from the same biogeographic realm
175 than between species from different ones (103). The observation that species more likely to be in
176 (direct or indirect) contact are also more likely to exchange TEs supports a role for ecological
177 relationships in shaping HTT. This is in line with a series of studies reporting HTT between animal
178 hosts and their parasites (47, 78, 128, 137, 141), but not with a study that did not detect HTT
179 between *Drosophila* species and two of their parasitoid wasps (99). Given the relatively high rate of
180 HTT in insects (103), it is likely that future studies implementing appropriate taxon sampling will
181 further delineate the types of ecological relationships, including host-parasite relationships, that
182 affect HTT patterns in insects (135). Interestingly, it was recently found that lepidopterans were
183 significantly more prone to HTT than other insect orders (112). The higher susceptibility of
184 lepidopterans to HTT may be explained by a number of different factors, one of which being
185 exposure to large double-stranded DNA viruses belonging to the Baculoviridae family. Most known
186 baculoviruses indeed infect lepidopterans and a large number of TEs are able to jump from infected
187 moth species to the genome of several baculoviruses, suggesting a role for these viruses as vectors of
188 HTT (46).

189 **1 - 3 Are insect TE landscapes shaped by ecological and life history traits?**

190 The replication dynamics of TEs may depend on certain life history traits of their hosts, as these traits
191 may condition the impact of TE insertions on fitness and how these insertions evolve in host
192 populations. One candidate trait is reproductive mode, since reduced recombination rates in asexual
193 taxa may lead to the accumulation of TE insertions, as seen in non-recombinant sex chromosomes
194 (18). However, asexual arthropods (including asexual wasps) do not have more TEs than their sexual
195 counterparts (6, 77, 119). By contrast, social complexity is negatively correlated with TE abundance
196 and TE diversity in bees, which may be explained by increased recombination rates in highly social
197 insects and/or the pronounced hygienic behavior in these insects, leading to a lower exposure to
198 parasites that may act as vectors of HTT (68). Yet, in social ants displaying hygienic behavior, TE
199 content and diversity are similar to non-solitary insects (42). Furthermore, in termites, the socially
200 more complex *Macrotermes natalensis* has a larger genome (1.31 Gb) and higher TE content (about
201 30%) than *Zootermopsis nevadensis* (562 Mb and about 16%, respectively) (76). Thus, whether or not
202 TE landscapes are shaped by levels of sociality in bees, the influence of this factor may not hold for
203 other social insects.

204 The ecological niche has been proposed as a potential factor shaping insect TE landscapes. For
205 example, the low TE content of the antarctic midge *B. antartica* (0.12%) is thought to result from the
206 paucity of contacts this extreme specialist has with other organisms in the species-poor polar
207 environment, combined to strong selective pressures due to pronounced physiological and ecological
208 constraints (71). In apparent agreement with a link between ecological niche and TE content, another
209 extreme specialist, the fig wasp *Ceratosolen solmsi* also has one of the lowest TE contents of all
210 insects (6.4%) (149). Yet, when comparing TE landscapes between *Drosophila* species in a
211 phylogenetic context, no significant difference was found between specialists and generalists (40).
212 The level of ecological specialization of *Drosophila* species, which is not as extreme as in *B. antartica*
213 and *C. solmsi*, may not be high enough to impact TE content. Thus, reevaluating TE content in a
214 controlled phylogenetic framework including related specialist and generalist species is required to
215 properly test the influence of ecological niche on this variable. More generally, how host physiology
216 and ecology govern TE replication dynamics deserves further studies. Such works may help to assess
217 how the similarity in TE contents among related species, despite sustained TE activity, reflects some
218 form of stabilizing/parallel evolution under similar constraints.

219

220 **2 – The fate and impact of TEs in insect genomes**

221 The development of next-generation sequencing technologies and analytical tools have enabled
222 studies of the population genomics of insect TEs, many of which have focussed on *D. melanogaster*
223 (3, 12). These studies have shown that a large fraction of the TEs inserted in the *D. melanogaster*
224 reference genome are not fixed in the species (106). In addition, thousands of non-reference TE
225 insertions segregate in *D. melanogaster* populations (25, 74, 80, 83, 109).

226 The majority of polymorphic TE insertions are present at lower frequencies than expected for neutral
227 variants, suggesting that purifying selection (deleterious effects) plays a major role in TE population
228 dynamics in *D. melanogaster* (10). A similar pattern of TE dynamics has been found in *D. simulans*
229 (75). The deleterious effect of TEs can in part be explained by insertional mutagenesis upon
230 integration in the genome. Consistently, more than half of spontaneous mutant phenotypes in *D.*
231 *melanogaster* are caused by TE insertions disrupting gene function (33) and very few TE insertions
232 are found in protein-coding genes in natural populations (74, 106). At the post-insertional level, an
233 important cause for TE deleteriousness is ectopic recombination between non allelic, homologous TE
234 insertions, which can generate deleterious genomic rearrangements (74, 106). It will be interesting to
235 assess to what extent TE insertions are deleterious for insects other than *Drosophila*.

236 **2 - 1 Insect adaptation**

237 Even though most TE insertions are deleterious or neutral, some insertions are expected to be
238 beneficial to their carriers. This is the case of several TE-mediated mutations underlying resistance to
239 insecticides in the pink bollworm *Pectinophora gossypiella*, a major pest of cotton, and in *D.*
240 *melanogaster* (116). In *P. gossypiella*, several independent TE insertions disrupting the *PgCad1* gene
241 confer resistance to the widely used *Bacillus thuringiensis* Cry1Ac toxin (37, 138). In *D. melanogaster*,
242 *cis*-regulatory sequences of an *Accord* LTR retrotransposon inserted in the 5' regulatory region of the
243 *Cyp6g1* gene are responsible for *Cyp6g1* upregulation and increased resistance to DDT (21, 26).
244 Furthermore, an adaptive allelic series in *Cyp6g1* involving successive mutations (including *P* and
245 *HMS-Beagle* TE insertions) was later found to be associated with increasing DDT resistance levels
246 (120). Similarly, resistance to organophosphate insecticide is caused by a *Doc1420* LINE
247 retrotransposon that truncates the *CHKov1* gene and produces altered transcripts (1). Interestingly,
248 the new variant may have initially been selected as a defense against viral infections, thereby pre-
249 adapting flies to insecticides (86). Yet another mechanism underlies TE-mediated increased resistance
250 to cyclodiene dieldrin: *Rdl* gene duplication through ectopic recombination between *Roo* LTR
251 retrotransposons (113). DNA transposons can also be involved in xenobiotic resistance, as
252 exemplified by the *Pogo* TE affecting polyadenylation signal choice in the *CG11699* gene and

253 conferring resistance to carbofuran and benzaldehyde (89). These examples serve to highlight the
254 diversity of TE families and molecular mechanisms through which TEs can be adaptive to their hosts,
255 which is all the more spectacular with respect to insecticide resistance in *D. melanogaster*, when
256 considering that this species is not a pest and has not been targeted by insecticides.

257 The contribution of TEs to *D. melanogaster* adaptation is not restricted to insecticide resistance, as
258 genome-wide studies of TE insertion polymorphisms have identified dozens of candidate adaptive TE
259 insertions (50, 51, 74, 80, 111). Population frequency distributions of TE insertions suggest that some
260 may play a role in adaptation to temperate climates (*D. melanogaster* has originated in the
261 afrotropics), often by induction of regulatory changes in nearby genes (50, 51). Functional gene
262 categories such as stress response, behavior and development appear to be particularly prone to TE-
263 mediated adaptation (111). In some cases, ecologically-relevant fitness benefits have been clearly
264 connected to specific TE insertions, such as a *Bari1* DNA transposon mediating oxidative stress
265 response (52, 54), *P*, *Jockey* and *Roo* elements involved in thermotolerance (81, 93) and an *invader4*
266 retrotransposon inducing faster development time (133). Interestingly, negative fitness effects of
267 such TE insertions have sometimes been identified, which may represent costs of selection and may
268 explain why the TE insertions have not reached fixation (52, 133).

269 Adaptive TE insertions have also been found in various insects other than *D. melanogaster*. For
270 example, in the peppered moth *Biston betularia*, industrial melanism is caused by a *carb-TE* DNA
271 transposon in the first intron of the *cortex* gene which affects gene expression (60). This mutation
272 underlies the replacement of a pale form by a black form driven by the interplay between bird
273 predation and coal pollution during the Industrial Revolution in the UK. Wing color polymorphism is
274 also associated with a TE insertion in the *Colias crocea* butterfly, conferring developmental and
275 reproductive advantages (147). In Chinese populations of the migratory locust (*Locusta migratoria*),
276 an *Lm1* SINE insertion in the third exon of the *Hsp90* gene produces an alternative splicing form
277 associated with faster development and higher developmental synchrony (20). Remarkably, only
278 heterozygotes are present in natural populations, suggesting there is an heterozygote advantage that
279 is maintained by balancing selection. It has also been proposed that TEs may be powerful agents of
280 rapid adaptation in invasive species (126), an hypothesis that has received empirical support from
281 several insects such as the ant *Cardiocondyla obscurior* (121) and the Asian tiger mosquito *Aedes*
282 *albopictus* (53).

283 While the aforementioned examples of adaptive TEs consider individual copies, the repetitive nature
284 of TEs and existence of multiple homologous sequences scattered in genomes offer the perspective
285 for TEs to collectively impact cellular processes. For example, *G2/Jockey-3* retrotransposons appear

286 to contribute to the structure and function of centromeres in *D. melanogaster* and *D. simulans* (19).
287 TEs may also rewire regulatory networks by supplying *cis* regulatory elements at chromosomal scale,
288 as shown with the recruitment of *Helitron* elements to regulate dosage compensation in *D. miranda*
289 sex chromosomes (34, 35). There is however no formal demonstration that TEs have actually
290 improved these cellular processes from their ancestral state. The involvement of TEs in these
291 processes could represent neutral or even slightly deleterious mutational changes.

292 **2 – 2 Antiviral immunity**

293 In addition to their role in adaptation of insect populations, recent studies are setting TEs as an
294 important component of insect antiviral immunity. In insects, viruses are mainly restricted by RNA
295 interference (RNAi) (134). This pathway relies on the recognition and cleavage of intracellular long
296 viral double-stranded (ds) RNAs by the endoribonuclease Dicer2, yielding 21-nucleotide small
297 interfering RNAs (siRNAs). One strand of siRNAs is then used by the endoribonuclease Argonaute 2 to
298 target and cleave complementary long single-stranded viral RNAs, resulting in viral restriction. While
299 this pathway confers immunity to infected insect cells, it has long remained unclear whether such
300 immunity could spread systemically. In plants and nematodes, systemic RNAi spread relies on
301 amplification of dsRNA molecules by RNA-dependent RNA-polymerases (RdRp) (59, 124), which are
302 absent in insects (82). Yet, Goic et al. (48, 49) showed that antiviral RNAi can be amplified through a
303 hitherto unknown mechanism in *Drosophila* flies and *Aedes* mosquitoes, which relies on the
304 formation of viral DNA (vDNA). Remarkably, vDNAs are produced through reverse transcription of
305 viral RNAs by insect retrotransposon proteins, instead of an RdRp. This process primarily takes place
306 in hemocytes, in which viral dsRNAs released by infected cells accumulate (107, 131). vDNAs are then
307 transcribed and they trigger the formation of secondary viral siRNAs which are loaded into exosome-
308 like vesicles. They are then secreted in the extracellular environment and spread over the entire
309 insect body, conferring systemic antiviral immunity (131). vDNAs are generated as both circular and
310 linear molecules, some of which may end up being integrated into the host genome (132). Isolation
311 and sequencing of episomal circular DNA from infected mosquito cells and *Drosophila* flies revealed
312 that many circular vDNAs (cvDNAs) correspond to virus-LTR retrotransposon chimeras. Strikingly, the
313 amount of circular DNA containing virus-LTR retrotransposon chimeras produced by mosquito cells is
314 typically much higher than that containing chimeras of non-virus host sequence and
315 retrotransposons (132). Furthermore, the viral portion of virus-LTR retrotransposon chimeras is
316 enriched for defective viral genomes (107). Together, these observations suggest that viral defective
317 RNAs are recognized and preferentially reverse-transcribed over non-viral RNAs by LTR
318 retrotransposon-encoded reverse transcriptases, through a process involving copy-choice
319 recombination and seemingly depending on Dicer2 (107, 131, 132). Importantly, inhibition of reverse

320 transcriptase activity in flies and mosquitoes leads to accelerated death of infected individuals (48,
321 49). Thus, in the context of viral infections, the presence of LTR retrotransposons capable of
322 producing active reverse transcriptases is crucial for fly and mosquito survival. In principle, as long as
323 sources of reverse transcriptase activity are available throughout the evolutionary history of insects,
324 this antiviral protection system does not require co-option of a specific TE copy that would become
325 stationary and evolve under purifying selection like a regular gene. Thus, while in conflict with their
326 hosts because of the overall deleterious consequences of transposition, insect LTR retrotransposons
327 may become beneficial when host individuals incur viral infections.

328 Even more remarkably, insect retrotransposons have recently been shown to catalyse vDNA
329 integration into piRNA clusters of an *Aedes aegypti* cell line, leading to formation of endogenous viral
330 elements (EVE) (132, 143). Such EVEs are co-transcribed with other TE remnants from piRNA clusters,
331 leading to the production of anti-sense viral piRNAs that provide antiviral immunity. Thus, in addition
332 to their role in the amplification and systemic spread of antiviral immunity, insect retrotransposons
333 and their piRNA-mediated host surveillance system have the potential to confer transgenerational
334 antiviral immunity to their hosts (132, 143). The finding that LTR retrotransposons may be essential
335 to insect antiviral immunity opens new perspectives on the way we conceive insect/TE relationships.
336 Much like other TEs such as *TBE* DNA transposons in the ciliate *Oxytricha trifallax* (136) or the
337 telomeric non-LTR retrotransposons in *Drosophila* flies (118), and much like cellular endosymbionts
338 such as *Wolbachia* and *Cardinium* (44, 65, 142), the position of insect LTR retrotransposons on the
339 continuum of host/symbiont interactions may vary in unexpected ways between conflict and
340 cooperation, depending on context (23).

341 **2 – 3 Aging**

342 Aging is typically associated with the progressive alteration of genome regulation, notably due to the
343 loss of repressive heterochromatin marks (145). Several studies have shown that this dysregulation is
344 associated with an increase of TE expression in various eukaryotic organisms including yeasts (91),
345 nematodes (30), mice (29) and human cell lines (28). Thus, it has been proposed that expression and
346 transposition of TEs that are silenced in young individuals may strongly affect cell and genome
347 integrity in old individuals, triggering or reinforcing aging symptoms (31, 145). A series of elegant
348 experiments performed in *D. melanogaster* seemingly support this model. In particular, it was shown
349 that Dicer2-mutant individuals had more DNA double-strand breaks, presumably caused by activated
350 TEs, than controls in the nuclei of fat body cells (146). This is consistent with the known role of Dicer2
351 in the formation of repressive heterochromatin around repeated DNA (including TEs) via the
352 recruitment of the Su(var)3-9 histone methyl-transferase (38, 104). Importantly, decreasing TE

353 activity in these Dicer2 mutants through the addition of a reverse-transcriptase inhibitor led to
354 reduced transposition and increased lifespan. Thus, TE activity rather than the mere deterioration of
355 chromatin structure could be directly implicated in aging in *D. melanogaster* (146). In apparent
356 agreement, the lower lifespan of male versus female *D. melanogaster* flies has been attributed to a
357 higher amount of heterochromatin in males, which possess a highly repeat- and heterochromatin-
358 rich Y chromosome (16, 88).

359 The finding that TEs largely contribute to aging in *D. melanogaster* has recently been complemented
360 by studies in social insects. These insects are ideal models in aging research because individuals from
361 a given colony sharing an identical genotype show large differences in lifespan, depending on the
362 caste they belong to. In the termite *Macrotermes bellicosus* for example, reproductive castes (kings
363 and queens) can live for as long as 20 years whereas the lifespan of major and minor workers never
364 exceeds a few months. Elsner et al. (36) have shown that, while overall TE and gene expression levels
365 in heads were stable through the lifetime of kings and queens, several hundreds of TE copies were
366 expressed at higher levels in old versus young major workers. The higher TE expression in old
367 workers was associated with down-regulation of four genes involved in the piRNA pathway,
368 suggesting that aging in major workers may be due to a decrease in TE suppression. Since these
369 genes were expressed at equal levels in old and young reproductive castes, it was proposed that the
370 longer lifespan of kings and queens evolved thanks to cooption of the piRNA pathway (36) to
371 suppress TEs in their somatic tissues (here heads). Though interesting, this hypothesis does not
372 explain why piRNA genes are expressed (and TEs suppressed) in heads of young major workers (85).
373 In fact, somatic expression of the piRNA pathway has been inferred to be ancestral to all arthropods,
374 with only few species (including *D. melanogaster*), having lost this pathway in the soma (82). Thus,
375 rather than cooption of the piRNA pathway in heads of *M. bellicosus* reproductives, observations
376 may be more consistent with a secondary loss of this pathway in heads of old major workers.

377

378 **3 – Conclusions and perspectives**

379 Major breakthroughs in our understanding of eukaryote genome regulation and evolution have been
380 made through the study of insect TEs. Our knowledge of TE landscapes and their impact on insect
381 genomes and phenotypes has rapidly increased over the last ten years thanks to the availability of an
382 increasing number of genome sequences. Current large-scale surveys of insect TE landscapes must be
383 interpreted cautiously as TEs have been thoroughly mined only in a handful of insect genomes and
384 new TE families are still being discovered even in the best annotated genomes (148). Yet, global
385 trends emerge, suggesting that while TE landscapes can be highly variable both within and across

386 insect orders, phylogenetic relatedness generally correlates with similarity in TE content overall (84,
387 105, 122, 130, 148), even in cases where most extant TEs are not inherited from shared ancestors.
388 Vertical inheritance, horizontal transfer and the ecology/physiology of hosts are likely involved in
389 shaping insect TE landscapes, and it will be interesting to assess their relative contribution along the
390 insect phylogeny.

391 Because of their high diversity and the wide spectrum of molecular mechanisms through which they
392 can generate evolutionary innovations (including insertion, deletion, rearrangement, dispersion of
393 cis-regulatory elements and TE protein sequences), TEs appear to be involved in a variety of adaptive
394 events in many insect species. Thus, insects may be good models to quantify the respective
395 contribution of TE-mediated genomic change versus other mutations in adaptation.

396 The finding that retrotransposons are at the heart of antiviral response in some insects emerges as
397 one of the most important discoveries made in invertebrate immunity in the last few years (94). Yet,
398 the range of viruses that are targeted by TE-mediated small RNA responses in the wild remains to be
399 defined and it is unclear to what extent retrotransposons play a role in suppressing viruses beyond *D.*
400 *melanogaster* and *Aedes* mosquitoes. Whether and how retrotransposons involved in this response
401 vary among insects is also unknown. In addition, it will be interesting to further decipher the
402 mechanisms by which insect retrotransposons selectively recognize and reverse-transcribe viral RNAs
403 over cellular RNAs.

404 Monitoring and manipulating insect TE expression in old versus young insects uncovered a likely
405 causal role for TE activity in aging, in agreement with the retrotransposon theory of aging (31, 145).
406 In social insects, it will be interesting to assess whether TE activity in old workers is associated with a
407 deterioration of heterochromatin structure, as observed in *D. melanogaster*. Furthermore, a general
408 prediction of the retrotransposon theory of aging is that individuals with higher heterochromatin
409 loads should be shorter lived than individuals with low amounts of heterochromatin. While this
410 hypothesis seems to hold in *D. melanogaster* (16), testing it could also take advantage of species in
411 which B chromosomes, known to be largely heterochromatic, are present at substantial frequencies
412 (57). More generally, these results call for a detailed evaluation of the impact of somatic
413 transposition on insect biology.

414

415 **Figure legend**

416 Figure 1. Proportions of DNA transposons, LTR, LINE and SINE retrotransposons in insect genomes.
417 TEs were automatically annotated in 195 insect species (103). Because of space constraints, only one

418 species per clade that are ≤ 45 My old is shown here (to the exception of the pair *D. melanogaster*
419 and *D. simulans*). The "Unclassified" category of TEs represents elements that were not classified
420 (and categorized as "unknown") by the procedure. These exclude satellites and other repeat
421 elements that are unlikely to be TEs. The design of the figure is inspired from figure 1 of ref. (105).
422 The insect phylogeny on the left is that used in ref. (103). The data used to build the figure is
423 available upon request.

424

425 **References**

- 426 1. Aminetzach YT. 2005. Pesticide Resistance via Transposition-Mediated Adaptive Gene Truncation
427 in *Drosophila*. *Science*. 309(5735):764–67
- 428 2. Attardo GM, Abd-Alla AMM, Acosta-Serrano A, Allen JE, Bateta R, et al. 2019. Comparative
429 genomic analysis of six *Glossina* genomes, vectors of African trypanosomes. *Genome Biol.*
430 20(1):187
- 431 3. Barrón MG, Fiston-Lavier A-S, Petrov DA, González J. 2014. Population Genomics of Transposable
432 Elements in *Drosophila*. *Annual Review of Genetics*. 48(1):561–81
- 433 4. Bartolome C, Bello X, Maside X. 2009. Widespread evidence for horizontal transfer of
434 transposable elements across *Drosophila* genomes. *Genome Biol.* 10:R22
- 435 5. Bartolomé C, Maside X, Charlesworth B. 2002. On the abundance and distribution of
436 transposable elements in the genome of *Drosophila melanogaster*. *Mol. Biol. Evol.* 19(6):926–37
- 437 6. Bast J, Schaefer I, Schwander T, Maraun M, Scheu S, Kraaijeveld K. 2016. No Accumulation of
438 Transposable Elements in Asexual Arthropods. *Mol. Biol. Evol.* 33(3):697–706
- 439 7. Bergman CM, Quesneville H, Anxolabéhère D, Ashburner M. 2006. Recurrent insertion and
440 duplication generate networks of transposable element sequences in the *Drosophila*
441 *melanogaster* genome. *Genome Biol.* 7(11):R112
- 442 8. Biémont C. 2010. A Brief History of the Status of Transposable Elements: From Junk DNA to
443 Major Players in Evolution: Figure 1.—. *Genetics*. 186(4):1085–93
- 444 9. Biessmann H, Valgeirsdottir K, Lofsky A, Chin C, Ginther B, et al. 1992. HeT-A, a transposable
445 element specifically involved in “healing” broken chromosome ends in *Drosophila melanogaster*.
446 *Mol. Cell. Biol.* 12(9):3910–18
- 447 10. Blumenstiel JP, Chen X, He M, Bergman CM. 2014. An age-of-allele test of neutrality for
448 transposable element insertions. *Genetics*. 196(2):523–38
- 449 11. Bonasio R, Zhang G, Ye C, Mutti NS, Fang X, et al. 2010. Genomic comparison of the ants
450 *Camponotus floridanus* and *Harpegnathos saltator*. *Science*. 329(5995):1068–71

- 451 12. Bourgeois Y, Boissinot S. 2019. On the Population Dynamics of Junk: A Review on the Population
452 Genomics of Transposable Elements. *Genes*. 10(6):419
- 453 13. Bourque G, Burns KH, Gehring M, Gorbunova V, Seluanov A, et al. 2018. Ten things you should
454 know about transposable elements. *Genome Biology*. 19(1):
- 455 14. Bowen NJ, McDonald JF. 2001. Drosophila euchromatic LTR retrotransposons are much younger
456 than the host species in which they reside. *Genome Res*. 11(9):1527–40
- 457 15. Brennecke J, Aravin AA, Stark A, Dus M, Kellis M, et al. 2007. Discrete small RNA-generating loci
458 as master regulators of transposon activity in Drosophila. *Cell*. 128(6):1089–1103
- 459 16. Brown EJ, Nguyen AH, Bachtrog D. 2019. The Y chromosome contributes to sex-specific aging in
460 Drosophila. *bioRxiv*
- 461 17. Bucheton A, Paro R, Sang HM, Pelisson A, Finnegan DJ. 1984. The molecular basis of I-R hybrid
462 Dysgenesis in drosophila melanogaster: Identification, cloning, and properties of the I factor.
463 *Cell*. 38(1):153–63
- 464 18. Chalopin D, Volff J-N, Galiana D, Anderson JL, Schartl M. 2015. Transposable elements and early
465 evolution of sex chromosomes in fish. *Chromosome Research*. 23(3):545–60
- 466 19. Chang C-H, Chavan A, Palladino J, Wei X, Martins NMC, et al. 2019. Islands of retroelements are
467 major components of Drosophila centromeres. *PLOS Biology*. 17(5):e3000241
- 468 20. Chen B, Zhang B, Xu L, Li Q, Jiang F, et al. 2017. Transposable Element-Mediated Balancing
469 Selection at *Hsp90* Underlies Embryo Developmental Variation. *Molecular Biology and Evolution*,
470 p. msx062
- 471 21. Chung H, Bogwitz MR, McCart C, Andrianopoulos A, ffrench-Constant RH, et al. 2007. *Cis* -
472 Regulatory Elements in the *Accord* Retrotransposon Result in Tissue-Specific Expression of the
473 *Drosophila melanogaster* Insecticide Resistance Gene *Cyp6g1*. *Genetics*. 175(3):1071–77
- 474 22. Cordaux R, Batzer MA. 2009. The impact of retrotransposons on human genome evolution. *Nat*
475 *Rev Genet*. 10:691–703
- 476 23. Cosby RL, Chang N-C, Feschotte C. 2019. Host-transposon interactions: conflict, cooperation, and
477 cooption. *Genes Dev*. 33(17–18):1098–1116
- 478 24. Craig, Chandler, Gellert, Lambowitz, Rice, Sandmeyer, eds. 2015. *Mobile DNA III*. American
479 Society of Microbiology
- 480 25. Cridland JM, Macdonald SJ, Long AD, Thornton KR. 2013. Abundance and Distribution of
481 Transposable Elements in Two Drosophila QTL Mapping Resources. *Molecular Biology and*
482 *Evolution*. 30(10):2311–27
- 483 26. Daborn PJ, Yen JL, Bogwitz MR, Le Goff G, Feil E, et al. 2002. A single p450 allele associated with
484 insecticide resistance in Drosophila. *Science*. 297(5590):2253–56

- 485 27. Daniels SB, Peterson KR, Strausbaugh LD, Kidwell MG, Chovnick A. 1990. Evidence for horizontal
486 transmission of the P transposable element between *Drosophila* species. *Genetics*. 124:339–55
- 487 28. De Cecco M, Criscione SW, Peckham EJ, Hillenmeyer S, Hamm EA, et al. 2013. Genomes of
488 replicatively senescent cells undergo global epigenetic changes leading to gene silencing and
489 activation of transposable elements. *Aging Cell*. 12(2):247–56
- 490 29. De Cecco M, Criscione SW, Peterson AL, Neretti N, Sedivy JM, Kreiling JA. 2013. Transposable
491 elements become active and mobile in the genomes of aging mammalian somatic tissues. *Aging*
492 (*Albany NY*). 5(12):867–83
- 493 30. Dennis S, Sheth U, Feldman JL, English KA, Priess JR. 2012. *C. elegans* Germ Cells Show
494 Temperature and Age-Dependent Expression of Cer1, a Gypsy/Ty3-Related Retrotransposon.
495 *PLoS Pathogens*. 8(3):e1002591
- 496 31. Driver CJ, McKechnie SW. 1992. Transposable elements as a factor in the aging of *Drosophila*
497 *melanogaster*. *Ann. N. Y. Acad. Sci.* 673:83–91
- 498 32. *Drosophila* 12 Genomes Consortium, Clark AG, Eisen MB, Smith DR, Bergman CM, et al. 2007.
499 Evolution of genes and genomes on the *Drosophila* phylogeny. *Nature*. 450(7167):203–18
- 500 33. Eickbush T. 2002. Fruit flies and humans respond differently to retrotransposons. *Current*
501 *Opinion in Genetics & Development*. 12(6):669–74
- 502 34. Ellison CE, Bachtrog D. 2013. Dosage Compensation via Transposable Element Mediated
503 Rewiring of a Regulatory Network. *Science*. 342(6160):846–50
- 504 35. Ellison CE, Bachtrog D. 2015. Non-allelic gene conversion enables rapid evolutionary change at
505 multiple regulatory sites encoded by transposable elements. *eLife*. 4:
- 506 36. Elsner D, Meusemann K, Korb J. 2018. Longevity and transposon defense, the case of termite
507 reproductives. *Proceedings of the National Academy of Sciences*. 115(21):5504–9
- 508 37. Fabrick JA, Mathew LG, Tabashnik BE, Li X. 2011. Insertion of an intact CR1 retrotransposon in a
509 cadherin gene linked with Bt resistance in the pink bollworm, *Pectinophora gossypiella*: CR1
510 retrotransposon and Bt resistance. *Insect Molecular Biology*. 20(5):651–65
- 511 38. Fagegaltier D, Bougé A-L, Berry B, Poisot É, Sismeiro O, et al. 2009. The endogenous siRNA
512 pathway is involved in heterochromatin formation in *Drosophila*. *Proceedings of the National*
513 *Academy of Sciences*. 106(50):21258–63
- 514 39. Feschotte C, Pritham EJ. 2007. DNA transposons and the evolution of eukaryotic genomes. *Annu*
515 *Rev Genet*. 41:331–68
- 516 40. Fonseca PM, Moura RD, Wallau GL, Loreto ELS. 2019. The mobilome of *Drosophila incompta*, a
517 flower-breeding species: comparison of transposable element landscapes among generalist and
518 specialist flies. *Chromosome Res*. 27(3):203–19

- 519 41. Fraser MJ, Smith GE, Summers MD. 1983. Acquisition of Host Cell DNA Sequences by
520 Baculoviruses: Relationship Between Host DNA Insertions and FP Mutants of *Autographa*
521 *californica* and *Galleria mellonella* Nuclear Polyhedrosis Viruses. *Journal of Virology*. 47:287–300
- 522 42. Gadau J, Helmkampf M, Nygaard S, Roux J, Simola DF, et al. 2012. The genomic impact of 100
523 million years of social evolution in seven ant species. *Trends Genet*. 28(1):14–21
- 524 43. Gahan LJ, Gould F, Heckel DG. 2001. Identification of a gene associated with Bt resistance in
525 *Heliothis virescens*. *Science*. 293(5531):857–60
- 526 44. Gavotte L, Mercer DR, Stoeckle JJ, Dobson SL. 2010. Costs and benefits of *Wolbachia* infection in
527 immature *Aedes albopictus* depend upon sex and competition level. *Journal of Invertebrate*
528 *Pathology*. 105(3):341–46
- 529 45. Gilbert C, Feschotte C. 2018. Horizontal acquisition of transposable elements and viral
530 sequences: patterns and consequences. *Current Opinion in Genetics & Development*. 49:15–24
- 531 46. Gilbert C, Peccoud J, Chateigner A, Moumen B, Cordaux R, Herniou EA. 2016. Continuous Influx
532 of Genetic Material from Host to Virus Populations. *PLoS Genetics*. 12:e1005838
- 533 47. Gilbert C, Schaack S, Pace JK, Brindley PJ, Feschotte C. 2010. A role for host-parasite interactions
534 in the horizontal transfer of transposons across phyla. *Nature*. 464:1347–50
- 535 48. Goic B, Stapleford KA, Frangeul L, Doucet AJ, Gausson V, et al. 2016. Virus-derived DNA drives
536 mosquito vector tolerance to arboviral infection. *Nat Commun*. 7:12410
- 537 49. Goic B, Vodovar N, Mondotte JA, Monot C, Frangeul L, et al. 2013. RNA-mediated interference
538 and reverse transcription control the persistence of RNA viruses in the insect model *Drosophila*.
539 *Nature Immunology*. 14:396–403
- 540 50. González J, Karasov TL, Messer PW, Petrov DA. 2010. Genome-Wide Patterns of Adaptation to
541 Temperate Environments Associated with Transposable Elements in *Drosophila*. *PLoS Genetics*.
542 6(4):e1000905
- 543 51. González J, Lenkov K, Lipatov M, Macpherson JM, Petrov DA. 2008. High Rate of Recent
544 Transposable Element–Induced Adaptation in *Drosophila melanogaster*. *PLoS Biology*. 6(10):e251
- 545 52. Gonzalez J, Macpherson JM, Petrov DA. 2009. A Recent Adaptive Transposable Element Insertion
546 Near Highly Conserved Developmental Loci in *Drosophila melanogaster*. *Molecular Biology and*
547 *Evolution*. 26(9):1949–61
- 548 53. Goubert C, Henri H, Minard G, Valiente Moro C, Mavingui P, et al. 2017. High-throughput
549 sequencing of transposable element insertions suggests adaptive evolution of the invasive Asian
550 tiger mosquito towards temperate environments. *Molecular Ecology*. 26(15):3968–81
- 551 54. Guio L, Barrón MG, González J. 2014. The transposable element *Bari-Jheh* mediates oxidative
552 stress response in *Drosophila*. *Molecular Ecology*. 23(8):2020–30

- 553 55. Han M-J, Zhou Q-Z, Zhang H-H, Tong X, Lu C, et al. 2016. iMITEdb: the genome-wide landscape of
554 miniature inverted-repeat transposable elements in insects. *Database*. 2016:baw148
- 555 56. Handler AM, McCombs SD, Fraser MJ, Saul SH. 1998. The lepidopteran transposon vector,
556 piggyBac, mediates germ-line transformation in the Mediterranean fruit fly. *Proceedings of the*
557 *National Academy of Sciences*. 95(13):7520–25
- 558 57. Hanlon S, Hawley R. 2018. B Chromosomes in the *Drosophila* Genus. *Genes*. 9(10):470
- 559 58. Harrison MC, Jongepier E, Robertson HM, Arning N, Bitard-Feildel T, et al. 2018. Hemimetabolous
560 genomes reveal molecular basis of termite eusociality. *Nat Ecol Evol*. 2(3):557–66
- 561 59. Himber C, Dunoyer P, Moissiard G, Ritzenthaler C, Voinnet O. 2003. Transitivity-dependent and -
562 independent cell-to-cell movement of RNA silencing. *EMBO J*. 22(17):4523–33
- 563 60. Hof AE van't, Campagne P, Rigden DJ, Yung CJ, Lingley J, et al. 2016. The industrial melanism
564 mutation in British peppered moths is a transposable element. *Nature*. 534(7605):102–5
- 565 61. Holt RA, Subramanian GM, Halpern A, Sutton GG, Charlab R, et al. 2002. The genome sequence
566 of the malaria mosquito *Anopheles gambiae*. *Science*. 298(5591):129–49
- 567 62. Honeybee Genome Sequencing Consortium. 2006. Insights into social insects from the genome
568 of the honeybee *Apis mellifera*. *Nature*. 443(7114):931–49
- 569 63. Hua-Van A, Le Rouzic A, Boutin TS, Filee J, Capy P. 2011. The struggle for life of the genome's
570 selfish architects. *Biol Direct*. 6:19
- 571 64. International Aphid Genomics Consortium. 2010. Genome sequence of the pea aphid
572 *Acyrtosiphon pisum*. *PLoS Biol*. 8(2):e1000313
- 573 65. Joshi D, McFadden MJ, Bevins D, Zhang F, Xi Z. 2014. *Wolbachia* strain wAlbB confers both fitness
574 costs and benefit on *Anopheles stephensi*. *Parasites & Vectors*. 7(1):336
- 575 66. Kaminker JS, Bergman CM, Kronmiller B, Carlson J, Svirskas R, et al. 2002. The transposable
576 elements of the *Drosophila melanogaster* euchromatin: a genomics perspective. *Genome Biol*.
577 3(12):research0084.1
- 578 67. Kanost MR, Arrese EL, Cao X, Chen YR, Chellapilla S, et al. 2016. Multifaceted biological insights
579 from a draft genome sequence of the tobacco hornworm moth, *Manduca sexta*. *Insect Biochem*
580 *Mol Biol*. 76:118–47
- 581 68. Kapheim KM, Pan H, Li C, Salzberg SL, Puiu D, et al. 2015. Social evolution. Genomic signatures of
582 evolutionary transitions from solitary to group living. *Science*. 348(6239):1139–43
- 583 69. Kapitonov VV, Jurka J. 2003. Molecular paleontology of transposable elements in the *Drosophila*
584 *melanogaster* genome. *Proc. Natl. Acad. Sci. U.S.A.* 100(11):6569–74
- 585 70. Kelleher ES. 2016. Reexamining the *P*-Element Invasion of *Drosophila melanogaster* Through the
586 Lens of piRNA Silencing. *Genetics*. 203(4):1513–31

- 587 71. Kelley JL, Peyton JT, Fiston-Lavier A-S, Teets NM, Yee M-C, et al. 2014. Compact genome of the
588 Antarctic midge is likely an adaptation to an extreme environment. *Nat Commun.* 5:4611
- 589 72. Kidwell MG, Kidwell JF. 1975. Cytoplasm–chromosome interactions in *Drosophila melanogaster*.
590 *Nature.* 253(5494):755–56
- 591 73. Kofler R. 2019. Dynamics of Transposable Element Invasions with piRNA Clusters. *Molecular*
592 *Biology and Evolution.* 36(7):1457–72
- 593 74. Kofler R, Betancourt AJ, Schlötterer C. 2012. Sequencing of Pooled DNA Samples (Pool-Seq)
594 Uncovers Complex Dynamics of Transposable Element Insertions in *Drosophila melanogaster*.
595 *PLoS Genetics.* 8(1):e1002487
- 596 75. Kofler R, Nolte V, Schlötterer C. 2015. Tempo and Mode of Transposable Element Activity in
597 *Drosophila*. *PLOS Genetics.* 11(7):e1005406
- 598 76. Korb J, Poulsen M, Hu H, Li C, Boomsma JJ, et al. 2015. A genomic comparison of two termites
599 with different social complexity. *Frontiers in Genetics.* 6:
- 600 77. Kraaijeveld K, Zwanenburg B, Hubert B, Vieira C, De Pater S, et al. 2012. Transposon proliferation
601 in an asexual parasitoid. *Mol. Ecol.* 21(16):3898–3906
- 602 78. Kuraku S, Qiu H, Meyer A. 2012. Horizontal transfers of Tc1 elements between teleost fishes and
603 their vertebrate parasites, lampreys. *Genome Biol Evol.* 4:929–36
- 604 79. Le Rouzic A, Dupas S, Capy P. 2007. Genome ecosystem and transposable elements species.
605 *Gene.* 390(1–2):214–20
- 606 80. Lerat E, Goubert C, Guirao-Rico S, Merenciano M, Dufour A, et al. 2019. Population-specific
607 dynamics and selection patterns of transposable element insertions in European natural
608 populations. *Molecular Ecology.* 28(6):1506–22
- 609 81. Lerman DN, Feder ME. 2005. Naturally occurring transposable elements disrupt hsp70 promoter
610 function in *Drosophila melanogaster*. *Mol. Biol. Evol.* 22(3):776–83
- 611 82. Lewis SH, Quarles KA, Yang Y, Tanguy M, Frézal L, et al. 2018. Pan-arthropod analysis reveals
612 somatic piRNAs as an ancestral defence against transposable elements. *Nature Ecology &*
613 *Evolution.* 2(1):174–81
- 614 83. Linheiro RS, Bergman CM. 2012. Whole Genome Resequencing Reveals Natural Target Site
615 Preferences of Transposable Elements in *Drosophila melanogaster*. *PLoS ONE.* 7(2):e30008
- 616 84. Lower SS, Johnston JS, Stanger-Hall KF, Hjelman CE, Hanrahan SJ, et al. 2017. Genome Size in
617 North American Fireflies: Substantial Variation Likely Driven by Neutral Processes. *Genome*
618 *Biology and Evolution.* 9(6):1499–1512
- 619 85. Lucas ER, Keller L. 2018. New explanation for the longevity of social insect reproductives:
620 Transposable element activity. *Proc. Natl. Acad. Sci. U.S.A.* 115(21):5317–18

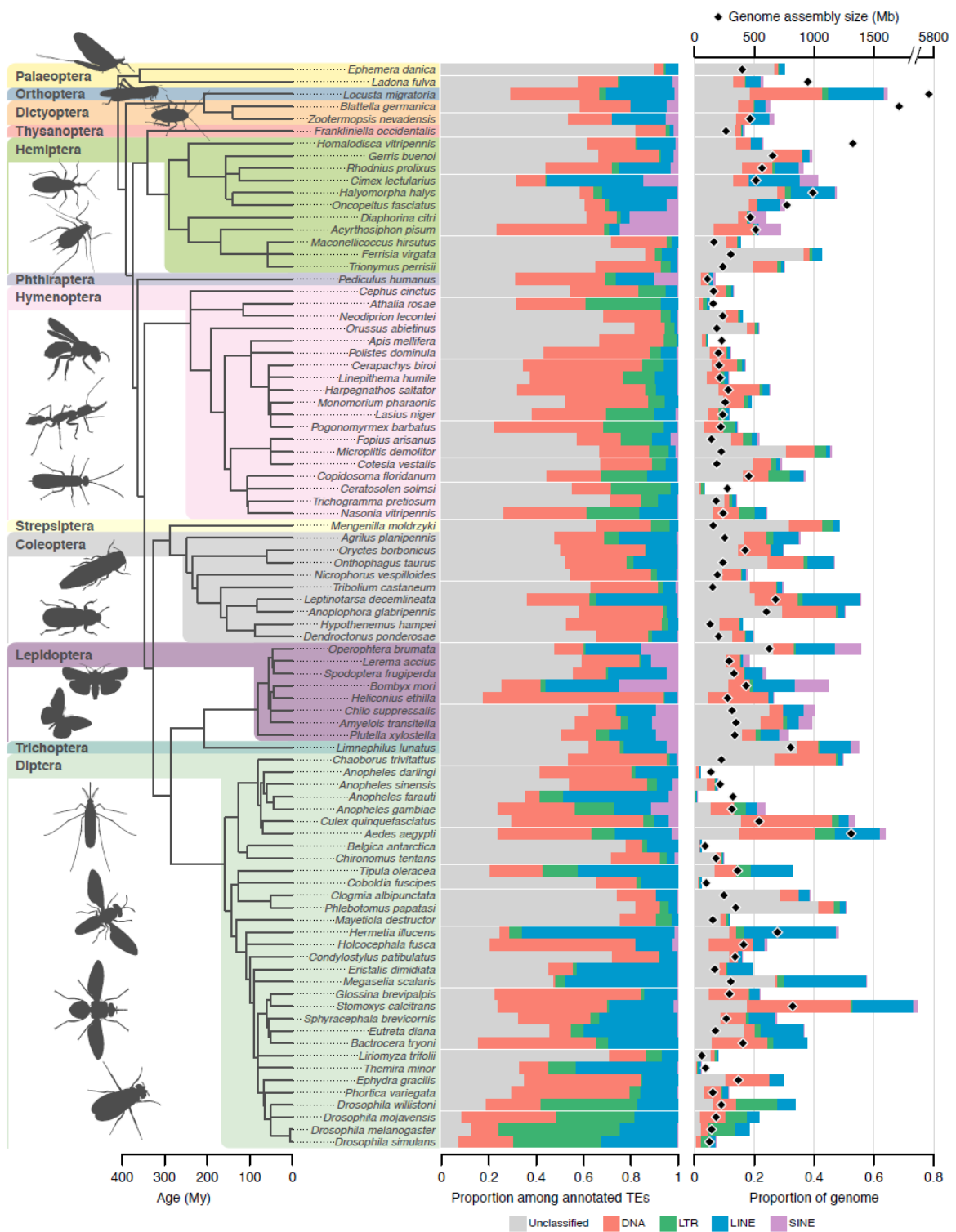
- 621 86. Magwire MM, Bayer F, Webster CL, Cao C, Jiggins FM. 2011. Successive Increases in the
622 Resistance of *Drosophila* to Viral Infection through a Transposon Insertion Followed by a
623 Duplication. *PLoS Genetics*. 7(10):e1002337
- 624 87. Majumdar S, Rio DC. 2015. P Transposable Elements in *Drosophila* and other Eukaryotic
625 Organisms. *Microbiol Spectr*. 3(2):MDNA3-0004–2014
- 626 88. Marais GAB, Gaillard J-M, Vieira C, Plotton I, Sanlaville D, et al. 2018. Sex gap in aging and
627 longevity: can sex chromosomes play a role? *Biol Sex Differ*. 9(1):33
- 628 89. Mateo L, Ullastres A, González J. 2014. A Transposable Element Insertion Confers Xenobiotic
629 Resistance in *Drosophila*. *PLoS Genetics*. 10(8):e1004560
- 630 90. Maumus F, Fiston-Lavier AS, Quesneville H. 2015. Impact of transposable elements on insect
631 genomes and biology. *Current Opinion in Insect Science*. 7:30–36
- 632 91. Maxwell PH, Burhans WC, Curcio MJ. 2011. Retrotransposition is associated with genome
633 instability during chronological aging. *Proceedings of the National Academy of Sciences*.
634 108(51):20376–81
- 635 92. McClintock B. 1950. The origin and behavior of mutable loci in maize. *Proceedings of the
636 National Academy of Sciences*. 36(6):344–55
- 637 93. Merenciano M, Ullastres A, de Cara MAR, Barrón MG, González J. 2016. Multiple Independent
638 Retroelement Insertions in the Promoter of a Stress Response Gene Have Variable Molecular and
639 Functional Effects in *Drosophila*. *PLOS Genetics*. 12(8):e1006249
- 640 94. Miesen P, Joosten J, van Rij RP. 2016. PIWIs Go Viral: Arbovirus-Derived piRNAs in Vector
641 Mosquitoes. *PLOS Pathogens*. 12(12):e1006017
- 642 95. Miller WJ, McDonald JF, Nouaud D, Anxolabéhère D. 1999. Molecular domestication--more than
643 a sporadic episode in evolution. *Genetica*. 107(1–3):197–207
- 644 96. Neafsey DE, Waterhouse RM, Abai MR, Aganezov SS, Alekseyev MA, et al. 2015. Mosquito
645 genomics. Highly evolvable malaria vectors: the genomes of 16 *Anopheles* mosquitoes. *Science*.
646 347(6217):1258522
- 647 97. Nene V, Wortman JR, Lawson D, Haas B, Kodira C, et al. 2007. Genome sequence of *Aedes
648 aegypti*, a major arbovirus vector. *Science*. 316(5832):1718–23
- 649 98. Oliver KR, Greene WK. 2012. Transposable elements and viruses as factors in adaptation and
650 evolution: an expansion and strengthening of the TE-Thrust hypothesis. *Ecology and Evolution*.
651 2(11):2912–33
- 652 99. Ortiz MF, Wallau GL, Graichen DA, Loreto EL. 2015. An evaluation of the ecological relationship
653 between *Drosophila* species and their parasitoid wasps as an opportunity for horizontal
654 transposon transfer. *Molecular Genetics and Genomics*. 290:67–78

- 655 100. Osanai-Futahashi M, Suetsugu Y, Mita K, Fujiwara H. 2008. Genome-wide screening and
656 characterization of transposable elements and their distribution analysis in the silkworm,
657 *Bombyx mori*. *Insect Biochem. Mol. Biol.* 38(12):1046–57
- 658 101. Pardue M-L, DeBaryshe PG. 2011. Retrotransposons that maintain chromosome ends. *Proc.*
659 *Natl. Acad. Sci. U.S.A.* 108(51):20317–24
- 660 102. Paricio N, Pèrez-Alonso M, Martínez-Sebastián maria J, de Frutos R. 1991. P sequences of
661 *Drosophilla Subobscura* lack exon 3 and may encode a 66 kd repressor-like protein. *Nucleic Acids*
662 *Research.* 19(24):6713–18
- 663 103. Peccoud J, Loiseau V, Cordaux R, Gilbert C. 2017. Massive horizontal transfer of transposable
664 elements in insects. *Proc. Natl. Acad. Sci. U.S.A.* 114(18):4721–26
- 665 104. Peng JC, Karpen GH. 2007. H3K9 methylation and RNA interference regulate nucleolar
666 organization and repeated DNA stability. *Nat. Cell Biol.* 9(1):25–35
- 667 105. Petersen M, Armisén D, Gibbs RA, Hering L, Khila A, et al. 2019. Diversity and evolution of the
668 transposable element repertoire in arthropods with particular reference to insects. *BMC Evol.*
669 *Biol.* 19(1):11
- 670 106. Petrov DA, Fiston-Lavier A-S, Lipatov M, Lenkov K, Gonzalez J. 2011. Population Genomics of
671 Transposable Elements in *Drosophila melanogaster*. *Molecular Biology and Evolution.*
672 28(5):1633–44
- 673 107. Poirier EZ, Goic B, Tomé-Poderti L, Frangeul L, Boussier J, et al. 2018. Dicer-2-Dependent
674 Generation of Viral DNA from Defective Genomes of RNA Viruses Modulates Antiviral Immunity
675 in Insects. *Cell Host & Microbe.* 23(3):353-365.e8
- 676 108. Quesneville H, Nouaud D, Anxolabehere D. 2005. Recurrent Recruitment of the THAP DNA-
677 Binding Domain and Molecular Domestication of the P-Transposable Element. *Molecular Biology*
678 *and Evolution.* 22(3):741–46
- 679 109. Rahman R, Chirn G, Kanodia A, Sytnikova YA, Brembs B, et al. 2015. Unique transposon
680 landscapes are pervasive across *Drosophila melanogaster* genomes. *Nucleic Acids Research.*
681 43(22):10655–72
- 682 110. Ray DA, Grimshaw JR, Halsey MK, Korstian JM, Osmanski AB, et al. 2019. Simultaneous TE
683 Analysis of 19 Heliconiine Butterflies Yields Novel Insights into Rapid TE-Based Genome
684 Diversification and Multiple SINE Births and Deaths. *Genome Biol Evol.* 11(8):2162–77
- 685 111. Rech GE, Bogaerts-Márquez M, Barrón MG, Merenciano M, Villanueva-Cañas JL, et al. 2019.
686 Stress response, behavior, and development are shaped by transposable element-induced
687 mutations in *Drosophila*. *PLOS Genetics.* 15(2):e1007900

- 688 112. Reiss D, Mialdea G, Miele V, de Vienne DM, Peccoud J, et al. 2019. Global survey of mobile
689 DNA horizontal transfer in arthropods reveals Lepidoptera as a prime hotspot. *PLoS Genetics*.
690 15(2):e1007965
- 691 113. Remnant EJ, Good RT, Schmidt JM, Lumb C, Robin C, et al. 2013. Gene duplication in the
692 major insecticide target site, *Rdl*, in *Drosophila melanogaster*. *Proceedings of the National*
693 *Academy of Sciences*. 110(36):14705–10
- 694 114. Rius N, Guillen Y, Delprat A, Kapusta A, Feschotte C, Ruiz A. 2016. Exploration of the
695 *Drosophila buzzatii* transposable element content suggests underestimation of repeats in
696 *Drosophila* genomes. *BMC Genomics*. 17:344
- 697 115. Robillard É, Le Rouzic A, Zhang Z, Capy P, Hua-Van A. 2016. Experimental evolution reveals
698 hyperparasitic interactions among transposable elements. *Proceedings of the National Academy*
699 *of Sciences*. 113(51):14763–68
- 700 116. Rostant WG, Wedell N, Hosken DJ. 2012. Transposable Elements and Insecticide Resistance.
701 In *Advances in Genetics*. 78:169–201. Elsevier
- 702 117. Sadd BM, Barribeau SM, Bloch G, de Graaf DC, Dearden P, et al. 2015. The genomes of two
703 key bumblebee species with primitive eusocial organization. *Genome Biol*. 16:76
- 704 118. Saint-Leandre B, Nguyen SC, Levine MT. 2019. Diversification and collapse of a telomere
705 elongation mechanism. *Genome Res*. 29(6):920–31
- 706 119. Schaack S, Pritham EJ, Wolf A, Lynch M. 2010. DNA transposon dynamics in populations of
707 *Daphnia pulex* with and without sex. *Proc. Biol. Sci*. 277(1692):2381–87
- 708 120. Schmidt JM, Good RT, Appleton B, Sherrard J, Raymant GC, et al. 2010. Copy Number
709 Variation and Transposable Elements Feature in Recent, Ongoing Adaptation at the *Cyp6g1*
710 Locus. *PLoS Genetics*. 6(6):e1000998
- 711 121. Schrader L, Kim JW, Ence D, Zimin A, Klein A, et al. 2014. Transposable element islands
712 facilitate adaptation to novel environments in an invasive species. *Nature Communications*. 5(1):
- 713 122. Sessegolo C, Burlet N, Haudry A. 2016. Strong phylogenetic inertia on genome size and
714 transposable element content among 26 species of flies. *Biology Letters*. 12(8):20160407
- 715 123. Siguier P, Gourbeyre E, Chandler M. 2014. Bacterial insertion sequences: their genomic
716 impact and diversity. *FEMS Microbiology Reviews*. 38(5):865–91
- 717 124. Sijen T, Fleenor J, Simmer F, Thijssen KL, Parrish S, et al. 2001. On the Role of RNA
718 Amplification in dsRNA-Triggered Gene Silencing. *Cell*. 107(4):465–76
- 719 125. Spradling A, Rubin G. 1982. Transposition of cloned P elements into *Drosophila* germ line
720 chromosomes. *Science*. 218(4570):341–47
- 721 126. Stapley J, Santure AW, Dennis SR. 2015. Transposable elements as agents of rapid adaptation
722 may explain the genetic paradox of invasive species. *Molecular Ecology*. 24(9):2241–52

- 723 127. Suen G, Teiling C, Li L, Holt C, Abouheif E, et al. 2011. The genome sequence of the leaf-cutter
724 ant *Atta cephalotes* reveals insights into its obligate symbiotic lifestyle. *PLoS Genet.*
725 7(2):e1002007
- 726 128. Suh A, Witt CC, Menger J, Sadanandan KR, Podsiadlowski L, et al. 2016. Ancient horizontal
727 transfers of retrotransposons between birds and ancestors of human pathogenic nematodes.
728 *Nat Commun.* 7:11396
- 729 129. Szitenberg A, Cha S, Opperman CH, Bird DM, Blaxter ML, Lunt DH. 2016. Genetic Drift, Not
730 Life History or RNAi, Determine Long-Term Evolution of Transposable Elements. *Genome Biol*
731 *Evol.* 8(9):2964–78
- 732 130. Talla V, Suh A, Kalsoom F, Dincă V, Vila R, et al. 2017. Rapid Increase in Genome Size as a
733 Consequence of Transposable Element Hyperactivity in Wood-White (Leptidea) Butterflies.
734 *Genome Biology and Evolution.* 9(10):2491–2505
- 735 131. Tassetto M, Kunitomi M, Andino R. 2017. Circulating Immune Cells Mediate a Systemic RNAi-
736 Based Adaptive Antiviral Response in *Drosophila*. *Cell.* 169(2):314-325.e13
- 737 132. Tassetto M, Kunitomi M, Whitfield ZJ, Dolan PT, Sánchez-Vargas I, et al. 2019. Control of RNA
738 viruses in mosquito cells through the acquisition of vDNA and endogenous viral elements. *eLife.*
739 8:
- 740 133. Ullastres A, Petit N, González J. 2015. Exploring the Phenotypic Space and the Evolutionary
741 History of a Natural Mutation in *Drosophila melanogaster*. *Molecular Biology and Evolution.*
742 32(7):1800–1814
- 743 134. van Rij RP, Saleh M-C, Berry B, Foo C, Houk A, et al. 2006. The RNA silencing endonuclease
744 Argonaute 2 mediates specific antiviral immunity in *Drosophila melanogaster*. *Genes &*
745 *Development.* 20(21):2985–95
- 746 135. Venner S, Miele V, Terzian C, Biémont C, Daubin V, et al. 2017. Ecological networks to unravel
747 the routes to horizontal transposon transfers. *PLOS Biology.* 15(2):e2001536
- 748 136. Vogt A, Goldman AD, Mochizuki K, Landweber LF. 2013. Transposon domestication versus
749 mutualism in ciliate genome rearrangements. *PLoS Genet.* 9(8):e1003659
- 750 137. Walsh AM, Kortschak RD, Gardner MG, Bertozzi T, Adelson DL. 2013. Widespread horizontal
751 transfer of retrotransposons. *Proc. Natl. Acad. Sci. U.S.A.* 110(3):1012–16
- 752 138. Wang L, Wang J, Ma Y, Wan P, Liu K, et al. 2019. Transposon insertion causes cadherin mis-
753 splicing and confers resistance to Bt cotton in pink bollworm from China. *Scientific Reports.* 9(1):
- 754 139. Wang S, Lorenzen MD, Beeman RW, Brown SJ. 2008. Analysis of repetitive DNA distribution
755 patterns in the *Tribolium castaneum* genome. *Genome Biol.* 9(3):R61
- 756 140. Wang X, Fang X, Yang P, Jiang X, Jiang F, et al. 2014. The locust genome provides insight into
757 swarm formation and long-distance flight. *Nat Commun.* 5:2957

- 758 141. Wang X, Liu X. 2016. Close ecological relationship among species facilitated horizontal
759 transfer of retrotransposons. *BMC Evol Biol.* 16:201
- 760 142. White JA, Kelly SE, Cockburn SN, Perlman SJ, Hunter MS. 2011. Endosymbiont costs and
761 benefits in a parasitoid infected with both *Wolbachia* and *Cardinium*. *Heredity.* 106(4):585–91
- 762 143. Whitfield ZJ, Dolan PT, Kunitomi M, Tassetto M, Seetin MG, et al. 2017. The Diversity,
763 Structure, and Function of Heritable Adaptive Immunity Sequences in the *Aedes aegypti*
764 Genome. *Current Biology.* 27(22):3511-3519.e7
- 765 144. Wicker T, Sabot F, Hua-Van A, Bennetzen JL, Capy P, et al. 2007. A unified classification
766 system for eukaryotic transposable elements. *Nat. Rev. Genet.* 8(12):973–82
- 767 145. Wood JG, Helfand SL. 2013. Chromatin structure and transposable elements in organismal
768 aging. *Front Genet.* 4:274
- 769 146. Wood JG, Jones BC, Jiang N, Chang C, Hosier S, et al. 2016. Chromatin-modifying genetic
770 interventions suppress age-associated transposable element activation and extend life span in
771 *Drosophila*. *Proc. Natl. Acad. Sci. U.S.A.* 113(40):11277–82
- 772 147. Woronik A, Tunström K, Perry MW, Neethiraj R, Stefanescu C, et al. 2019. A transposable
773 element insertion is associated with an alternative life history strategy. *Nature Communications.*
774 10(1):
- 775 148. Wu C, Lu J. 2019. Diversification of Transposable Elements in Arthropods and Its Impact on
776 Genome Evolution. *Genes (Basel).* 10(5):
- 777 149. Xiao J-H, Yue Z, Jia L-Y, Yang X-H, Niu L-H, et al. 2013. Obligate mutualism within a host drives
778 the extreme specialization of a fig wasp genome. *Genome Biol.* 14(12):R141
- 779 150. Zanni V, Eymery A, Coiffet M, Zytnicki M, Luyten I, et al. 2013. Distribution, evolution, and
780 diversity of retrotransposons at the flamenco locus reflect the regulatory properties of piRNA
781 clusters. *Proc. Natl. Acad. Sci. U.S.A.* 110(49):19842–47
- 782



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