Functional & Integrative Genomics (2023) 23:180
https://doi.org/10.1007/s10142-023-01072-6

REVIEW

Mosquito gene targeted RNAi studies for vector control

Mahima Yadav[1] · Nisha Dahiya[1] · Neelam Sehrawat[1]

Received: 16 February 2023 / Revised: 24 April 2023 / Accepted: 25 April 2023 / Published online: 25 May 2023

Abstract

Vector-borne diseases are serious public health concern. Mosquito is one of the major vectors responsible for the transmission of a number of diseases like malaria, Zika, chikungunya, dengue, West Nile fever, Japanese encephalitis, St. Louis encephalitis, and yellow fever. Various strategies have been used for mosquito control, but the breeding potential of mosquitoes is such tremendous that most of the strategies failed to control the mosquito population. In 2020, outbreaks of dengue, yellow fever, and Japanese encephalitis have occurred worldwide. Continuous insecticide use resulted in strong resistance and disturbed the ecosystem. RNA interference is one of the strategies opted for mosquito control. There are a number of mosquito genes whose inhibition affected mosquito survival and reproduction. Such kind of genes could be used as bioinsecticides for vector control without disturbing the natural ecosystem. Several studies have targeted mosquito genes at different developmental stages by the RNAi mechanism and result in vector control. In the present review, we included RNAi studies conducted for vector control by targeting mosquito genes at different developmental stages using different delivery methods. The review could help the researcher to find out novel genes of mosquitoes for vector control.

Keywords RNA interference · Vector control · Anopheles · Aedes · Culex · Delivery methods

Intoduction

Infectious diseases spread by vectors account for 17% of all communicable diseases and cause 7,00,000 deaths per year worldwide (World Health Organization 2020a). Globally, cases of mosquito-borne disease have been increasing, and after the COVID-19 pandemic, mosquito-borne diseases have been resurging from the disease-eradicated region (Franklinos et al. 2019; Ong et al. 2022). In 2021, 247 million cases of malaria were reported globally (WHO report 2022k), and recent outbreak of dengue, yellow fever, chikungunya, and Zika poses a serious threat in many areas (Rana et al. 2021; Bagcchi 2023; Islam et al. 2022; Cortes-Escamilla et al. 2022; Tuells et al. 2022; Vairo et al. 2019; Pielnaa et al. 2020). It is expected that by 2050, about half of the population of the world would be at risk of arbovirus transmission (Kraemer et al. 2019). Vector-borne disease can arise from parasites, viruses, or bacteria, and mosquito acts as a host for a number of disease-causing pathogens like *West Nile virus*, *Zika virus*, *DENV* virus, *Flavivirus*, *CHIKV*, *Plasmodium*, and *Wuchereria bancrofti* that pose a serious threat to human health. Mosquitoes belonging to genera *Aedes*, *Anopheles*, and *Culex* play an important role in the transmission of vector-borne disease. *Aedes* and *Anopheles* are the primary vectors for the viral pathogen and parasites. *Culex* is the vector for both the parasite and viruses (Sultana et al. 2020). The mosquito-borne diseases, host, causing pathogen, symptoms, outbreaks, and vaccine have been mentioned in the supplementary file. Although the mosquito population has been reduced to some extent by the use of insecticide-treated nets, indoor residual spraying, mosquito repellant, sterilant, insecticide, targeting of mosquito breeding habitat, and sound traps, these methods did not appear to be very successful (Benelli et al. 2016). Due to the lack of effective drugs and vaccines against most vector-borne diseases, the emergence of resistance in mosquitoes against insecticides like DDT, pyrethroids, carbamates, organophosphates, and organochlorines and the destruction of the ecosystem via reiteration use of insecticides made humans compelled to use another alternative approach for vector control (Sultana et al. 2020; Airs & Bartholomay 2017).

✉ Neelam Sehrawat
neelamsehrawat@mdurohtak.ac.in

Mahima Yadav
mahimayadav8682@gmail.com

Nisha Dahiya
dahiyanisha994@gmail.com

[1] Department of Genetics, Maharshi Dayanand University, Rohtak, Haryana, India

There is a requirement to use another environment-friendly approach for controlling the mosquito population as it is the most effective way to combat life-threatening vector-borne diseases (Mysore et al. 2021).

RNA interference is an innovative in vivo approach in which the effect of mRNA transcript is reduced through posttranscriptional modification on the basis of sequence complementarity with double-stranded RNA (Airs & Bartholomay 2017; Balakrishna Pillai et al. 2017). The pathway required two core proteins, Dicer protein (endonuclease) which recognizes dsRNA and generates small RNAs and Argonaut protein that takes generated RNAs and screens complementary target mRNA. Target mRNA is degraded or its translation is inhibited during the process known as posttranslational gene silencing (Azimzadeh Jamalkandi et al. 2014). Fire et al. (1998) discovered this phenomenon in the nematode *Caenorhabditis elegans* via the introduction of dsRNA into the body cavity to manipulate gene expression resulting in sequence-specific gene silencing (Reis 2017). In the field of mosquito genomics, RNAi is one of the best methods being used to suppress the effect of mosquito endogenous genes and genes encoding for pathogens in vivo. RNAi provided new insight into fundamental research to disrupt the physiology of the mosquito life cycle by suppressing the gene associated with fecundity, behavior pattern, survival, and vector status so that burden of mosquito-borne disease on the human population could be reduced. As this technology is more popular in agriculture in terms of managing insect pests, it is interesting to consider the implementation of RNAi in mosquito control as a bioinsecticide (Airs & Bartholomay 2017). CRISPR/Cas is the more advance tool that could be used to explore genome editing (Li et al. 2022). A number of mosquito genes have been targeted for vector control by RNAi mechanism. Two reviews have briefly explained the application of RNAi for controlling the mosquito population. Balakrishna Pillai et al. (2017) elucidated the implementation of RNAi for understanding vector-pathogen interaction by using various delivery methods targeted at different developmental stages, insecticide resistance genes of vector, and Munawar et al. (2020) explained different methods used for targeting larva genes to overcome the mosquito burden. In the present review, we have focused on the genes targeted at different developmental stages whose inhibition by RNAi is associated with direct mortality of individuals, physical or physiological abnormalities, vectoral capacity, and pesticide susceptibility. We tried to avoid the gene targeted to understand mosquito biology by RNAi in terms of their specific function as explained in Balakrishna Pillai et al. (2017) review. Our main goal is to find out novel mosquito candidate genes that can be used as bioinsecticides in the near future without depleting natural resources in order to overcome the burden of pesticide resistance in mosquitoes over a period of time. We also did not include the mosquito gene on which the RNAi study had been taken, but their inhibition effect did not affect mosquito survival.

Methods

Articles for this review were searched through the database PubMed, Scopus, and ScienceDirect and from the reference list of relevant articles. The WHO site was used for collecting information regarding mosquito-borne disease, disease-causing pathogens, symptoms, outbreaks, and vaccine availability (https://www.who.int/). Research Gate was also used for some articles which were not in full text on PubMed. Search term "RNAi based strategy for mosquito control" was used while using the PubMed, Scopus, and ScienceDirect databases. Title and abstract of the research and review articles were screened individually. Research articles and reviews relevant to the topic were included in the study. Last literature search was performed on 30 January 2023.

Results

Figure 1 illustrates the results of the search. A total of 1526 articles were identified with the search term "RNAi based strategy for mosquito control" using PubMed, Scopus, and ScienceDirect databases. A total of 55 articles have been included in the study after reading the full text. The RNAi studies targeted mosquito gene candidate results in the mortality, abnormality, susceptibility towards insecticide, and affect fecundity of mosquitoes have been discussed in the present review. Mosquito gene-based RNAi studies that did not provide the significant result or low mortality results have been excluded.

Egg stage targeted genes

There are a few RNAi studies have been done on the eggs of mosquitoes for vector control. Meleshkevitch et al. (2013) performed a silencing experiment in *Ae. aegypti* by using Na^+ methionine transporter 5 (NAT5) via the soaking method. NAT5 is involved in the transport of L-Meth under the influence of Na^+, but the silencing effect was neutralized after the late larva stage and significant mortality of larvae was observed during ecdysis; the emergence of adults from pupae was also suppressed as well.

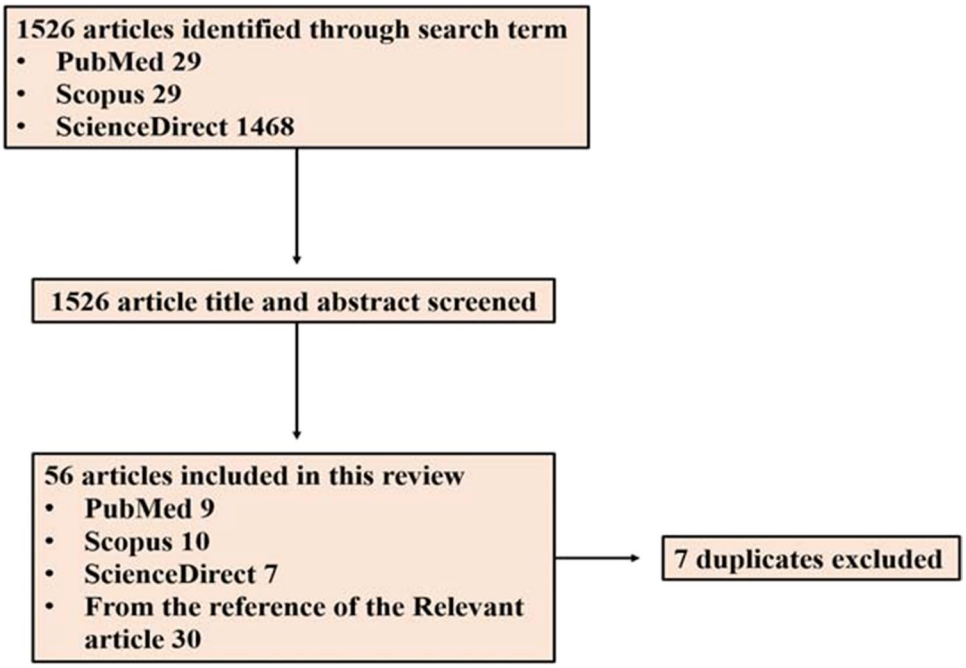

Fig. 1 A flow diagram of literature search

Larva targeted genes

The larval stage is one of the most important developmental stages of mosquitoes, at which genes targeted by the RNAi mechanism provided fruitful results in the larvae control strategy. Different methods have been used for the transfer of ds RNA of the gene of interest in mosquito larvae via microorganisms like bacteria (*E. coli*), fungi (*Saccharomyces* spp.), and algae (*Chlamydomonas*, *Chlorella*) and by various technical approaches like soaking, microinjection, and nanoparticles (Taracena et al. 2019; Mysore et al. 2017; Hapairai et al. 2020; Van Ekert et al. 2014; Khalil et al. 2021). The inhibition of gene expression is usually done by real-time PCR. With the deep analysis of the implementation of all methods on mosquito mortality, the yeast delivery system was found to be the most efficient in carrying the highest mortality of larvae (Mysore et al. 2021, Mysore et al. 2019a, b; Mysore et al. 2017). It might be due to the complete knockout of ds RNA, which is the biggest challenge of RNAi to tackle. Studies conducted on the inhibition effect of larvae-targeted genes on mortality by RNAi mechanism are mentioned in Table 1, and Fig. 2 shows the list of larva gene targets according to the category mentioned in the text.

The highest mortality targeted genes

Ataxin 2-binding protein (Mysore et al. 2021), *dopamine 1* (Hapairai et al. 2020), *leukocyte receptor complex 0.51* (Mysore et al. 2017), *synaptotagmin*, *semaphorin* (Mysore et al. 2019a, b), *offtrack* (Mysore et al. 2017), *shaker* (Mysore et al. 2020) gene-targeted via yeast, and *hr3* gene via algal delivery system affected the highest larvae survival. The microbial delivery method also gave a good result in *offtrack* and leukocyte receptor complex suppression and carrying high mortality of *An. gambiae* larvae (Mysore et al. 2017). *Juvenile acid methyl transferase* (Van Ekert et al. 2014) inhibition delayed pupation and eclosion rate as well as carried 80% mortality of *Ae. aegypti* larvae by fungal delivery method. A no. of scientists have worked on *chitin synthetase 1* and *2* or *chitin synthetase A* and *B* in different mosquitoes by using multiple delivery systems (Khalil et al. 2021; Lopez et al. 2019; Zhang et al. 2015, 2010; Singh et al. 2013). Among them, *chitin synthetase A* and *B* silencing carried out the highest ~ 80% mortality of larvae by the soaking method in *Ae. aegypti* (Lopez et al. 2019).

Medium range mortality targeted genes

Vacuolar adenosine triphosphatase (V-ATPase), *3-hydroxy kynurenine transaminase (3-HKT)*, *voltage-gated* Na^+ *channel (V-ATPase)*, *inhibitor of apoptosis* (*IAP1*), *dopamine 1*, *β-tubulin*, *steroid receptor coactivator (SRC)*, and *chitin synthetase* enzyme inhibition carried out a medium range of mortality of ~ 50–70% among larvae by various delivery methods (Khalil et al. 2021; Kumar et al. 2013; Bona et al. 2016; Hapairai et al. 2020; Singh et al. 2013; Das et al. 2015). *Vacuolar sorting protein* (*SNF7*) and *steroid receptor coactivator* (*SRC*) inhibition affected high mortality of larvae by quantum dot nanoparticle than only chitosan nanoparticle. *Chitin synthetase 1*, *heat shock protein* gene, and *3,4-dihydroxyphenylacetaldehyde synthetase* gene inhibition results in three times higher mortality of larvae through

Table 1 Effect of larva targeted gene on mosquito survival

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
1	*Ataxin 2-binding protein (A2BP1)* genes/*rbfox1*	An important factor for neural and muscle development	*Ae. aegypti* (laboratory strain)	siRNA	Yeast ATSB feeding (attractive targeted sugar baits)	77% mortality of larvae was observed with consumption of *rbfox1* yeast ATSB [$n = 20$ per treatment—13 replicates]	Mysore et al. 2021
			Ae. albopictus (laboratory strain)			90% mortality of larvae was observed with consumption of *rbfox1* yeast ATSB [$n = 20$ per treatment—13 replicates]	
			An. gambiae (laboratory strain)			~90% mortality of larvae was observed with consumption of *rbfox1* yeast ATSB [$n = 20$ per treatment—13 replicates]	
			C. quinquefasciatus (laboratory strain)			~91% mortality of larvae was observed with the consumption of *rbfox1* yeast ATSB [$n = 20$ per treatment—13 replicates]	
2	*Dopamine 1 receptor (dop1)*	Member of the GPCR family expressed in the developmental and adult stage of the mosquito	*Ae. aegypti* (laboratory strain)	sh RNA	Yeast delivery system	~92% mortality in larvae of indoor environments and ~93% mortality in larvae from semifield were found with the treatment of *dop1.462* shRNA [$n = 25$ per treatment—triplicates]	Hapairai et al. 2020
				si RNA	Soaking	~70% mortality was found in larvae treated with *dop1.462* si RNA [$n = 20$ per treatment—duplicates]	
3	*Leukocyte receptor complex member (lrc.51)*	Neural gene	*An. gambiae* (laboratory strain)	shRNA	Yeast delivery system	100% mortality was observed with the treatment of *lrc.51* shRNA [$n = 20$ per treatment—two biological replicates each with triplicates]	Mysore et al. 2017
				siRNA	Microinjection	55% mortality was observed with the treatment of *lrc.51* siRNA [$n = 30$ per treatment—duplicate]	
	Leukocyte receptor complex member (lrc.2)			siRNA	*E. coli*	99% mortality was observed with the treatment of *lrc.2* siRNA [$n = 20$ per treatment—2 replicates]	
				siRNA	Soaking	29% mortality was observed with the treatment of *lrc.2* siRNA [$n = 20$ per treatment—duplicate]	
					Microinjection	42% mortality was observed with the treatment of *lrc.2* siRNA [$n = 30$ per treatment—duplicate]	

Table 1 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
4	*Suppressor of actin* (*sac1.1*)	Neural gene	*An. gambiae* (laboratory strain)	shRNA	Yeast delivery system	89% mortality was observed with the treatment of *sac1.1* shRNA RNA [$n = 20$ per treatment—two biological replicates—each with triplicates]	Mysore et al. 2017
				siRNA	*E. coli*	43% mortality was observed with the treatment of *sac1.1* siRNA [$n = 20$ per treatment—two biological replicates each with triplicates]	
					Soaking	45% mortality was observed with the treatment of *sac1.1* siRNA [$n = 20$ per treatment—duplicate]	
					Microinjection	42% and 29% mortality was observed with the treatment of *sac1.1* siRNA and *sac1.91* [$n = 30$ per treatment—duplicate]	
5	*Offtrack gene (otk.16)*	Neural gene	*An. gambiae* (laboratory strain)	shRNA	Yeast delivery system	89% mortality was observed with the treatment of *otk.16* shRNA [$n = 20$ per treatment—two biological replicates each with triplicates]	Mysore et al. 2017
				siRNA	*E. coli*	84% mortality was observed with the treatment of *otk.16* siRNA [$n = 20$ per treatment—two biological replicates each with triplicates]	
					Soaking	28% mortality was observed with the treatment of *otk.16* siRNA [$n = 20$ per treatment—duplicate]	
					Microinjection	40% mortality was observed with the treatment of *otk.16* siRNA [$n = 30$ per treatment—duplicate]	
	Offtrack gene (otk.94)				Microinjection	40% mortality was observed with the treatment of *otk.94* siRNA [$n = 30$ per treatment—duplicate]	

Table 1 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
6	*Synaptotagmin*	Calcium-binding protein that acts as a calcium sensor and regulates the release of neurotransmitter	*Ae. aegypti* (laboratory strain)	shRNA	Dry inactivated yeast tablets	92.7% and 90.6% mortality was observed on treating laboratory-lived larvae and semifield lived larvae, respectively, with *syn.427* shRNA [laboratory assay—$n = 20$ per treatment—multiple replicates; semifield assay—$n = 20$ per treatment—three biological replicates each with three replicates]	Mysore et al. 2019a, b
			An. gambiae (laboratory strain)			92.0% mortality was observed on treating larvae with *syn.427* sh RNA [$n = 20$ per treatment—multiple replicates]	
			Ae. albopictus (laboratory strain)			92.0% mortality was observed on treating larvae with *syn.427* sh RNA [$n = 20$ per treatment—multiple replicates]	
			C. quinquefasciatus (laboratory strain)			92.0% mortality was observed on treating larvae with *syn.427* sh RNA [$n = 20$ per treatment—multiple replicates]	
			Ae. aegypti (laboratory strain)	siRNA	Soaking	32.5% mortality was found on treating larvae with *syn.427* siRNA [$n = 20$ per treatment—duplicate]	
			Ae. aegypti (laboratory strain)		Nanoparticle (chitosan)	Larvae and pupae treated with *syn* siRNA treatment encountered defects in the antenna lobe and neuron receptor and deformation in glomeruli [$n = 20$ per treatment—no replicates]	Zhang et al. 2015

Table 1 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
7	*Semaphorin 1 a (sema 1a)*	It plays an important role in the nervous system development of larvae as well as being involved in the formation of olfactory receptor	*Ae. aegypti* (laboratory strain)	shRNA	Dry inactivated yeast tablets	92%, 82%, and 91% mortality due to neural defect was observed with the treatment of yeast transformed with *sema* shRNA in laboratory-lived, simulated field, and semifield larvae, respectively [laboratory-lived larvae—$n = 20$ larvae per treatment—multiple biological replicates—each with 3 replicates; simulated field larvae—$n = 20$ larvae per treatment—multiple biological replicates—each with 3 replicates; semifield larvae $n = 20$ larvae per treatment—three biological replicates—each with 3 replicates]	Mysore et al. 2019a, b
			Ae. albopictus (laboratory strain)			93% mortality was observed with the treatment of *sema* shRNA transformed yeast tablets [$n = 20$ larvae per treatment—9 replicates]	
			An. gambiae (laboratory strain)			90% mortality was observed with the treatment of *sema* shRNA transformed yeast tablets [$n = 20$ larvae per treatment—12 replicates]	
			Cx. quinquefasciatus (laboratory strain)			90% mortality was observed with the treatment of *sema* shRNA transformed yeast tablets [$n = 20$ larvae per treatment—12 replicates]	
			Ae. aegypti (laboratory strain)	siRNA	Nanoparticle (chitosan) soaking	44% of siRNA-treated mosquitoes encounter defects in the antenna lobe because of a decrease in the no. of neurons targeting the antenna lobe and a reduction in the no. of synapses in the antenna lobe of larva and pupae was found in siRNA-treated mosquitoes [$n = 100$ (total)—two or three replicates]	Mysore et al. 2013
					Soaking	75% mortality was observed with the treatment of *sema* siRNA treatment [$n = 20$ per treatment—two replicates]	Mysore et al. 2019a, b

Table 1 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
8	*Juvenile acid methyl transferase* (JHAMT)	Involved in the jasmonic hormone biosynthesis pathway	*Ae. aegypti* (laboratory strain)	Long hairpin RNA	*Pichia pastoris* (fungus)	Pupation was delayed by 20–24 days and high mortality at early and after adult eclosion was observed and 80% mortality rate was found in larvae treated with LHP-transformed *P. pastoris* cells [$n = 20$ per treatment—triplicates]	Van Ekert et al. 2014
9	*3-Hydroxy kynurenine transaminase* (3-HKT)	Catalyze transmission reaction of 3HK in tryptophan catabolism pathway, an auto oxidative agent that produces reactive oxygen species under normal condition	*An. stephensi* (laboratory strain)	dsRNA	*Chlamydomonas reinhardtii* (algae)	50% larva mortality was found with the treatment of ds *3hkt* RNA [$n = 20$–30 per treatment]	Kumar et al. 2013
			Ae. aegypti (laboratory strain)		*Chlorella vulgaris*	6.7–43% increment in mortality of larvae fed transgenic *chlorella* algae [$n = 10$ per treatment—triplicates]	Fei et al. 2021
					Chlamydomonas reinhardtii	60–100% mortality of larvae fed transgenic *Chlamydomonas* was observed [$n = 10$ per treatment—triplicates]	
10	*hr3*	Involved in the metamorphosis process	*Ae. aegypti* (laboratory strain)	dsRNA	*Chlamydomonas reinhardtii* (algae)	Larvae fed transgenic algal strain suffered from a damaged epidermis, distorted muscles, and disintegrated midgut and had only a 1.3% survival rate [$n = 10$ per treatment—triplicates]	Fei et al. 2020
11	*Doublesex*	Required for sex differentiation during embryonic development	*An. gambiae* (laboratory strain)	siRNA	Soaking	50% of larvae failed to develop into adults after treatment with ds *dsx* RNA, i.e., RNAi-affected females failed to develop and the remaining fertile females that were produced failed to feed blood, mate, and survive [$n = 100$ per treatment—6 replicates]	Whyard et al. 2015
				dsRNA	*E. coli* HT115 (DE3)	72.1% male and 27.8% female progeny were produced from ds *Agdsx*-treated larvae and female adults emerged out from ds *Agdsx* larvae produced 37.1% less progeny than control ones [$n = 20$ per treatment—triplicates]	Taracena et al. 2019
12	*gas8* + *doublesex*	*gas8 is* required for spermatogenesis and *doublesex* acts as a transcriptional factor that regulates female-specific gene	*Ae. aegypti* (laboratory strain)	dsRNA	Soaking	All ds-treated larvae emerged out as male progeny of which 96% of male mosquitoes were found to be sterile and the remaining 4% were found to be partially sterile [$n = 100$ per treatment—6 replicates]	Whyard et al. 2015

Table 1 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
13	*p Glycoprotein*	ATP-dependent efflux pump that carries out transport of substrate across the membrane	*Ae. aegypti* (laboratory strain)	dsRNA	Soaking	The mortality rate of *p glycoprotein*-deficient larvae was found to be 82% more than the control ones on treating larvae with insecticide temephos [$n = 100$ per treatment—triplicates]	Figueira-Mansur et al. 2013
14	*Voltage-gated sodium channel* (VSGC)	Involved in detoxification of insecticides	*Ae. aegypti* (field-collected strain)	dsRNA	Soaking	ds *vsgc*-treated larvae encountered 50% higher mortality than the untreated larvae with the treatment of insecticide pyrethroid [$n = 100$ per treatment—triplicates]	Bona et al. 2016
15	*abcg4 transporter*	Involved in detoxification of insecticides	*An. stephensi* (laboratory strain)	ds RNA	Soaking	Silencing of *abcg 4* results in increased larva mortality and increased pyrethroid efficacy as *abcg 4* carry out detoxification of insecticides [$n = 50$ larvae per treatment—triplicates]	Negri et al. 2019
16	Testis gene *[(boule (bol); fuzzy onions (fzo); growth arrest-specific protein 8 (gas8); no-hitter (nht); and zero population growth (zpg)]*	Involved in spermatogenesis	*Ae. aegypti* (laboratory strain)	dsRNA	Soaking	Silencing of testis-specific gene induced 72–92% sterility in male mosquitoes at high concentrations of dsRNA treatment and the remaining 8–18% dsRNA-treated fertile males had reduced fecundity [$n = 100$ per treatment—5 biological replicates]	Whyard et al. 2015
				dsRNA	*E. coli*	62–90% sterility was achieved by feeding of dsRNA expressed *E. coli* to larvae [$n = 100$ per treatment—5 biological replicates]	
17	*Inhibitor of apoptosis 1 (IAP1)*	It is an inhibitor of caspase and crucial for cell survival	*Cx. quinquefasciatus* (laboratory strain)	dsRNA	Soaking	~53–54% mortality of larvae observed due to ds *IAP1* treatment and ~26–27% of ds IAP1-treated larvae were able to emerge into adult mosquitoes [$n = 30$ per treatment—triplicates]	Khalil et al. 2021
					Nanoparticle (chitosan)	~64.67% mortality of larvae and a significant reduction of 9.33% in the emergence of adults were observed with treatment of ds *IAP1* nanoparticles [$n = 30$ per treatment—triplicates]	
					Nanoparticle (chitosan-sodium tripolyphosphate)	60% mortality of larvae was observed with the treatment of ds *IAP1*-CSTPP (chitosan-sodium tripolyphosphate) nanoparticles [$n = 5$–7 per treatment—triplicates]	Dhandapani et al. 2019

Table 1 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
18	*Vacuolar adenosine triphosphatase (V-ATPase)*	Play an important role in the transport of proton across the cell membrane	*Cx. quinquefasciatus* (laboratory strain)	dsRNA	Soaking	~63–65% mortality of larvae was observed due to ds *V-ATPase* treatment and only ~18.8% of ds *V-ATPase* treated larvae were able to emerge into adult mosquitoes [$n = 30$ per treatment—triplicates]	Khalil et al. 2021
					Nanoparticle (chitosan)	~56.67% mortality of larvae and a significant reduction of 22% in the emergence of adults was observed with the treatment of ds *V-ATPase* nanoparticles [$n = 30$ per treatment—triplicates]	
19	*Single-minded gene (sim)*	Regulator of mosquito olfactory receptor	*Ae. aegypti* (laboratory strain)	si RNA	Nanoparticle (chitosan)	Effect in odor tracking behavior, multiple defects in antenna lobe was observed [$n = 30$ per treatment—two replicates]	Zhang et al. 2015
20	*snf 7 (vacuolar sorting protein)*	Involved in transport and required for survival of mosquito	*Ae. aegypti* (laboratory strain)	dsRNA	Nanoparticles (chitosan)	46.7% mortality of larvae observed with seven days treatment of ds *snf7* chitosan-treated nanoparticles [n = not mentioned]	Das et al. 2015
					Nanoparticles (carbon quantum dot)	53.33% mortality of larvae observed with seven days' treatment of ds *snf7* quantum dot nanoparticles [n = not mentioned]	
21	*Sterol carrier protein 2*	Enhance cholesterol uptake	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	42% mortality rate increased in adults emerged from ds *scp-2* [$n = 40$–50 per treatments—duplicates] treated larvae, egg hatchability affected by *scp2* silencing—only 15% of eggs laid by ds *scp2* female able to hatch [$n = 43$ per treatments—duplicates]	Blitzer et al. 2005
22	*src*	Steroid receptor coactivator	*Ae. aegypti* (laboratory strain)	dsRNA	Nanoparticles (chitosan)	26.67% mortality of larvae observed with seven days' treatment of ds *src* chitosan-treated nanoparticles [n = not mentioned]	Das et al. 2015
					Nanoparticles (carbon quantum dot)	75% mortality of larvae observed with 7 days' treatment of ds *src* carbon quantum dot-treated nanoparticles [n = not mentioned]	

Table 1 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
23	*3,4-Dihydroxyphenylacetaldehyde synthetase (DOPAL)*	Required for flexible cuticle formation	*Ae. aegypti* (laboratory strain)	dsRNA	Nanoparticle (chitosan) soaking	The mortality rate of larvae fed ds *dopal* synthetase had three times more than the control group, length, molting rate, and growth rate were also reduced in ds *dopal* synthetase-treated larvae [$n = 100$ per treatment—3 biological replicates]	Chen et al. 2019
24	*Vestigial gene (Vg)*	Carry out wing development, morphogenesis, 3rd instar larva development	*Aedes aegypti* (laboratory strain)	dsRNA	Nanoparticle (chitosan)	*vg* silencing carried significant mortality and delayed pupa and adult stage and caused malformation of adult wings [$n = 25$ per treatment—5 biological replicates—each with triplicates]	Kumar et al. 2016

Table 1 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
25	*Chitin synthase 1*	Carry out chitin formation in the cuticular exoskeleton, foregut, hindgut, trachea, and epidermal and ectodermal tissue	*Cx. quinquefasciatus* (laboratory strain)	dsRNA	Nanoparticle (chitosan)	61.33% mortality of larvae and ~ 20–22% reduction in the emergence of adults were observed on treating larva with ds *chs1* nanoparticles [$n = 30$ per treatment—triplicates]	Khalil et al. 2021
					Soaking	55–56% mortality of larvae observed due to ds *chs1* treatment and ~ 27.7% of ds *chs1*-treated larvae were able to emerge into adult mosquitoes [$n = 30$ per treatment—triplicates]	
			An. gambiae (laboratory strain)		Nanoparticle (chitosan)	Knockdown of *chs1* increased the susceptibility of mosquitoes to the insecticide diflubenzene [$n = 20$ per treatment—triplicates]	Zhang et al. 2015
			Ae. aegypti (laboratory strain)		Soaking	ds-treated larvae showed a reduction in growth, and the mortality rate was found three times higher than the control one; the larva survived after ds *ch*1 treatment and showed a 1/3 reduction in length as well as failed to develop in adults [$n = 10$–20 per treatment—triplicates]	Singh et al. 2013
	Chitin synthase 1 (two fragments taken—F1, F2)		*An. gambiae* (laboratory strain)		Nanoparticle (chitosan)	Mortality increased by 26.5% in larvae treated with ds *chs1* nanoparticles; ds *chs1*-treated larvae were found to be more susceptible to diflubenzuron (insecticide) [$n = 15$–20 per treatment—triplicates]	Zhang et al. 2010
	Chitin synthase A and chitin synthase B (*CHSA and CHSB*)		*Ae. aegypti* (laboratory strain)		Soaking	The survival rate of ds *chsa*_1928 (a fragment of *CHS* gene)-treated larvae decreased drastically, only 20% of larvae after treatment with dsRNA were able to reach the pupa stage, and surviving adult mosquitoes emerged from pupae found to develop abnormally in morphological features like wings, size, and more fragile than the control group [$n = 30$ per treatment—triplicates] Silencing of *chsa* increased the susceptibility of larvae towards insecticide diflubenzuron results in 75% mortality on the 6^{th} day of treatment [$n = 15$ per treatment—triplicates]	Lopez et al. 2019

Table 1 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
26	*Chitin synthase 2*	Carry out chitin biosynthesis in the peritrophic matrix	*An. gambiae* (laboratory strain)	dsRNA	Nanoparticle (chitosan)	Knockdown of *chs2* increased the effect of the insecticide calcofluor white and dithiothreitol that increased the mortality rate of mosquitoes [$n = 20$ per treatment—triplicates]	Zhang et al. 2015
	Chitin synthase 2 (two fragments taken—F1, F2)				Nanoparticle (chitosan)	Mortality of ds *chs2* nanoparticle-treated larvae increased by 29.3%. Larva mortality increased by 48% when treated larvae were exposed to calcofluor white (insecticide) or DTT [$n = 15$–20 per treatment—triplicates]	Zhang et al. 2010
27	*β-Tubulin*	Component of the cell cytoskeleton	*Ae. aegypti* (laboratory strain)	dsRNA	Soaking	Only ~ 52.1% of larvae were able to survive after treatment with ds *β-tubulin* RNA [n = 20 per treatment—triplicates]	Singh et al. 2013
28	*Heat shock protein 83*	Carry out folding and unfolding of proteins under stressed condition	*Ae. aegypti* (laboratory strain)	dsRNA	Soaking	*hsp 83*-treated ds larvae showed three times higher mortality than control ones [$n = 20$ per treatment—triplicates]	Singh et al. 2013
29	*Shaker gene*	Encode voltage-gated potassium ion channel subunit	*Ae. aegypti* (laboratory strain)	siRNA	Soaking	48–52% mortality of larvae was observed with the treatment of *sh.463* siRNA compared with control larvae [$n = 20$ larvae per treatment—duplicate]	Mysore et al. 2020
				shRNA	Yeast ATSB feeding	92% mortality of larvae was observed with the treatment of *sh.463* dried inactivated yeast tablets, and in semifield condition, 93–94% mortality was observed with treatment of *sh.463* expressing ATSB inactivated yeast tablets [$n = 20$ per treatment—3 biological replicates]	
			Ae. albopictus	shRNA	Yeast delivery system	91–92% mortality of larvae was observed with the treatment of *sh.463* RNA [$n = 20$ per treatment—3 biological replicates]	
			An. gambiae	shRNA	Yeast delivery system	92–93% mortality of larvae was observed with the treatment of *sh.463* RNA [$n = 20$ per treatment—3 biological replicates]	
			Cx. quinquefasciatus	shRNA	Yeast delivery system	92–93% mortality of larvae was observed with the treatment of *sh.463* RNA [$n = 20$ per treatment—3 biological replicates]	

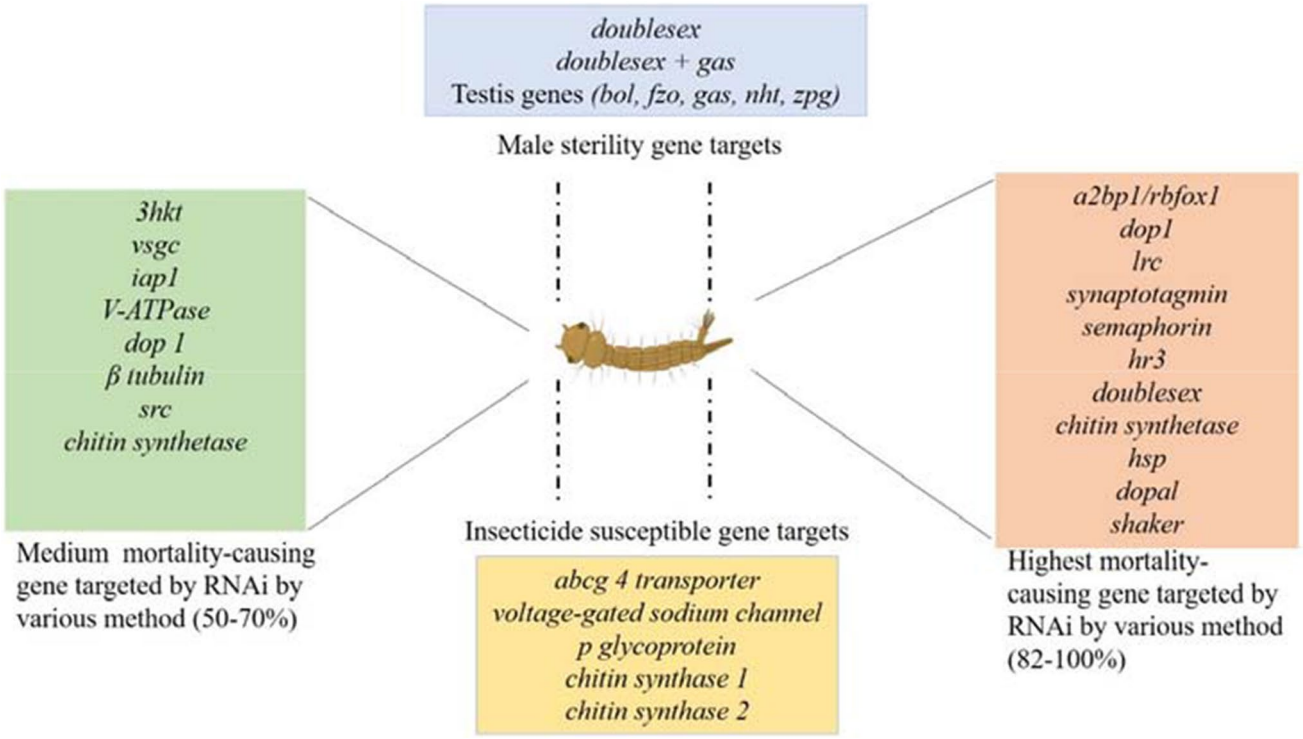

Fig. 2 Larva gene targeted by RNAi for vector control

soaking and nanoparticle method, respectively (Singh et al. 2013; Chen et al. 2019).

Sterility-causing targeted genes

Sex-specific genes like testis genes, *gas* and *doublesex* gene silencing with the soaking method results in the emergence of a maximum no. of sterile male progeny. *Doublesex* gene inhibition affected half of larva survival, and females that emerged from ds-treated larvae failed to develop and reproduce (Whyard et al. 2015).

Insecticide susceptible targeted genes

Several gene expression inhibition elevated the susceptibility of mosquitoes towards insecticides as the insecticide resistance in mosquitoes has been increased with continuous exposure. *Abcg4 transporter* (Negri et al. 2019) and *voltage-gated sodium channel* (Bona et al. 2016) increased the susceptibility of larvae towards pyrethroid and *p glycoprotein* (Figueira-Mansur et al. 2013) susceptibility towards temephos by the soaking method. *Chitin synthase 1* (Zhang et al. 2015, 2010) and *chitin synthase 2* (Zhang et al. 2010) inhibition increases sensitivity towards diflubenzene and calcofluor white or dithiothretol, respectively, by the nanoparticle method.

Pupa targeted genes

Pupa genes are a good target for controlling the mosquito population. Knockdown at the pupa stage can persist during developmental interval time between pupae and can extend up to the adult stage (Regna et al. 2016). Most RNAi studies conducted to target pupa genes hindered the eclosion process or carried physiological abnormalities in the adults that emerged from treated pupae. *Prophenoloxidase III* inhibition in Zika virus potential vector *Ar. subalbatus* allowed survival of only 3–4% of emerged adults with malformed wings and legs (Tsao et al. 2009). *Laccase2* and *tyrosine hydroxylase* inhibition in malarial vector *An. sinensis* inhibited the eclosion process and affected cuticles and survival rate as well (Du et al. 2017; Qiao et al. 2016). *Semaphorin 1a* and *cecropin B* gene inhibition carried physiological abnormalities like defective antenna lobes and the inability of adults to detach from pupae resulting in the death of individuals (Mysore et al. 2013; Liu et al. 2017). Testis genes *boule (bol)*, *fuzzy onions (fzo)*, *growth arrest specific protein 8 (gas8)*, *no-hitter (nht)*, and *zero population growth (zpg)* inhibition

Table 2 Effect of pupa targeted gene on mosquito survival

Sr no	Gene	Function	Vector studied	Method	Type of RNA used for interference	Effect	Reference
1	*Laccase 2*	Required for cuticle formation and immunity maintenance via the production of melanin	*An. sinensis* (laboratory strain)	Microinjection	dsRNA	ds *lac2* treated pupae produced soft, thin, and unpigmented cuticles and hindered the eclosion process, and survival rate was also reduced. Adult progeny from ds *lac2* pupae was found to be more susceptible to microorganism infection [n = not mentioned]	Du et al. 2017
2	*Tyrosine hydroxylase*	Carry out catalysis of tyrosine in dopa which is an important melanin precursor	*An. sinensis* (laboratory strain)	Microinjection	dsRNA	Eclosion rate is reduced by 30% in ds *TH*-treated individual than the control one and failed to develop melanin pigment in cuticles as well as during sclerotization leading to the death of the individual. Knockdown of *tyrosine hydroxylase* carried out an impairment in the immunity of individuals that reduced the survival rate and life span of pupae severely [n = not mentioned—triplicates]	Qiao et al. 2016
3	*Prophenoloxidase III*	Involved in melanization and sclerotization	*Ar. subalbatus* (laboratory strain)	Microinjection	ds RNA	The mortality rate of pupae increased by ~ 68.3% after inoculation of ds *pro-III* for up to 5 days. Around 30% of adults emerged from ds-treated pupae, but most of them died due to the inability to detach from pupae exuvia. Only 3–4% of survived adults had malformed wing and legs [$n = 30$ per treatment—triplicate]	Tsao et al. 2009
4	*Semaphorin-1a (sema1a)*	Olfactory development	*Ae. aegypti* (laboratory strain)	Nanoparticle (chitosan) soaking	siRNA	32% of siRNA treated mosquitoes encounter defects in the antenna lobe because of a decrease in the no. of neurons targeting the antenna lobe, and a reduction in the no. of synapses in the antenna lobe of pupae was found in si RNA-treated mosquitoes [$n = 100$ per treatment—triplicate]	Mysore et al. 2013
5	Testis gene *[(boule (bol); fuzzy onions (fzo); growth arrest-specific protein 8 (gas8); no-hitter (nht); and zero population growth (zpg)]*	Involved in spermatogenesis	*Ae. aegypti* (laboratory strain)	Microinjection	dsRNA	Mating of adults emerged out from dsRNA-injected pupae resulted in reduction of fecundity and production of viable progeny by > 75% [$n = 20$ per treatment—3 biological replicates]	Whyard et al. 2015

Table 2 (continued)

Sr no	Gene	Function	Vector studied	Method	Type of RNA used for interference	Effect	Reference
6	*Cecropin B*	Antimicrobial peptide	*Ae. aegypti* (laboratory strain)	Microinjection	dsRNA	~58.67% mortality was observed with dsRNA treatment and adults emerged from injected pupae unable to detach from exuvia; 21% of adults emerged completely had deformed legs and wings resulting in the death of individuals [$n = 30$ per treatment—5 replicate]	Liu et al. 2017

results in fecundity reduction and the progeny produced from mating of adults (emerged adults from testis gene ds RNA-treated pupae) found to be less viable (Whyard et al. 2015). Table 2 shows the list of pupa genes targeted by the RNAi mechanism.

Adult-stage targeted genes

A number of RNAi studies focused on adult stage genes in order to manage vector population. Adult stage is easy to handle to carry delivery of RNA as comparison to egg and pupa stage. A number of methods had been used to deliver RNA to inhibit the target gene expression. Most of gene targeted at adult stage affected reproductive capacity in terms of egg production and some genes inhibition affected survival leading to mortality of individuals.

Mortality causing targeted genes

Ataxin 2-binding protein (Mysore et al. 2021) and *dopamine 1 receptor* (Hapairai et al. 2020) gene silencing carried high mortality among different vectors including *An. gambiae*, *Cx. quinquefasciatus*, *Ae. albopictus*, and *Ae. aegypti* via yeast attractive targeted sugar bait delivery method. *Coatomer protein 1* (Isoe et al. 2011) and *stearoyl Co-A desaturase* (Ferdous et al. 2021) gene expression inhibition led to high mortality of adult mosquitoes through microinjection delivery method. *Ataxin 2-binding protein* (Mysore et al. 2021), *ecdysone receptor* (Maharaj et al. 2022), and *akirin* (Letinić et al. 2020) gene suppression executed an effective mortality in adult mosquito microinjection delivery method. *Epsilon glutathione transferase* (GST) gene inhibition increased the susceptibility of mosquitoes towards insecticide deltamethrin (Lumjuan et al. 2011). In *Ae. aegypti*, *3,4-dihydroxyphenylacetaldehyde synthetase* (Chen et al. 2019) gene inhibition and *shaker* gene (Mysore et al. 2020) inhibition by microinjection cause more than 50% mortality in different vectors including *Ae. aegypti*, *Ae. albopictus*, *An. gambiae*, and *Cx. quinquefasciatus.*

Male targeted genes

A few studies executed silencing of male mosquito gene and mating of these specific gene-deficient mosquitoes with virgin females affected fecundity rate adversely. Male sex-specific gene *heme peroxidase 12*-deficient mosquitoes mating with female results in reduction of fecundity capacity by ~ 50% (Kumari et al. 2022). Ammonia transporter is a crucial factor for sperm viability and fertility; silencing also affected fecundity rate of female mosquitoes (Durant & Donini 2020).

Table 3 Adult stage targeted gene

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
1	*Ataxin 2-binding protein (A2BP1)* genes/*rbfox1.457*	An important factor for neural and muscle development	*Ae. aegypti* (laboratory strain)	siRNA	Yeast ATSB feeding (attractive targeted sugar baits)	~ 77% mortality of adults was observed with the consumption of *rbfox1* yeast ATSB [$n = 150$ (total)—triplicates]	Mysore et al., 2021
			An. gambiae (laboratory strain)			93% mortality of adults was observed with the consumption of *rbfox1* yeast ATSB [$n = 75$ (total)—triplicates]	
			Ae. albopictus (laboratory strain)			~ 89% mortality of adults was observed with the consumption of *rbfox1* yeast ATSB [$n = 204$ (total) — triplicates]	
			Cx. quinquefasciatus (laboratory strain)			~ 81% mortality of adults was observed with the consumption of *rbfox1* yeast ATSB [$n = 225$ (total) — triplicates]	
			Ae. aegypti (laboratory strain)		Microinjection	45% mortality of adults was observed with the treatment of si *rbfox1* RNA [$n = 20$ per treatment—triplicates]	
2	*Juvenile acid methyl transferase (JHAMT)*	Involved in the jasmonic hormone biosynthesis pathway	*Ae. aegypti* (laboratory strain)	dsRNA	Feeding by capillary glass	Egg development is inhibited by 3.6–5.6 folds in 47% of females treated with *jmtA* dsRNA [*n* = not mentioned—duplicate]	Van Ekert et al. 2014
					Microinjection	Among all female mosquitoes treated with *jmtA* dsRNA, 45% of females encountered inhibition in egg development, as well as yolk length of oocyst, decreased by 2.5 folds shorter than the control dsRNA [$n = 67$ per treatment—duplicate]	
3	*ras homolog enriched in brain GTPase* (*Rheb*)	Activate the target of rapamycin (TOR) pathways that is involved in the activation of the reproductive cycle of the mosquito	*Ae. aegypti* (laboratory strain)	dsRNA	Soaking	*Vitellogenin* (*Vg*) expression (initiator of vitellogenesis and egg development), ovary size, size of matured eggs, no. of eggs were reduced in ds *Rheb*-reduced mosquito, some ds *Rheb*-reduced female mosquitoes found to be devoid of development eggs [$n = 10$ per treatment triplicates]	Roy and Raikhel 2011

Table 3 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
4	*Stearoyl co-A desaturase*	It converts the saturated fatty acid into unsaturated fatty acid and is essential for maintaining membrane fluidity	*An. coluzzii* (laboratory strain)	dsRNA	Microinjection	The survival rate of knockout mosquitoes decreased by 100% and 52% after feeding blood by membrane feeding assay and direct feeding on human blood, respectively. With the deficiency of *stearoyl co-A desaturase* enzyme midgut of mosquitoes became swollen up, and got fragile as well as rigidity also decreased. Egg development was also affected as oocyst failed to mature [n = not mentioned]	Ferdous et al. 2021
5	*Coatomer protein 1*	It involves cellular process and carries out transport between the endoplasmic reticulum and Golgi	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	88–95% mortality was found with injecting ds *cop I* in female mosquitoes after seven days post blood and midgut epithelial cells were found to be more fragile and lighter, and premature defecation of blood was also found. 89% mortality was observed after 72 h blood feed in mosquitoes treated with ds *γcopI* (subunit of *copI*) as well as ds *γcopI*-deficient mosquitoes showed delayed blood digestion, egg production, and follicle and ovary found reduced in size, eggs were found without eggshell [n = not mentioned—triplicates]	Isoe et al. 2011
6	*Ribosomal proteins s6* and *s26*	Involved in cellular processes	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	Reproductive output is reduced by 96% and 91%, respectively, during the 1st oviposition and a significant reduction in fecundity during the 2nd oviposition in *rps6* [$n = 102$ per treatment—7 biological replicates] and *rps26* [$n = 85$ per treatment—7 biological replicates] silenced mosquito	Estep et al. 2016

Table 3 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
7	*Akirin*	Play an essential role in innate immunity, embryonic development	*An. arabiensis* (laboratory strain)	siRNA	Microinjection	si RNA-mediated silencing of a*kirin* carried a 17% reduction in fecundity rate, 23% reduction in fertility rate, and 23% survival rate of siRNA a*kirin*-treated mosquito [$n = 20$ per treatment—5 replicates]	Letinić et al. 2020
				dsRNA		ds RNA-mediated silencing of a*kirin* carried a 25% reduction in fecundity rate, 29% reduction in fertility rate, and 48% survival rate of dsRNA a*kirin*-treated mosquito [$n = 20$ per treatment—5 replicates]	
8	*aeSigP-66,427*	Na+/Ca2 exchanger	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	Knockdown of a*eSigP-66,427* disrupted egg production and reduced sperm motility [not mentioned]	Pascini et al. 2020
9	*Ecdysone receptor*	It is an essential factor for mosquito longevity as well as helps in the transmission of malaria	*An. funestus* (laboratory strain)	dsRNA	Microinjection	The survival rate and longevity of *EcR*-depleted mosquitoes were decreased by ~ 10.5 times and 50%, respectively, than control ones; among all *EcR*-depleted females, only 32% of females were able to produce eggs, i.e., fertility was also reduced in *EcR*-depleted females [$n = 83$ (total)—3 biological replicates]	Maharaj et al. 2022
10	*HR38*	Carry out glycogen accumulation, reduction in trehalose	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	*hr38*-deficient mosquitoes encounter a 23.1% reduction in the length of ovarian follicles than wild-type and control mosquitoes and egg count was also reduced by 59% and 52% in comparison with wild-type and control mosquitoes, respectively [*n* = not mentioned—triplicates]	Dong et al. 2018

Table 3 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
11	*Ammonia transporter/methyl-ammonium permease*	It carries out specific transfer of ammonia throughout the cell membrane to avoid NH_3/NH_4^+ toxicity and regulate osmoregulation and excretion as well as an essential component for sperm viability and fertility	*Ae. aegypti* (laboratory strain)	siRNA	Microinjection	Mated female mosquitoes with *Amt* knockout males produced a reduced number of eggs significantly [$n = 46$ per treatment—triplicates]	Durant & Donini 2020
12	Autophagic genes (*ATG1, ATG6, ATG8*)	Involved in autophagy initiation, vesicle nucleation, and vesicle formation, respectively	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	The second gonadotrophic cycle of the autophagic gene-deficient mosquito was affected severely. The length of the secondary ovarian follicle and the size of the ovary was reduced [ATG1—$n = 10$; ATG1 + ATG6—$n = 15$; ATG8—$n = 12$; ATG1 + ATG8—$n = 12$]	Bryant and Raikhel 2011
13	*Transferrin*	Iron-binding protein that helps in the utilization, mobilization, and storing of iron	*An. culicifacies* (laboratory strain)	dsRNA	Microinjection	~ 23% reduction in oocyst number was observed in *transferrin*-deficient mosquitoes [$n = 10$ per treatment—triplicates]	Rani et al. 2022
14	*Heme peroxidase 12*	The cellular factor that protects sperm from oxidative stress	*An. stephensi* (laboratory strain)	dsRNA	Microinjection	*hpx12*-deficient male mosquitoes lost sperm viability, motility, and sperm head qualities and expression of the accessory protein of the accessory gland also decreased. Virgin females mated with *hpx12*-deficient males produced ~ 50–52% less no. of eggs and ~ 37–40% eggs were unable to hatch out [$n = 30$ per treatment—triplicates]	Kumari et al. 2022
15	*Trehalase*	It plays an important role in energy metabolization under different physiological condition	*An. stephensi* (laboratory strain)	dsRNA	Microinjection	~ 50% reduction in egg laying capacity in *trehalase*-deficient mosquitoes was observed [$n = 15$–25 per treatment—triplicates]	Tevatiya et al. 2020
16	*Epsilon glutathione transferase (GST)*	Carry out detoxification of foreign compound	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	Silencing of *gst* increased the susceptibility of mosquitoes towards deltamethrin insecticide [$n = 20$–26 per treatment—triplicates]	Lumjuan et al. 2011

Table 3 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
17	*Dopamine 1 receptor*	Member of the GPCR family expressed in the developmental and adult stage of the mosquito	*Ae. aegypti* (laboratory strain)	siRNA	ATSB (attractive targeted sugar baits)	~ 88% of *dop1.462* siRNA-treated mosquitoes encountered death after treatment, and the remaining 12% of mosquitoes failed to fly and were unable to coordinate in terms of walking behavior [$n = 34$ per treatment—triplicate]	Hapairai et al. 2020
			Ae. albopictus (laboratory strain)			~ 91% mortality was found in mosquitoes treated with *dop1.462* siRNA [$n = 34$ per treatment—triplicate]	
			An. gambiae (laboratory strain)			~ 91% mortality was found in mosquitoes treated with dop1.462 siRNA [$n = 34$ per treatment—triplicate]	
			Ae. aegypti (laboratory strain)		Microinjection	~ 48–49% higher mortality rate was found in dop1.462 siRNA-deficient mosquito than the control ones. Deficiency of dop1.462 siRNA causes disruption of neural function [$n = 20$ per treatment—triplicate]	
			Ae. albopictus (laboratory strain)			~ 55% higher mortality rate was found in dop1.462 siRNA-deficient mosquito than the control ones [$n = 60$ per treatment—triplicate]	
			An. gambiae (laboratory strain)			~ 42% higher mortality rate was found in dop1.462 siRNA-deficient mosquito than the control ones [$n = 60$ per treatment—triplicate]	
18	*Target of rapamycin kinase (TOR kinase)*	An important enzyme of TOR signaling cascade transduction	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	90% of female mosquitoes treated with ds *tor* kinase failed to develop eggs because of the inability to produce yolk sacs and oocytes failed to enlarged [n = not mentioned]	Hansen et al. 2005

Table 3 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
19	*Protein tyrosine phosphatase homolog (PTP homolog)*	Important enzyme for cell differentiation, cell growth, and metabolism	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	Silencing of *ptp* homolog affected the production of yolk protein vitellogenin and carried a 30% reduction in egg production [$n = 30$ per treatment triplicates]	Moretti et al. 2014
20	*Kruppel homolog 1*	Play an important role in the juvenile hormone signaling pathway	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	ds *kruppel*-treated females carried a 46% reduction in egg production than the control [$n = 40$ per treatment—triplicates]	Ojani et al. 2018
21	*3,4-Dihydroxyphenylacetaldehyde synthetase (DOPAL)*	Required for flexible cuticle formation	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	The mortality rate of ds *dopal*-treated adults was more than 50% [$n = 20$ per treatment (total—100 male + 100 female)—triplicates]	Chen et al. 2019
22	*Inward rectifier potassium (kir1)*	Involved in osmoregulation and urine production	*An. gambiae* (laboratory strain)	dsRNA	Microinjection	ds *kier1*-treated produced 10% less egg than the control mosquitoes [$n = 151$ per treatment—3 biological replicates]	Raphemot et al. 2014
23	*Frizzled 2 (fz2)*	Transmembrane receptor of the Wnt signaling pathway	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	A significant reduction in the no. of eggs was observed in *fz2*-silenced mosquitoes compared with control mosquitoes [$n = 20$ per treatment—3 biological replicates]	Weng & Shiao 2015
24	*Regulator of ribosome synthesis 1 (RRS1)*	Regulate ribosome synthesis	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	Follicle length and egg no. were decreased significantly in ds *RRS1*-treated mosquitoes compared with control mosquitoes	Wang et al. 2017
25	*Ribosomal protein large subunit 32 (RpL32)*	Ribosomal protein	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	Follicle length and egg no. were decreased significantly in ds *RpL32*-treated mosquitoes compared with control mosquitoes	Wang et al. 2017
26	*Methoprene-tolerant (Met)*	Involved in ribosome biogenesis	*Ae. aegypti* (laboratory strain)	dsRNA	Microinjection	Follicle length and egg no. were decreased significantly in ds *Met*-treated mosquitoes compared with control mosquitoes	Wang et al. 2017

Table 3 (continued)

Sr no	Gene	Function	Vector studied	Type of RNA used for interference	Targeted methods	Effect	Reference
27	*Shaker gene (sh.463)*	Encode voltage-gated potassium ion channel subunit	*Ae. albopictus* (laboratory strain)	si RNA	Microinjection	60% mortality of adults was observed with the treatment of *sh.463* siRNA	Mysore et al. 2020
			Ae. aegypti (laboratory strain)	siRNA	Microinjection	63–64% mortality of adults was observed with the treatment of *sh.463* siRNA [$n = 20$ per treatment—two replicates]	
			An. gambiae (laboratory strain)	siRNA	Microinjection	53–54% mortality was observed with the treatment of *sh.463* siRNA [$n = 20$ per treatment—3 biological replicates]	
			Cx. quinquefasciatus (laboratory strain)	siRNA	Microinjection	58–59% mortality was observed with the treatment of *sh.463* siRNA [$n = 20$ per treatment—3 biological replicates]	

Reproductive output targeted genes

A number of adult targeted gene silencing affected ovary size, ovarian follicle length, oocyst maturation, oocyst number, egg development, and fecundity rate and reduced reproductive output carried out by mosquitoes. *Juvenile acid methyl transferase* (Van Ekert et al. 2014), *ras homolog enriched in brain GTPase* (Roy & Raikhel 2011), *coatomer protein 1* (Isoe et al. 2011), *ribosomal proteins S6 and S26* (Estep et al. 2016), *AeSigP-66,427* (Pascini et al. 2020), *hr38* (Dong et al. 2018), *autophagic genes* (Bryant & Raikhel 2011), *transferrin* (Rani et al. 2022), *trehalase* (Tevatiya et al. 2020), *target of rapamycin kinase* (Hansen et al., 2005), *protein tyrosine phosphatase homolog* (Moretti et al. 2014), and *kruppel homolog 1* (Ojani et al. 2018) gene silencing decreased the ability to reproduce and provided rewarding result to control mosquito population. *Inward rectifier potassium* (Raphemot et al. 2014) and *frizzled 2* (Weng & Shiao 2015) gene silencing by microinjection interfered with egg production in *An. gambiae* and *Ae. aegypti*, respectively. In *Ae. aegypti*, *regulator of ribosome synthesis*, *ribosome protein large subunit 32*, and *methoprene-tolerant* (Wang et al. 2017) gene inhibition by microinjection results in a reduction in follicle length and egg number. The silencing effect of the mentioned gene is listed in Table 3, and Fig. 3 is showing the adult stage targeted genes by RNAi.

Conclusion

Mosquito-borne diseases are posing a major threat to mankind for many decades. The only way to tackle these diseases is to use an effective vaccine. But there are a number of mosquito-borne disease like chikungunya, elephantiasis, and Zika virus for which no vaccine is available and some developed vaccines have lower efficacy like RTS/01 for malaria. In future time, mosquito could be a potential vector for other perilous diseases. In this situation, mosquito control approach is the only route to overcome this extreme burden. A number of approaches have been used for controlling the mosquito population, but the population of mosquitoes has been growing despite the adoption of a variety of treatments due to their rapid rate of reproduction. Consistent use of chemical insecticide disturbed the air, water, and soil environment and also made mosquito to evolve with greater extent to counteract the effect of insecticides. At present time, RNAi has emerged as a novel strategy in the field of functional genomics study of organisms and has been used for mosquito control by targeting a particular mosquito gene. Inhibition of the mosquito gene, which is

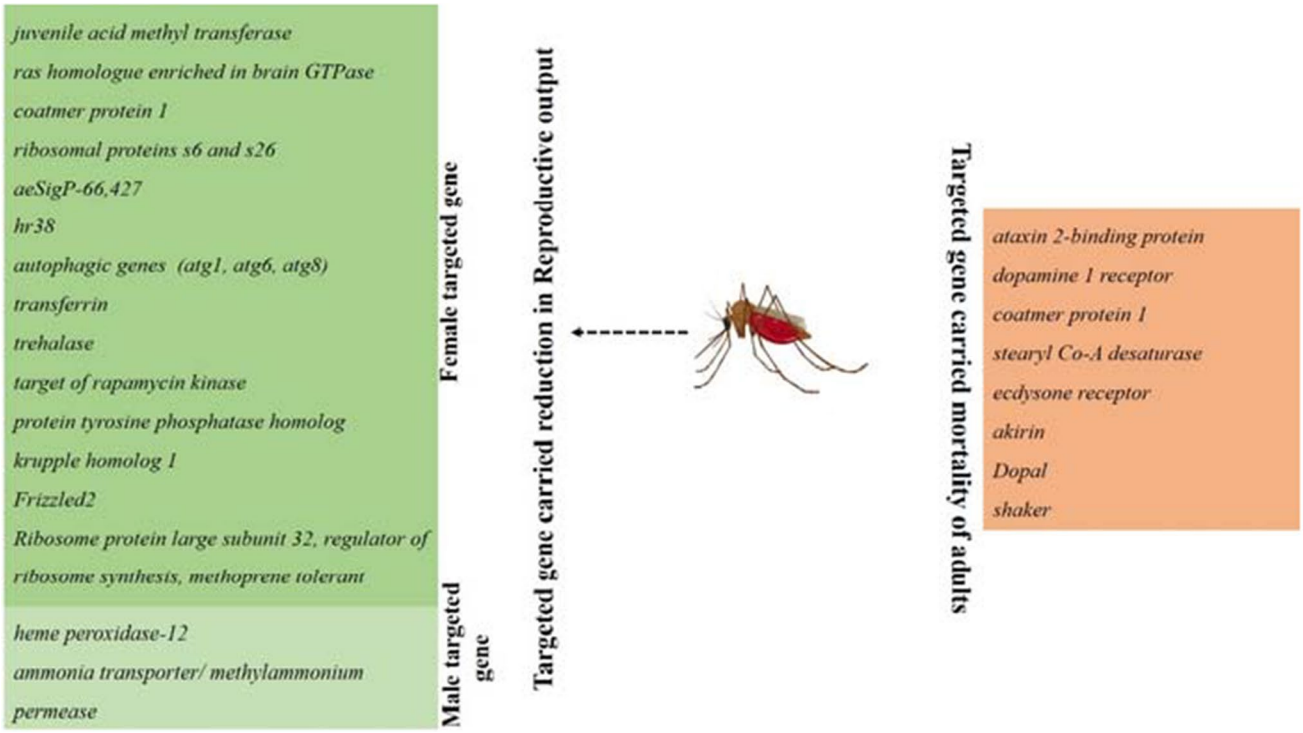

Fig. 3 Adult stage gene targeted by RNAi for vector control

essential to its survival, may result in mosquito death. A number of researchers used RNAi method to inhibit mosquito gene expression to find out the outcomes of gene inhibition. In the present review, we explained different studies conducted on RNAi-mediated silencing effect on vector survival by targeting mosquito genes of different developmental stages via different delivery methods. With literature finding, we concluded that larva genes *ataxin 2-binding protein*, *dopamine 1*, *leukocyte receptor complex 0.51*, *synaptotagmin*, *semaphorin*, *offtrack*, *hr3*, *juvenile acid methyl transferase*, *chitin synthetase A* and *B*, and *shaker* gene silencing targeted by different methods provided the most effective results as shown in Table 1. At the larval stage, *shaker*, *synaptotagmin*, *and semaphorin* gene inhibition has also been applied in semifield conditions and provided fruitful results in larva control. Most of the pupa stage targeted genes provided effective results in terms of abnormalities, generated due to gene inhibition assay. *Prophenoloxidase III* and *cecropin B* gene suppression at the pupal stage is found to be more efficient by microinjection method and adult stage targeted gene *ataxin 2-binding protein*, *dopamine 1 receptor*, *coatomer protein 1*, and *stearoyl co-A desaturase* gene silencing carried the highest mortality in adults. With deep analysis of all result findings, it was concluded that yeast delivery method is the most efficient method in carrying the highest mortality among different mosquito species, i.e., yeast delivery method is capable of complete inhibition of the target gene. This review is providing the information all about the mosquito gene target that can be used for further bioinsecticide for mosquito control without depleting the natural ecosystem. We need to find the most efficient delivery method so that complete inhibition of gene could carry out maximum mortality of gene of interest for vector control so that vector-borne disease could be controlled. No doubt, stability and large-scale production at lower cost are the major challenges in the implementation of RNAi in field conditions. In vivo strategies could solve the problem of cost and yield. It is regarded that using bacterial expression system could solve the dsRNA cost and large-scale production. Further studies are required in this area to implement RNAi for vector control in the field.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10142-023-01072-6.

Author contribution Writing—original draft preparation: Mahima Yadav; writing—review and editing: Nisha Dahiya; conceptualization, supervision, review, and editing: Neelam Sehrawat.

Data availability Not applicable.

Declarations

Ethical approval Not applicable.

Competing interests The authors declare no competing interests.

References

Ahmed A, Ali Y, Elduma A, Eldigail MH, Mhmoud RA, Mohamed NS, Ksiazek TG, Dietrich I, Weaver SC (2020) Unique outbreak of Rift Valley fever in Sudan, 2019. Emerg Infect Dis 26(12):3030–3033. https://doi.org/10.3201/eid2612.201599

Airs PM, Bartholomay LC (2017) RNA interference for mosquito and mosquito-borne disease control. Insects 8(1):4. https://doi.org/10.3390/insects8010004

Azimzadeh Jamalkandi S, Azadian E, Masoudi-Nejad A (2014) Human RNAi pathway: crosstalk with organelles and cells. Funct Integr Genomics 14:31–46. https://doi.org/10.1007/s10142-013-0344-1

Bagcchi S (2023) Nepal faces an outbreak of dengue. Lancet Infect Dis 23(1):35. https://doi.org/10.1016/S1473-3099(22)00821-0

Balakrishna Pillai A, Nagarajan U, Mitra A, Krishnan U, Rajendran S, Hoti SL, Mishra RK (2017) RNA interference in mosquito: understanding immune responses, double-stranded RNA delivery systems and potential applications in vector control. Insect Mol Biol 26(2):127–139. https://doi.org/10.1111/imb.12282

Benelli G, Jeffries CL, Walker T (2016) Biological control of mosquito vectors: past, present, and future. Insects 7(4):52. https://doi.org/10.3390/insects7040052

Besnard M, Lastere S, Teissier A, Cao-Lormeau VM, Musso D (2014) Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014. Euro Surveill 19(13):20751

Bhardwaj U, Pandey N, Rastogi M, Singh SK (2021) Gist of Zika virus pathogenesis. Virology 560:86–95. https://doi.org/10.1016/j.virol.2021.04.008

Blitzer EJ, Vyazunova I, Lan Q (2005) Functional analysis of AeSCP-2 using gene expression knockdown in the yellow fever mosquito. Aedes Aegypti Insect Molecular Biology 14(3):301–307. https://doi.org/10.1111/j.1365-2583.2005.00560.x

Bona ACD, Chitolina RF, Fermino ML, de Castro PL, Weiss A, Lima JBP, Baldi N, Bernardes ES, Henen J, Maori E (2016) Larval application of sodium channel homologous dsRNA restores pyrethroid insecticide susceptibility in a resistant adult mosquito population. Parasit Vectors 9(1):1–14. https://doi.org/10.1186/s13071-016-1634-y

Bryant B, Raikhel AS (2011) Programmed autophagy in the fat body of Aedes aegypti is required to maintain egg maturation cycles. PloS one 6(11):e25502. https://doi.org/10.1371/journal.pone.0025502

Chen J, Lu HR, Zhang L, Liao CH, Han Q (2019) RNA interference-mediated knockdown of 3, 4-dihydroxyphenylacetaldehyde synthase affects larval development and adult survival in the mosquito Aedes aegypti. Parasit Vectors 12(1):1–11. https://doi.org/10.1186/s13071-019-3568-7

Cortes-Escamilla A, Roche B, Rodríguez-López MH, Gatell-Ramírez HL, Alpuche-Aranda CM (2022) Spatiotemporal patterns of dengue and Zika incidence during the 2015–2018 outbreak of Zika in Mexico. Salud pública de méxico 64(5 Sept-Oct):478–487

Cossaboom CM, Nyakarahuka L, Mulei S, Kyondo J, Tumusiime A, Baluku J, Akurut GG, Namanya D, Kamugisha K, Nansikombi HT, Nyabakira A, Mutesasira S, Whitmer S, Telford C, Lutwama J, Balinandi S, Montgomery J, Klena JD, Shoemaker T (2022) Rift Valley fever outbreak during COVID-19 surge, Uganda, 2021. Emerg Infect Dis 28(11):2290–2293. https://doi.org/10.3201/eid2811.220364

Couto-Lima D, Madec Y, Bersot MI, Campos SS, Motta MDA, Santos FBD, Vazeille M, Vasconcelos PFC, de-Oliveira RL, Failloux AB (2017) Potential risk of re-emergence of urban transmission of yellow fever virus in Brazil facilitated by competent Aedes populations. Sci Rep 7(1):1–12. https://doi.org/10.1038/s41598-017-05186-3

Das S, Debnath N, Cui Y, Unrine J, Palli SR (2015) Chitosan, carbon quantum dot, and silica nanoparticle mediated dsRNA delivery for gene silencing in Aedes aegypti: a comparative analysis. ACS Appl Mater Interfaces 7(35):19530–19535. https://doi.org/10.1021/acsami.5b05232

Dhandapani RK, Gurusamy D, Howell JL, Palli SR (2019) Development of CS-TPP-dsRNA nanoparticles to enhance RNAi efficiency in the yellow fever mosquito. Aedes Aegypti Sci Rep 9(1):1–11. https://doi.org/10.1038/s41598-019-45019-z

Dick OB, San Martín JL, Montoya RH, del Diego J, Zambrano B, Dayan GH (2012) The history of dengue outbreaks in the Americas. Am J Trop Med Hyg 87(4):584. https://doi.org/10.4269/ajtmh.2012.11-0770

Dong D, Zhang Y, Smykal V, Ling L, Raikhel AS (2018) HR38, an ortholog of NR4A family nuclear receptors, mediates 20-hydroxyecdysone regulation of carbohydrate metabolism during mosquito reproduction. Insect Biochem Mol Biol 96:19–26. https://doi.org/10.1016/j.ibmb.2018.02.003

Du MH, Yan ZW, Hao YJ, Yan ZT, Si FL, Chen B, Qiao L (2017) Suppression of Laccase 2 severely impairs cuticle tanning and pathogen resistance during the pupal metamorphosis of Anopheles sinensis (Diptera: Culicidae). Parasit Vectors 10(1):1–11. https://doi.org/10.1186/s13071-017-2118-4

Duffy MR, Chen TH, Hancock WT, Powers AM, Kool JL, Lanciotti RS, Pretrick M, Marfel M, Holzbauer S, Dubray C, Guillaumot L, Griggs A, Bel M, Lambert AJ, Laven J, Kosoy O, Panella A, Biggerstaff BJ, Fischer M, Hayes EB (2009) Zika virus outbreak on Yap Island, federated states of Micronesia. N Engl J Med 360(24):2536–2543. https://doi.org/10.1056/NEJMoa0805715

Durant AC, Donini A (2020) Ammonium transporter expression in sperm of the disease vector Aedes aegypti mosquito influences male fertility. Proc Natl Acad Sci 117(47):29712–29719. https://doi.org/10.1073/pnas.2011648117

Dwibedi B, Mohapatra N, Rathore SK, Panda M, Pati SS, Sabat J, Thakur B, Panda S, Kar SK (2015) An outbreak of Japanese encephalitis after two decades in Odisha. India. Indian J Med Res 142(Suppl 1):S30–S32. https://doi.org/10.4103/0971-5916.176609

Estep AS, Sanscrainte ND, Becnel JJ (2016) DsRNA-mediated targeting of ribosomal transcripts RPS6 and RPL26 induces long lasting and significant reductions in fecundity of the vector Aedes aegypti. J Insect Physiol 90:17–26. https://doi.org/10.1016/j.jinsphys.2016.05.001

European Centre for Disease Prevention and Control (ECDPC) (2016) Scientist share data from ECDPC- Zika virus epidemic in the Americas: potential association with microcephaly and Guillain-Barré syndrome (first update). https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/zika-virus-americas-association-withmicrocephaly-rapid-risk-assessment.pdf. Accessed Mar 2023

European Centre for Disease Prevention and Control (ECDPC) (2020) Scientists share data from ECDPC-Malaria Annual Epidemiological Report. https://www.ecdc.europa.eu/sites/default/files/documents/AER-malaria-2020.pdf. Accessed Mar 2023

European Centre for Disease Prevention and Control (ECDPC) (2021) Scientists share data from ECDPC-Communicable disease threats report. https://www.ecdc.europa.eu/sites/default/files/documents/Communicable-disease-threats-report-21-aug-public.pdf. Accessed Mar 2023

European Centre for Disease Prevention and Control (ECDPC) (2022) Scientists share data from ECDPC - Weekly Update: 2022 West Nile Transmission. https://www.ecdc.europa.eu/en/west-nile-fever/surveillance-and-disease-data/disease-data-ecdc. Accessed Mar 2023

Fei X, Zhang Y, Ding L, Li Y, Deng X (2020) Controlling the development of the dengue vector Aedes aegypti using HR3 RNAi transgenic Chlamydomonas. Plos One 15(10):e0240223. https://doi.org/10.1371/journal.pone.0240223

Fei X, Zhang Y, Ding L, Xiao S, Xie X, Li Y, Deng X (2021) Development of an RNAi-based microalgal larvicide for the control of Aedes aegypti. Parasit Vectors 14(1):1–11. https://doi.org/10.1186/s13071-021-04885-1

Ferdous Z, Fuchs S, Behrends V, Trasanidis N, Waterhouse RM, Vlachou D, Christophides GK (2021) Anopheles coluzzii stearoyl-CoA desaturase is essential for adult female survival and reproduction upon blood feeding. PLoS Pathogens 17(5):e1009486. https://doi.org/10.1371/journal.ppat.1009486

Figueira-Mansur J, Ferreira-Pereira A, Mansur JF, Franco TA, Alvarenga ESL, Sorgine MHF, Neves BC, Melo ACA, Leal WS, Masuda H, Moreira MF (2013) Silencing of P-glycoprotein increases mortality in temephos-treated Aedes aegypti larvae. Insect Mol Biol 22(6):648–658. https://doi.org/10.1111/imb.12052

Fire A, Xu S, Montgomery MK, Kostas SA, Driver SE, Mello CC (1998) Patent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans. Nature 391(6669):206–211. https://doi.org/10.1038/35888

Franklinos LH, Jones KE, Redding DW, Abubakar I (2019) The effect of global change on mosquito-borne disease. Lancet Infect Dis 19(9):e302–e312. https://doi.org/10.1016/S1473-3099(19)30161-6

Garske T, Van Kerkhove MD, Yactayo S, Ronveaux O, Lewis RF, Staples JE, Perea W, Ferguson NM, Committee YFE (2014) Yellow fever in Africa: estimating the burden of disease and impact of mass vaccination from outbreak and serological data. PLoS Med 11(5):e1001638. https://doi.org/10.1371/journal.pmed.1001638

Hansen IA, Attardo GM, Roy SG, Raikhel AS (2005) Target of rapamycin-dependent activation of S6 kinase is a central step in the transduction of nutritional signals during egg development in a mosquito. J Biol Chem 280(21):20565–20572. https://doi.org/10.1074/jbc.M500712200

Hapairai LK, Mysore K, Sun L, Li P, Wang CW, Scheel ND, Lesnik A, Scheel MP, Igiede J, Wei N, Severson DW, Duman-Scheel M (2020) Characterization of an adulticidal and larvicidal interfering RNA pesticide that targets a conserved sequence in mosquito G protein-coupled dopamine 1 receptor genes. Insect Biochem Mol Biol 120:103359. https://doi.org/10.1016/j.ibmb.2020.103359

Ingelbeen B, Weregemere NA, Noel H, Tshapenda GP, Mossoko M, Nsio J, Ronsse A, Ahuka-Mundeke S, Cohuet S, Kebela BI (2018) Urban yellow fever outbreak—Democratic Republic of the Congo, 2016: towards more rapid case detection. PLoS Negl Trop Dis 12(12):e0007029. https://doi.org/10.1371/journal.pntd.0007029

Integrated Disease Surveillance Program (IDSP) (2018) Scientists share data from IDSP-Weekly outbreak report. https://idsp.nic.in/WriteReadData/l892s/442018.pdf. Accessed Mar 2023

Islam MT, Rahman M, Sadia FJ (2022) Outbreak of dengue amid the COVID-19 pandemic: an emerged crisis for Bangladesh. Asia Pac J Public Health 34(4):467–468. https://doi.org/10.1177/10105395211072841

Isoe J, Collins J, Badgandi H, Day WA, Miesfeld RL (2011) Defects in coatomer protein I (COPI) transport cause blood feeding induced mortality in Yellow Fever mosquitoes. Proc Natl Acad Sci 108(24):E211–E217. https://doi.org/10.1073/pnas.1102637108

Khalil SM, Munawar K, Alahmed AM, Mohammed AM (2021) RNAi-mediated screening of selected target genes against Culex quinquefasciatus (Diptera: Culicidae). J Med Entomol 58(6):2177–2185. https://doi.org/10.1093/jme/tjab114

Kraemer MU, Reiner RC Jr, Brady OJ, Messina JP, Gilbert M, Pigott DM, Yi D, Johnson K, Earl L, Marczak LB, Shirude S, Weaver ND, Bisanzio D, Perkins TA, Lai S, Lu X, Jones P, Coelho GE, Carvalho RG et al (2019) Past and future spread of the arbovirus vectors Aedes aegypti and Aedes albopictus. Nat Microbiol 4(5):854–863. https://doi.org/10.1038/s41564-019-0440-7

Kumar A, Wang S, Ou R, Samrakandi M, Beerntsen BT, Sayre RT (2013) Development of an RNAi based microalgal larvicide to control mosquitoes. Malaria World J 4(6):1–7. https://doi.org/10.1186/s13071-021-04885-1

Kumar DR, Kumar PS, Gandhi MR, Al-Dhabi NA, Paulraj MG, Ignacimuthu S (2016) Delivery of chitosan/dsRNA nanoparticles for silencing of wing development vestigial (vg) gene in Aedes aegypti mosquitoes. Int J Biol Macromol 86:89–95. https://doi.org/10.1016/j.ijbiomac.2016.01.030

Kumari S, Tevatiya S, Rani J, Das De T, Chauhan C, Sharma P, Sah R, Singh S, Pandey KC, Pande V, Dixit R (2022) A testis-expressing heme peroxidase HPX12 regulates male fertility in the mosquito Anopheles stephensi. Sci Rep 12(1):1–13. https://doi.org/10.1038/s41598-022-06531-x

Letinić BD, Dahan-Moss Y, Koekemoer LL (2020) Characterising the effect of Akirin knockdown on Anopheles arabiensis (Diptera: Culicidae) reproduction and survival, using RNA-mediated interference. PloS one 15(2):e0228576. https://doi.org/10.1371/journal.pone.0228576

Li M, Yan C, Jiao Y, Xu Y, Bai C, Miao R, Jiang J, Liu J (2022) Site-directed RNA editing by harnessing ADARs: advances and challenges. Funt Integr Genomics 22(6):1089–1103. https://doi.org/10.1007/s10142-022-00910-3

Lindsey NP, Staples JE, Lehman JA, Fischer M (2010) Surveillance for human West Nile virus disease—United states, 1999–2008. MMWR Surveill Summ 59(2):1–17

Liu WT, Tu WC, Lin CH, Yang UC, Chen CC (2017) Involvement of cecropin B in the formation of the Aedes aegypti mosquito cuticle. Sci Rep 7(1):1–17. https://doi.org/10.1038/s41598-017-16625-6

Lopez SBG, Guimarães-Ribeiro V, Rodriguez JVG, Dorand FA, Salles TS, Sá-Guimarães TE, Alvarenga ESL, Melo ANA, Almeida RV, Moreira MF (2019) RNAi-based bioinsecticide for Aedes mosquito control. Sci Rep 9(1):1–13. https://doi.org/10.1038/s41598-019-39666-5

Lumjuan N, Rajatileka S, Changsom D, Wicheer J, Leelapat P, Prapanthadara LA, Somboon P, Lycett G, Ranson H (2011) The role of the Aedes aegypti Epsilon glutathione transferases in conferring resistance to DDT and pyrethroid insecticides. Insect Biochem Mol Biol 41(3):203–209. https://doi.org/10.1016/j.ibmb.2010.12.005

Maharaj S, Ekoka E, Erlank E, Nardini L, Reader J, Birkholtz LM, Koekemoer LL (2022) The ecdysone receptor regulates several key physiological factors in Anopheles funestus. Malar J 21(1):1–13. https://doi.org/10.1186/s12936-022-04123-8

Mansfield KL, Banyard AC, McElhinney L, Johnson N, Horton DL, Hernández-Triana LM, Fooks AR (2015) Rift Valley fever virus: a review of diagnosis and vaccination, and implications for emergence in Europe. Vaccine 33(42):5520–5531. https://doi.org/10.1016/j.vaccine.2015.08.020

McDonald E, Mathis S, Martin SW, Staples JE, Fischer M, Lindsey NP (2021) Surveillance for West Nile virus disease—United States, 2009–2018. Am J Transplant 21(5):1959–1974. https://doi.org/10.1111/ajt.16595

McMillen CM, Hartman AL (2018) Rift Valley fever in animals and humans: current perspectives. Antiviral Res 156:29–37. https://doi.org/10.1016/j.antiviral.2018.05.009

McNaughton H, Singh A, Khan SA (2018) An outbreak of Japanese encephalitis in a non-endemic region of north-east India. J Royal College Phys Edinburgh 48(1):25–29. https://doi.org/10.4997/JRCPE.2018.10

Meleshkevitch EA, Voronov DA, Miller MM, Penneda M, Fox JM, Metzler R, Boudko DY (2013) A novel eukaryotic Na+methionine selective symporter is essential for mosquito development. Insect Biochem Mol Biol 43(8):755–767. https://doi.org/10.1016/j.ibmb.2013.05.008

Mir D, Delatorre E, Bonaldo M, Lourenço-de-Oliveira R, Vicente AC, Bello G (2017) Phylodynamics of yellow fever virus in the Americas: new insights into the origin of the 2017 Brazilian outbreak. Sci Rep 7(1):7385. https://doi.org/10.1038/s41598-017-07873-7

Moretti DM, Ahuja LG, Nunes RD, Cudischevitch CO, Daumas-Filho CRO, Medeiros-Castro P, Ventura-Martins G, Jablonka W, Gazos-Lopes F, Senna R, Sorgine MHF, Hartfelder K, Capurro M, Atella GC, Mesquita RD, Silva-Neto MAC (2014) Molecular analysis of Aedes aegypti classical protein tyrosine phosphatases uncovers an ortholog of mammalian PTP-1B implicated in the control of egg production in mosquitoes. PloS One 9(8):e104878. https://doi.org/10.1371/journal.pone.0104878

Munawar K, Alahmed AM, Khalil SMS (2020) Delivery methods for RNAi in mosquito larvae. J Insect Sci 20(4):12. https://doi.org/10.1093/jisesa/ieaa074

Mysore K, Flannery EM, Tomchaney M, Severson DW, Duman-Scheel M (2013) Disruption of Aedes aegypti olfactory system development through chitosan/siRNA nanoparticle targeting of semaphorin-1a. PLoS Negl Trop Dis 7(5):e2215. https://doi.org/10.1371/journal.pntd.0002215

Mysore K, Hapairai LK, Sun L, Harper EI, Chen Y, Eggleson KK, Realey JS, Scheel ND, Severson DW, Wei N, Duman-Scheel M (2017) Yeast interfering RNA larvicides targeting neural genes induce high rates of Anopheles larval mortality. Malar J 16(1):461. https://doi.org/10.1186/s12936-017-2112-5

Mysore K, Li P, Wang CW, Hapairai LK, Scheel ND, Realey JS, Sun L, Roethele JB, Severson DW, Wei N, Duman-Scheel M (2019a) Characterization of a yeast interfering RNA larvicide with a target site conserved in the synaptotagmin gene of multiple disease vector mosquitoes. PLoS Negl Trop Dis 13(5):e0007422. https://doi.org/10.1371/journal.pntd.0007422

Mysore K, Li P, Wang CW, Hapairai LK, Scheel ND, Realey JS, Sun L, Severson DW, Wei N, Duman-Scheel M (2019b) Characterization of a broad-based mosquito yeast interfering RNA larvicide with a conserved target site in mosquito semaphorin-1a genes. Parasit Vectors 12(1):256. https://doi.org/10.1186/s13071-019-3504-x

Mysore K, Hapairai LK, Sun L, Li P, Wang CW, Scheel ND, Lesnik A, Igiede J, Scheel MP, Wei N, Severson DW, Duman-Scheel M (2020) Characterization of a dual-action adulticidal and larvicidal interfering RNA pesticide targeting the Shaker gene of multiple disease vector mosquitoes. PLoS Negl Trop Dis. 14(7):e0008479. https://doi.org/10.1371/journal.pntd.0008479

Mysore K, Sun L, Hapairai LK, Wang CW, Roethele JB, Igiede J, Scheel MP, Scheel ND, Li P, Wei N, Severson DW, Duman-Scheel M (2021) A broad-based mosquito yeast interfering RNA pesticide targeting Rbfox1 represses Notch signaling and kills both larvae and adult mosquitoes. Pathogens. 10(10):1251. https://doi.org/10.3390/pathogens10101251

Nabatanzi M, Ntono V, Kamulegeya J, Kwesiga B, Bulage L, Lubwama B, Ario AR, Harris J (2022) Malaria outbreak facilitated by increased mosquito breeding sites near houses and cessation of indoor residual spraying, Kole district, Uganda, January-June 2019. BMC Public Health 22(1):1898. https://doi.org/10.1186/s12889-022-14245-y

Negri A, Ferrari M, Nodari R, Coppa E, Mastrantonio V, Zanzani S, Porretta D, Bandi C, Urbanelli S, Epis S (2019) Gene silencing through RNAi and antisense Vivo-Morpholino increases the efficacy of pyrethroids on larvae of Anopheles stephensi. Malar J 18(1):294. https://doi.org/10.1186/s12936-019-2925-5

Niriella MA, Ediriweera DS, De Silva AP, Premarathna BHR, Jayasinghe S, De Silva HJ (2021) Dengue and leptospirosis infection during the coronavirus 2019 outbreak in Sri Lanka. Trans R Soc Trop Med Hyg 115(9):944–946. https://doi.org/10.1093/trstmh/trab058

Nomhwange T, Jean Baptiste AE, Ezebilo O, Oteri J, Olajide L, Emelife K, Hassan S, Nomhwange ER, Adejoh K, Ireye F, Nora EE, Ningi A, Bathondeli B, Tomori O (2021) The resurgence of yellow fever outbreaks in Nigeria: a 2-year review 2017–2019. BMC Infect Dis 21(1):1054. https://doi.org/10.1186/s12879-021-06727-y

Ojani R, Fu X, Ahmed T, Liu P, Zhu J (2018) Krüppel homologue 1 acts as a repressor and an activator in the transcriptional response to juvenile hormone in adult mosquitoes. Insect Mol Biol 27(2):268–278. https://doi.org/10.1111/imb.12370

Ong SQ, Pauzi MBM, Gan KH (2022) Text mining in mosquito-borne disease: A systematic review. Acta Trop 231:106447. https://doi.org/10.1016/j.actatropica.2022.10644

Pan American Health Organisation (PAHO) (2016) Scientists share data from PHAO. https://www3.paho.org/hq/index.php?option=com_content&view=article&id=11599:regional-zika-epidemiological-updateamericas&Itemid=41691&lang=en#gsc.tab=0

Pascini TV, Ramalho-Ortigão M, Ribeiro JM, Jacobs-Lorena M, Martins GF (2020) Transcriptional profiling and physiological roles of Aedes aegypti spermathecal-related genes. BMC Genomics 21(1):1–18. https://doi.org/10.1186/s12864-020-6543-y

Pielnaa P, Al-Saadawe M, Saro A, Dama MF, Zhou M, Huang Y, Huang J, Xia Z (2020) Zika virus-spread, epidemiology, genome, transmission cycle, clinical manifestation, associated challenges, vaccine and antiviral drug development. Virology 543:34–42. https://doi.org/10.1016/j.virol.2020.01.015

Public Health Agency of Canada (PHAC) (2022) Scientists share data from PHAC- Surveillance of West Nile virus. https://www.canada.ca/en/public-health/services/diseases/west-nile-virus/surveillance-west-nile-virus.html. Accessed Mar 2023

Qiao L, Du M, Liang X, Hao Y, He X, Si F, Mei T, Chen B (2016) Tyrosine hydroxylase is crucial for maintaining pupal tanning and immunity in Anopheles sinensis. Sci Rep 6(1):29835. https://doi.org/10.1038/srep29835

Rana MS, Ikram A, Alam MM, Salman M (2021) Novel coronavirus outbreak in Pakistan: beware of dengue. J Formos Med Assoc 120(1):765. https://doi.org/10.1016/j.jfma.2020.07.027

Rani J, De TD, Chauhan C, Kumari S, Sharma P, Tevatiya S, Chakraborti S, Pandey KC, Singh N, Dixit R (2022) Functional disruption of transferrin expression alters reproductive physiology in Anopheles culicifacies. PLoS One 17(3):e0264523. https://doi.org/10.1371/journal.pone.0264523

Raphemot R, Estévez-Lao TY, Rouhier MF, Piermarini PM, Denton JS, Hillyer JF (2014) Molecular and functional characterization of Anopheles gambiae inward rectifier potassium (Kir1) channels: a novel role in egg production. Insect Biochem Mol Biol 51:10–19. https://doi.org/10.1016/j.ibmb.2014.05.002

Regna K, Harrison RM, Heyse SA, Chiles TC, Michel K, Muskavitch MA (2016) RNAi trigger delivery into Anopheles gambiae pupae. JoVE (Journal of Visualized Experiments) 109:e53738. https://doi.org/10.3791/53738

Reis RS (2017) The entangled history of animal and plant microRNAs. Funct Integr Genomics 17(2–3):127–134. https://doi.org/10.1007/s10142-016-0513-0

Rodríguez JCP, Olivera MJ, Herrera MCP, Abril EP (2022) Malaria epidemics in Colombia, 1970–2019. Rev Soc Bras de Med Trop 55:e05592021. https://doi.org/10.1590/0037-8682-0559-2021

Roth A, Mercier A, Lepers C, Hoy D, Duituturaga S, Benyon E, Guillaumot L, Souares Y (2014) Concurrent outbreaks of dengue,

chikungunya and Zika virus infections–an unprecedented epidemic wave of mosquito-borne viruses in the Pacific 2012–2014. Euro Surveill 19(41):20929. https://doi.org/10.2807/1560-7917.es2014.19.41.20929

Roy SG, Raikhel AS (2011) The small GTPase Rheb is a key component linking amino acid signaling and TOR in the nutritional pathway that controls mosquito egg development. Insect Biochem Mol Biol 41(1):62–69. https://doi.org/10.1016/j.ibmb.2010.10.001

Seo HJ, Kim HC, Klein TA, Ramey AM, Lee JH, Kyung SG, Park JY, Cho YS, Cho IS, Yeh JY (2013) Molecular detection and genotyping of Japanese encephalitis virus in mosquitoes during a 2010 outbreak in the Republic of Korea. PloS One 8(2):e55165. https://doi.org/10.1371/journal.pone.0055165

Singh AD, Wong S, Ryan CP, Whyard S (2013) Oral delivery of double-stranded RNA in larvae of the yellow fever mosquito, Aedes aegypti: Implications for Pest Mosquito Control. J Insect Sci 13:69. https://doi.org/10.1673/031.013.6901

Sultana N, Raul PK, Goswami D, Das D, Islam S, Tyagi V, Das B, Gogoi HK, Chattopadhyay P, Raju PS (2020) Bio-nanoparticle assembly: a potent on-site biolarvicidal agent against mosquito vectors. RSC Adv 10(16):9356–9368. https://doi.org/10.1039/c9ra09972g

Taracena ML, Hunt CM, Benedict MQ, Pennington PM, Dotson EM (2019) Downregulation of female doublesex expression by oral-mediated RNA interference reduces number and fitness of Anopheles gambiae adult females. Parasit Vectors 12(1):1–11. https://doi.org/10.1186/s13071-019-3437-4

Tevatiya S, Kumari S, Sharma P, Rani J, Chauhan C, De TD, Pandey KC, Pande V, Dixit R (2020) Molecular and functional characterization of trehalase in the mosquito anopheles stephensi. Front Physiol 11:575718. https://doi.org/10.3389/fphys.2020.575718

Tsao IY, Lin US, Christensen BM, Chen CC (2009) Armigeres subalbatus prophenoloxidase III: cloning, characterization and potential role in morphogenesis. Insect Biochem Mol Biol 39(2):96–104. https://doi.org/10.1016/j.ibmb.2008.10.007

Tuells J, Henao-Martínez AF, Franco-Paredes C (2022) Yellow fever: a perennial threat. Arch Med Res 53(7):649–657. https://doi.org/10.1016/j.arcmed.2022.10.005

Uchenna Emeribe A, Nasir Abdullahi I, Ajagbe OR, Egede Ugwu C, Oloche Onoja S, Dahiru Abubakar S, Umeozuru CM, Animasaun OS, Omosigho PO, Danmusa UM, MAB M, Aminu MS, Yahaya H, Oyewusi S (2021) Incidence, drivers and global health implications of the 2019/2020 yellow fever sporadic outbreaks in Sub-Saharan Africa. Pathog Dis 79(4):ftab017. https://doi.org/10.1093/femspd/ftab017

Vahey GM, Mathis S, Martin SW, Gould CV, Staples JE, Lindsey NP (2021) West Nile virus and other domestic nationally notifiable arboviral diseases—United States, 2019. Morb Mortal Wkly Rep 70(32):1069. https://doi.org/10.15585/mmwr.mm7032a1

Vairo F, Haider N, Kock R, Ntoumi F, Ippolito G, Zumla A (2019) Chikungunya: epidemiology, pathogenesis, clinical features, management, and prevention. Infect Dis Clin 33(4):1003–1025. https://doi.org/10.1016/j.idc.2019.08.006

Van Ekert E, Powell CA, Shatters RG Jr, Borovsky D (2014) Control of larval and egg development in Aedes aegypti with RNA interference against juvenile hormone acid methyl transferase. J Insect Physiol 70:143–150. https://doi.org/10.1016/j.jinsphys.2014.08.001

Wang LH, Fu SH, Wang HY, Liang XF, Cheng JX, Jing HM, Cai GL, Li XW, Ze WY, Lv XJ, Wang HQ, Zhang DL, Feng Y, Yin ZD, Sun XH, Shui TJ, Li MH, Li YX, Liang GD (2007) Japanese encephalitis outbreak, Yuncheng, China, 2006. Emerg Infect Dis 13(7):1123–1125. https://doi.org/10.3201/eid1307.070010

Wang JL, Saha TT, Zhang Y, Zhang C, Raikhel AS (2017) Juvenile hormone and its receptor methoprene-tolerant promote ribosomal biogenesis and vitellogenesis in the Aedes aegypti mosquito. J Biol Chem 292(24):10306–10315. https://doi.org/10.1074/jbc.M116.761387

Weng SC, Shiao SH (2015) Frizzled 2 is a key component in the regulation of TOR signaling-mediated egg production in the mosquito Aedes aegypti. Insect Biochem Mol Biol 61:17–24. https://doi.org/10.1016/j.ibmb.2015.03.010

Whyard S, Erdelyan CN, Partridge AL, Singh AD, Beebe NW, Capina R (2015) Silencing the buzz: a new approach to population suppression of mosquitoes by feeding larvae double-stranded RNAs. Parasit Vectors 8(1):1–11. https://doi.org/10.1186/s13071-015-0716-6

World Health Organization (2019). WHO Region of the Americas records highest number of dengue cases in history; cases spike in other regions. Retrived from https://www.who.int/news/item/21-11-2019-who-region-of-the-americas-records-highest-number-of-dengue-cases-in-history-cases-spike-in-other-regions. Last Accessed 20 Dec 2022

World Health Organization (WHO) (2000) Scientists share data from WHO- West Nile Fever-Israel. https://www.who.int/emergencies/disease-outbreak-news/item/2000_09_22-en. Accessed March 2023

World Health Organization (WHO) (2005) Scientists share data from WHO - Japanese Encephalitis-India. https://www.who.int/emergencies/disease-outbreak-news/item/2005_09_13a-en. Accessed Dec 2022

World Health Organization (WHO) (2019) Scientists share data from WHO - South Sudan Yellow fever. https://www.who.int/emergencies/emergency-events/item/yellow-fever. Accessed Mar 2023

World Health Organization (WHO) (2020a) Scientists share data from WHO-Vector borne Disease. https://www.who.int/newsroom/fact-sheets/detail/vector-borne-diseases.. Accessed Dec 2022

World Health Organization (WHO) (1996) Scientists share data from WHO - 1996- Nepal. https://www.who.int/emergencies/disease-outbreak-news/item/1996_10_04-en. Accessed Dec 2022.

World Health Organization (WHO) (2020b) Scientists share data from WHO -Yellow fever Senegal. https://www.who.int/emergencies/disease-outbreak-news/item/2020-DON303. Accessed Dec 2022

World Health Organization (WHO) (2020c) Scientists share data from WHO- Yellow fever Uganda. https://www.who.int/emergencies/disease-outbreak-news/item/2020-DON249. Accessed Mar 2023

World Health Organization (WHO) (2020d) Scientists share data from WHO- Yellow fever Guinea. https://www.who.int/emergencies/disease-outbreak-news/item/2020-DON302. Accessed Dec 2022

World Health Organization (WHO) (2020e) Scientists share data from WHO- Yellow fever South Sudan. https://www.who.int/emergencies/disease-outbreak-news/item/2020-DON262. Accessed Mar 2023

World Health Organization (WHO) (2020f) Scientists share data from WHO Yellow fever- Ethiopia. https://www.who.int/emergencies/disease-outbreak-news/item/2020-DON263. Accessed Mar 2023

World Health Organization (WHO) (2021a) Scientists share data from WHO. https://www.who.int. Accessed Dec 2022

World Health Organization (WHO) (2021b) Scientists share data from WHO- Dengue fever Pakistan. https://www.who.int/emergencies/disease-outbreak-news/item/dengue-fever-pakistan. Accessed Mar 2023

World Health Organization (WHO) (2022a) Scientists share data from WHO - Malaria- Pakistan. https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON413. Accessed Dec 2022

World Health Organization (WHO) (2022b) Scientists share data from WHO - Dengue Pakistan. https://www.who.int/emergencies/disease-outbreak-news/item/2022i-DON414. Accessed Dec 2022

World Health Organization (WHO) (2022c) Scientists share data from WHO - Dengue-Nepal. https://www.who.int/emergencies/disease-outbreak-news/item/2022h-DON412. Accessed Dec 2022

World Health Organization (WHO) (2022d) Scientists share data from WHO - Lymphatic filariasis (Elephentiasis). https://www.who.int/health-topics/lymphatic-filariasis#tab=tab_1. Accessed Dec 2022

World Health Organization (WHO) (2022e) Scientists share data from WHO - Rift valley fever - Mauritiania. https://www.who.int/emergencies/disease-outbreak-news/item/2022k-DON417. Accessed Dec 2022

World Health Organization (WHO) (2022f) Scientists share data from WHO - Dengue Timor-Leste. https://www.who.int/emergencies/disease-outbreak-news/item/dengue%2D%2D-timor-leste. Accessed Dec 2022

World Health Organization (WHO) (2022g) Scientists share data from WHO - Japanese enephalitis Australia. https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON365. Accessed Dec 2022

World Health Organization (WHO) (2022h) Scientists share data from WHO - Dengue and severe dengue. https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue. Accessed Dec 2022

World Health Organization (WHO) (2022i) Scientists share data from WHO - Dengue Bangladesh. https://www.who.int/emergencies/disease-outbreak-news/item/2022g-DON424. Accessed Dec 2022

World Health Organization (WHO) (2022j) Scientists share data from WHO - Dengue Sao Tome and Principe. https://www.who.int/emergencies/disease-outbreak-news/item/2022e-DON387. Accessed Dec 2022

World Health Organization Malaria Report (2022k) Scientists share data from https://www.who.int/publications/i/item/9789240064898

World Health Organization (WHO) (2023a) Scientists share data from WHO -Epidemiological update dengue, chikungunya and Zika. https://www.paho.org/en/documents/epidemiological-update-dengue-chikungunya-and-zika. Accessed Jan 2023

World Health Organization (WHO) (2023b) Scientists share data from WHO - Yellow fever African regions (AFRO). https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON431. Accessed Dec 2022

Youssouf H, Subiros M, Dennetiere G, Collet L, Dommergues L, Pauvert A, Rabarison P, Vauloup-Fellous C, Godais GL, Jaffar-Bandjee MC, Jean M, Paty MC, Noel H, Oliver S, Filleul L, Larsen C (2020) Rift valley fever outbreak, Mayotte, France, 2018–2019. Emerg Infect Dis 26(4):769–772. https://doi.org/10.3201/eid2604.191147

Zhang X, Zhang J, Zhu KY (2010) Chitosan/double-stranded RNA nanoparticle-mediated RNA interference to silence chitin synthase genes through larval feeding in the African malaria mosquito (Anopheles gambiae). Insect Mol Biol 19(5):683–693. https://doi.org/10.1111/j.1365-2583.2010.01029.x

Zhang X, Mysore K, Flannery E, Michel K, Severson DW, Zhu KY, Duman-Scheel M (2015) Chitosan/interfering RNA nanoparticle mediated gene silencing in disease vector mosquito larvae. J Vis Exp 97:52523. https://doi.org/10.3791/52523