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Current and proposed insect targets for gene drive development

A horizon scanning survey

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Summary of findings

- There are currently 32 insect targets from six different orders proposed or under development.¹
- While nine of the proposed insect targets are vectors of human disease², in particular malaria, the majority (21) are agricultural pests³, including four livestock pests or livestock disease vectors, which partially overlap with human disease vectors.
- Only three species are proposed as targets because of wider biodiversity impacts or combined economic loss and biodiversity impacts⁴, as well as one for forest management purposes and one for conservation⁵, the latter again overlapping with human disease vectors.
- The majority of gene drive proposals are based on eradication/suppression approaches. Only a very few are projects that are actually aiming to modify characteristics of insects in the wild.
- At the present time no projects are close to producing a usable and proven 'product'. But some are closer to potential field trials, pending on regulation, risk assessment and further (technical) developments.

Contextualisation

The emergence of gene drive technology opens-up unprecedented prospects of modifying, suppressing, or even eliminating wild species to serve human purposes. The consequences of choosing to go down this path are very difficult to foresee, especially in the longer term. To help frame further discussion on this topic, we have conducted a survey of gene drive development in insects, screening the the scientific literature up until April 2022. The survey also includes development of so-called 'x-shredders', a sex ratio distortion system with close similarities to gene drive technology.

We do not cover issues regarding risks, difficulties in performing robust risk assessments, or the lack of proven methods to confine, halt or reverse engineered gene drives.

Our survey gives an overview of:

- What research has taken place or is ongoing.
- Which species and taxa are current or proposed targets for gene drive development, and which types of gene drives are being put forward.⁶
- How far along developments have progressed and what the next stages of experimentation might be.

Summary of proposed insect targets

	Taxonomic Group	Taxonomic level	Common name	Number of proposed targets
*	CULICIDAE	family	mosquitoes	6
*	DIPTERA	order	flies - here excluding mosquitoes	10
* *	LEPIDOPTERA	order	moths, butterflies and skippers	2
۲	HEMIPTERA	order	true bugs	5
(*)	COLEOPTERA	order	beetles and weevils	5
* * * *	HYMENOPTERA	order	sawflies, bees, wasps and ants	3
*	THYSANOPTERA	order	thrips	1
	total			32

Detail of findings

The following table shows the detailed findings of our survey (pp. 3 - 17) and is sorted according to taxa, with those species or orders that are most advanced in gene drive development placed first. Please see page 17 for explanation of development levels of gene drives.

¹ The vast majority of the targets identified in the literature are single species or species complexes, however some early stage proposals relate to broader taxonomic groups, namely the *Glossina* genus (Testse flies - row 31), the *Scolytinae* subfamily (Bark beetles - row 44) and the *Thysanoptera* order (Thrips - row 51).

² All 6 mosquito species listed in rows 1-17, flies in rows 30 and 31, and the bug *Rhodnius prolixus* in rows 39-40.

³ Targets impacting crops are detailed in rows 18-25, 28, 32-38, 41-43, 45-47, 50-51; targets impacting livestock are listed in rows 26, 27, 29 and 31.

⁴ Targets impacting wider biodiversity (and economics) are detailed in rows 48-50.

⁵ Proposed targets for forestry are bark beetles in row 44, and for conservation is the mosquito *Culex quinquefasciatus*, a vector for bird malaria as well as for human and animal diseases, and listed in rows 13-15.

⁶ Many experimental gene drive systems are being developed and tested in the model organism *Drosophila melanogaster*. Because we are not aware of any plans to target this organism in the wild, a survey of work in this species is not included here but rather will be presented in a separate table.

	Species	Intended use	Type of gene drive (our categories)	Publications (where research	to e	expe	erim	is st enta						Project leader (corresponding author on publications)	Funders
	Geographic range (of target species)	Intended direct effect (of gene drive)	Developer's name for gene drive system	is described)	in t	he v	vild?	?						Institution	
	CULICIDAE (mosqu	uitoes) 🔭													
1	Anopheles gambiae African malaria mosquito Sub-Saharan	Reduction of transmission of malaria pathogen by this vector (to reduce morbidity and mortality from malaria in Sub-Saharan Africa) Population suppression	Autosomal sex distorter -'X-shredder' (I-Ppol based) 1 Synthetic sex ratio	 i. Galizi et al. 2014, ii. Facchinelli et al. 2019, iii. Bernardini et al. 2019 	1	2	3	4	5	6	7	8	9	A. Crisanti Imperial College + M.Q. Benedict CDC	Gates Foundation (via NIH); European Research Council
	Africa (Sinka et al 2012)		distortion system								-				
2			Homing CRISPR Gene drive targeting doublesex (<i>dsx</i> gene) or dsxF CRISPR gene drive	 i. Kyrou et al. 2018 ii. Hammond, Pollegioni, et al. 2021 iii. Garrood et al. 2021, Taxiarchi et al. 2021 	1	2	3	4	5	6	7	8	9	A. Crisanti Imperial College	Gates Foundation Open Philanthropy DARPA, BBSRC
3			Autosomal sex distorter - 'X-shredder' (CRISPR based) ¹ CRISPR-Cas9 sex ratio distortion system	Galizi et al. 2016	1	2	3	4	5	6	7	8	9	A. Crisanti Imperial College	Gates Foundation (via NIH)
4			Homing CRISPR + Sex Distorter (X-shredder) (male-biased) Sex- distorter gene drive (SDGD)	i. Simoni et al. 2020 ii. Garrood et al. 2021	1	2	3	4	5	6	7	8	9	A. Crisanti Imperial College	Gates Foundation

Species	Intended use	Type of gene drive (our categories)	Publications (where research	to	w cl expe	erime	ental						Project leader (corresponding author on publications)	Funders
Geographic range (of target species)	Intended direct effect (of gene drive)	Developer's name for gene drive system	is described)	in	the v	vild?							Institution	
		Homing CRISPR CRISPR-Cas9 gene drive system targeting female reproduction	 i. Hammond et al. 2015, ii. Hammond et al. 2017 iii. Garrood et al. 2021 	1	2	3	4	5	6	7	8	9	A. Crisanti Imperial College	Gates Foundatior (via NIH); European Research Counci
		Homing CRISPR CRISPR-Cas9 gene drive system targeting female reproduction	 i. Hammond, Karlsson, et al. 2021 ii. Garrood et al. 2021 iii. Taxiarchi et al. 2021 	1	2	3	4	5	6	7	8	9	A. Crisanti Imperial College	Gates Foundation
	Reduction of transmission of malaria pathogen by this vector (to reduce morbidity and mortality from malaria in Sub-Saharan Africa) Population modification	Homing CRISPR Cas9/gRNA gene drive	 i. Carballar-Lejarazú et al. 2020 ii. Carballar-Lejarazú et al. 2022 iii. Terradas et al. 2022 	1	2	3	4	5	6	7	8	9	A. James UC Irvine	Gates Foundation
	Population modification (to stop pathogen development within mosquito)	Split homing CRISPR variant (see technical table for details) Integral gene drive (IGD)	Hoermann et al. 2021	1	2	3	4	5	6	7	8	9	N. Windbichler Imperial College	Gates Foundation
Anopheles arabiensis	Reduction of transmission of malaria pathogen by this vector (to reduce morbidity and mortality from malaria in Sub-Saharan Africa)	Autosomal sex distorter -'X-shredder' ¹	Bernardini et al. 2019	1	2	3	4	5	6	7	8	9	A. Crisanti Imperial College	Gates Foundatior
Sub-Saharan Africa and a small part of Arabian peninsula - see map (Sinka et al 2012)	Population suppression	Synthetic sex ratio distortion system												

	Species Geographic range (of target species)	Intended use Intended direct effect (of gene drive)	Type of gene drive (our categories) Developer's name for gene drive system	Publications (where research is described)	to		erim	enta	train. / rele					Project leader (corresponding author on publications) Institution	Funders
10	Anopheles stephensi Asian malaria mosquito	Reduction of transmission of malaria pathogen by this vector (to reduce morbidity and mortality from malaria in India and surrounding regions)	Homing CRISPR	i. Gantz et al. 2015 ii. Pham et al. 2019	1	2	3	4	5	6	7	8	9	E. Bier & A. James UC San Diego, UC Irvine	NIH; Sarah Sandell and Michael Marshall; W. M. Keck Foundation; TATA Institute;
	Indian subcontinent and parts of middle east - see map (Sinka et al 2012)	Population modification to 'interrupt parasite transmission'	Cas9 mediated gene drive system for population modification												Gates Foundation; UC Irvine
11		Reduction of transmission of malaria pathogen by this vector Population modification – proof of principle	Homing CRISPR HDR based autonomous gene drive rescue system (HDR = homology directed repair)	i. Adolfi et al. 2020 ii. Terradas et al. 2022	1	2	3	4	5	6	7	8	9	A. James UC Irvine, US	NIH; TATA Institute; UC Irvine; DARPA
12	<i>Aedes aegypti</i> Yellow fever mosquito	Reduction of transmission of arboviruses (e.g. yellow fever, chikungunya, dengue, and Zika)	Split homing CRISPR gene drive	i. Li, Yang, et al. 2020 ii. Verkuijl et al. 2020 iii. Buchman et al. 2019	1	2	3	4	5	6	7	8	9	O. Akbari UC San Diego + L. Alphey	DARPA; UC Davis; US Centers for Disease Control
	'predicted to occur primarily in the tropics and sub-tropics, with concentrations in northern Brazil and southeast Asia including all of India'(Kraemer et al. 2015)	Population modification	CRISPR based split gene drive	iv. Buchman et al. 2020										Pirbright Institute	and Prevention (Li et al)

	Species Geographic range (of target species)	Intended use Intended direct effect (of gene drive)	Type of gene drive (our categories) Developer's name for gene drive system	Publications (where research is described)	to	expe		enta		/syst ease				Project leader (corresponding author on publications) Institution	Funders
13	<i>Culex quinquefasciatus</i> Southern house mosquito	Reduction of transmission of vector- borne diseases in humans, mammals and birds (e.g. avian malaria)	Unspecified - probably CRISPR based	 i. Anderson et al. 2020 ii. Anderson et al. 2019 iii. DARPA 2017 	1	2	3	4	5	6	7	8	9	L. Alphey Pirbright Institute [+ K. Esvelt MIT	DARPA; BBSRC; Welcome Trust
	(Samy et al 2016)	Unspecified	NA – preliminary studies only											On DARPA grant award]	
14			Unspecified - CRISPR based NA – preliminary study only	Feng et al. 2021	1	2	3	4	5	6	7	8	9	V. Gantz UC San Diego	UC San Diego; NIH; TATA
15			Unspecified - CRISPR based NA – preliminary study only	Li, Li, et al. 2020	1	2	3	4	5	6	7	8	9	O. Akbari University of California San Diego	In part: UC San Diego Start Up Funds
16	Anopheles funestus Predicted distribution	Reduction of transmission of malaria pathogen by this vector (to reduce morbidity and mortality from malaria in Sub-Saharan Africa)	Unspecified – probably would be derived from systems developed by Gates Foundation in <i>An.</i> <i>gambiae</i>	Ogola et al. 2019	1	2	3	4	5	6	7	8	9	D.P. Tchousassi International Centre of Insect Physiology and Ecology, Kenya	Gates Foundation (via NIH) DFiD Sida SDC
	(Sinka et al 2012)	Unspecified	NA – preliminary study only												Kenyan Govt
17		Morbidity and mortality from malaria in sub- Saharan Africa	Probably homing CRISPR – cites these drives as showing 'the most promise'	Quinn et al. 2021	1	2	3	4	5	6	7	8	9	T. Nolan Liverpool School of Tropical Medicine	BBSRC
		Not specified but does talk about 'control' of this vector	NA – preliminary study only												

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	Species	Intended use	Type of gene drive (our categories)	Publications (where research	Ho	ow cle expe	ose orim	is st enta	rain/ / rel(/syst	em			Project leader (corresponding	Funders
	Geographic range (of target species)	Intended direct effect (of gene drive)	Developer's name for gene drive system	is described)		the w					,			author on publications) Institution	
	DIPTERA (flies)	×									(this	order	r incl	ludes mosquitoes shown sep	arately above)
18	<i>Drosophila suzukii</i> Spotted wing drosophila (SWD)	Reduction of damage to soft fruit crops (e.g. cherries) caused by this species	MEDEA	Buchman et al. 2018	1	2	3	4	5	6	7	8	9	O. Akbari UC San Diego	California Cherry Board
	Bangladesh, Korea, Thailand. Spread into: Japan, Brazil, Argentine, Chile, Mexico, United States (esp. California), Canada, and Europe (esp. France) see map	Here providing proof of concept for MEDEA in <i>D. suzukii</i> for population suppression/ replacement	Synthetic <i>Medea</i> gene drive system												
	(Polo et al. 2016) (EPPO 2022)														
19		Reduction of damage to soft fruit crops (e.g. cherries) caused by this species	Propose homing CRISPR	Ni et al. 2021	1	2	3	4	5	6	7	8	9	J. Huang Zhejiang University,	Zhejiang Provincial Fund for Distinguished Young Scholars Fundamental
		Population suppression	NA – preliminary study only												Research Funds for the Zhejiang Provincial Universities
20	<i>Ceratitis capitata</i> Mediterranean fruit fly (medfly)	Reduction of damage to fruit crops caused by this species	Autosomal sex distorter - 'X-shredder'	Meccariello et al. 2021	1	2	3	4	5	6	7	8	9	N. Windbichler Imperial College	BBSRC BARD
	Africa, Mediterranean area Australasia, North and South America (FAO/IAEA 2017)	Population suppression	CRISPR based sex distortion												

	Species Geographic range (of target species)	Intended use Intended direct effect (of gene drive)	Type of gene drive (our categories) Developer's name for gene drive system	Publications (where research is described)	to	w cl e <i>xpe</i> the v	rime	enta						Project leader (corresponding author on publications) Institution	Funders
21			Homing CRISPR gene drive Cas9 based sex conversion suppression gene drive (note no constructs yet tested in <i>C. capitata</i>)	KaramiNejadRanjbar et al. 2018	1	2	3	4	5	6	7	8	9	E. Wimmer University of Gottingen	DAAD Excellence Foundation for the Promotion of the Max Planck Society IGI UC Berkeley DARPA
22			Preliminary study only, but development of CRISPR methods in this species points towards CRISPR based gene drive design NA – preliminary study only	Sim et al. 2019	1	2	3	4	5	6	7	8	9	S.M. Geib Daniel K. Inouye US Pacific Basin Agricultural Research Center	USDA
23	<i>Anastrepha ludens</i> Mexican fruit fly	Reduction of damage to fruit crops caused by this species	Preliminary study only, but development of CRISPR methods in this species points towards CRISPR based gene drive design	Sim et al. 2019	1	2	3	4	5	6	7	8	9	S.M. Geib Daniel K. Inouye US Pacific Basin Agricultural Research Center	USDA
	Mexico, Central America and parts of US (CABI 2022)	Population suppression	NA – preliminary study only												
24	<i>Bactrocera dorsalis</i> Oriental fruit fly	Reduction of damage to vegetable, fruit and nut crops caused by this species	Preliminary study only, but development of CRISPR methods in this species points towards CRISPR based gene drive design	Sim et al. 2019	1	2	3	4	5	6	7	8	9	S.M. Geib Daniel K. Inouye US Pacific Basin Agricultural Research Center	USDA
	(CABI 2022)	Population suppression	NA – preliminary study only												

	Species Geographic range	Intended use Intended direct effect	Type of gene drive (our categories) Developer's name for	Publications (where research is described)	to	w cl expe the v	erime	enta	rain, / rele	/sys ease	tem s			Project leader (corresponding author on publications)	Funders
	(of target species)	(of gene drive)	gene drive system											Institution	
25			Some form of CRISPR based gene drive	Zhao et al. 2019	1	2	3	4	5	6	7	8	9	R. Yan Hainan University	
			NA – preliminary study only												
26	<i>Cochliomyia hominivorax</i> New world screwworm	Reduction of disease and death of livestock caused by this species in South America and Caribbean	Propose homing CRISPR	i. Scott et al. 2020 ii. Paulo et al. 2019	1	2	3	4	5	6	7	8	9	M.J. Scott North Carolina State University	NCSU FAPESP USDA-ARS COPEG
	(CABI 2022)	Population suppression	NA – preliminary study only												STRI
27	<i>Lucilla cuprina</i> Australian sheep blowfly	Reduction of disease and death of livestock caused by this species in Australia and New Zealand	Probably homing CRISPR (in line with proposals for <i>C.</i> <i>hominivorax</i>)	Paulo et al. 2019	1	2	3	4	5	6	7	8	9	M.J. Scott North Carolina State University	FAPESP USDA-ARS COPEG STRI
	Throughout the world (needs warmer weather conditions)	Population suppression	NA – preliminary study only												
28	<i>Bactrocera oleae</i> Olive fruit fly	Reduction of harm to olive harvests caused by this species	Homing CRISPR	Koidou et al. 2020	1	2	3	4	5	6	7	8	9	J. Vontas Foundation for Research & Technology, Hellas, Greece	
	(CABI 2022)	Population suppression	NA – preliminary study only												

Lucilla sericata Green bottle fly Throughout the world Lutzomyia longipalpis	Reduction of disease and death of livestock caused by this species Population suppression	Propose Homing CRISPR	Davis et al. 2021	1	2	3								
-	Population suppression					5	4	5	6	7	8	9	M.J. Scott North Carolina State University	DARPA
Lutzomyia longipalpis		NA – preliminary study only												
species complex Sand Fly	Reduction in transmission of <i>Leishmania infantum</i> by this vector (to reduce occurrence of visceral leishmaniasis disease)	Propose homing CRISPR	Wellcome 2017	1	2	3	4	5	6	7	8	9	M. Yeo London School of Hygiene and Tropical Medicine	Wellcome
Primarily central and South America (Sosa- Estani and Leonor Segura 2015)	Population modification	NA – preliminary study only												
<i>Glossina</i> genus Tsetse flies	Reduction in transmission of trypanosome parasites by this vector (to reduce occurrence of sleeping sicknessin humans and livestock, esp. European cattle breeds.)	NA – proposal only	Bier 2022	1	2	3	4	5	6	7	8	9	E. Bier UC San Diego	NIH; Allan Frontiers Group Gates Foundatior TATA trusts
	Not stated – proposal only	NA – proposal only												
	South America (Sosa- Estani and Leonor Segura 2015) Glossina genus	Ieishmaniasis disease)Primarily central and South America (Sosa- Estani and Leonor Segura 2015)Population modificationGlossina genus Tsetse fliesReduction in transmission of trypanosome parasites by this vector (to reduce occurrence of sleeping sicknessin humans and livestock, esp. European cattle breeds.)Mot stated – proposal only	Ieishmaniasis disease)Primarily central and South America (Sosa- Estani and Leonor Segura 2015)Population modification onlyNA – preliminary study onlyGlossina genus Tsetse fliesReduction in transmission of trypanosome parasites by this vector (to reduce occurrence of sleeping sicknessin humans and livestock, esp. European cattle breeds.)NA – proposal onlyMot stated – proposal onlyNA – proposal only	leishmaniasis disease)Primarily central and South America (Sosa- Estani and Leonor Segura 2015)Population modification onlyNA – preliminary study onlyGlossina genus Tsetse fliesReduction in transmission of trypanosome parasites by this vector (to reduce occurrence of sleeping sicknessin humans and livestock, esp. European cattle breeds.)NA – proposal onlyBier 2022Image: ten state of the proposal onlyNA – proposal onlyBier 2022	leishmaniasis disease)NA - preliminary study onlyHeishmaniasis disease)Image: State of the state of t	Ieishmaniasis disease)NA - preliminary study onlyIeishmaniasis disease)Ieishmaniasis diseaseIeishmaniasis disease </td <td>Ieishmaniasis disease)NA - preliminary study onlyBier 2022I23Glossina genus Tsetse fliesReduction in transmission of trypanosome parasites by this vector (to reduce of sleeping sicknessin humans and livestock, esp. 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European cattle breeds.)12345678Image: Comparison of trypanosome parasites trypanosome parasites trypanosome parasites by this vector (to reduce trypanosome parasites trypanosome parasites trypanosome parasites trypanosome parasites trypanosome parasites trypanosome parasites8<t< td=""><td>Ieishmaniasis disease) NA - preliminary study only Bier 2022 1 2 3 4 5 6 7 8 9 Glossina genus Segura 2015) Reduction in transmission of trypanosome parasites by this vector (to reduce cattle breeds.) NA - proposal only Bier 2022 1 2 3 4 5 6 7 8 9 Mathematical breeds. NA - proposal only Bier 2022 1 2 3 4 5 6 7 8 9 Mathematical breeds. NA - proposal only Bier 2022 1 2 3 4 5 6 7 8 9 Mathematical breeds. NA - proposal only Bier 2022 1 2 3 4 5 6 7 8 9 Mathematical breeds. NA - proposal only NA - proposal only NA - proposal only 1 1 2 3 4 5 6 7 8 9 Mathematical breeds. 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	Species Geographic range (of target species)	Intended use Intended direct effect (of gene drive)	Type of gene drive (our categories) Developer's name for gene drive system	Publications (where research is described)	to	ow cl <i>expe</i> the v	erime	enta						Project leader (corresponding author on publications) Institution	Funders
	LEPIDOPTERA (mo	ths, butterflies and s	kippers) 😿	*											
32	<i>Plutella xylostella</i> Diamond back moth	Reduction of damage to cruciferous crops by this species	Split homing CRISPR	Xu et al. 2022	1	2	3	4	5	6	7	8	9	M.S. You Fujian Agriculture and Forestry University	BBSRC EU Chinese
	Top – year round range Bottom – seasonal range (Zalucki et al. 2012)	Not stated	CRISPR-Cas9 based gene drive in the diamondback moth											+ L. Alphey Pirbright Institute	government
33		Reduction of damage to cruciferous crops by this species	Drive type not specified in detail	Harvey-Samuel et al. 2019	1	2	3	4	5	6	7	8	9	L. Alphey Pirbright Institute	EU BBSRC
		Population suppression	Proposed system is termed 'RIDL-with- Drive' (RIDL - Release of Insects carrying Dominant Lethal)												
34		Reduction of damage to cruciferous crops by this species	Not specified but study uses CRISPR- Cas9 gene knockout methodology, so homing CRISPR seems likely	i. Peng et al. 2020 ii. Chen et al. 2019	1	2	3	4	5	6	7	8	9	M.S. You Fujian Agriculture and Forestry University	National Natural Science Foundation of China, National Natural Science Foundation of Fujian Province,
		Population suppression	NA preliminary study												Major Project of Fujian Province
35	<i>Plodia interpunctella</i> Indian meal moth	Reduction of damage to dry food stores (e.g. cereals) caused by this species	NA – proposal only	Goldsmith et al. 2022	1	2	3	4	5	6	7	8	9	C. Goldsmith Texas A&M University	USDA
	Present on all continents except Antarctica (CABI 2022)	Not stated – proposal only	NA – proposal only												

	Species	Intended use	Type of gene drive (our categories)	Publications		w cl								Project leader (corresponding author on publications)	Funders
	Geographic range (of target species)	Intended direct effect (of gene drive)	Developer's name for gene drive system	is described)		the v								Institution	
	HEMIPTERA (true b	ougs)													
36	<i>Diaphorina citri</i> Asian citrus psyllid	Reduction in transmission of citrus greening disease, and resulting harm to citrus fruit. This species acts as a vector for <i>Candidatus Liberibacter</i> spp. bacteria which cause the disease.	Not stated – no details of design published	Described by Jones et al. 2019 and Turpen 2017 (Report to USDA)	-	8	3	4	x	x	x	x	x	T. Turpen Citrus Research and Development Foundation, Florida	USDA
	Central and South America, India, South East Asia and Saudi Arabia (Grafton-Cardwell et al. 2005)	Population replacement or modification	Not stated – no details of design published												
37		As above	Propose homing CRISPR	Wheatley and Yang 2021	1	2	3	4	5	6	7	8	9	Y. Yang Pennsylvania State	USDA Hatch
		Population modification or suppression proposed	NA – proposal only											University	appropriations
38	<i>Lygus hesperus</i> Western tarnished plant bug	Reduction in damage to cotton and other crops caused by this species	Probably CRISPR based – various forms of CRISPR drive cited	Heu et al. 2022	1	2	3	4	5	6	7	8	9	J. Fabrick U.S. Arid Land Agricultural Research Center	Cotton Incorporated
	Mainly western US, also reported in US state of Georgia (CABI 2022)	Population suppression	NA – preliminary study											Center	
39	<i>Rhodnius prolixus</i> Kissing bug	Reduction in transmission of the parasite <i>Trypanosoma</i> <i>cruzi</i> by this vector (to reduce occurrence of Chagas disease)	Propose homing CRISPR	Wellcome 2017	1	2	3	4	5	6	7	8	9	M. Yeo London School of Hygiene and Tropical Medicine	Wellcome
	Venezuala, Columbia and parts of Central America (Sosa-Estani and Leonor Segura 2015)	Population modification	NA – no research published yet												

	Species Geographic range (of target species)	Intended use Intended direct effect (of gene drive)	Type of gene drive (our categories) Developer's name for gene drive system	Publications (where research is described)	to	w cl expe the v	erim	enta	rain / rele	/sys ease	tem s			Project leader (corresponding author on publications) Institution	Funders
40		Reduction in transmission of the parasite <i>Trypanosoma</i> <i>cruzi</i> by this vector (to reduce occurrence of Chagas disease)	Probably homing CRISPR	Berni et al. 2020	1	2	3	4	5	6	7	8	9	H. Araujo Federal University of Rio de Janeiro	Not stated
		Population modification or suppression	NA – unpublished preliminary study only												
41	<i>Bemisia tabaci</i> species complex Silverleaf whitefly	Reduction of damage to crops caused by transmission of begomoviruses by this vector species	Homing CRISPR	Li, Aidlin Harari, et al. 2020	1	2	3	4	5	6	7	8	9	B.E. Tabashnik University of Arizona	United States— Israel Binational Agricultural Research and Development Fund
	(Kriticos et al. 2020)	Population modification	NA – preliminary theoretical study												
42	<i>Trioza eryteae</i> African citrus psyllid (vector of citrus greening disease)	Reduction in transmission of citrus greening disease, and resulting harm to citrus fruit. This species acts as a vector for <i>Candidatus Liberibacter</i> spp. bacteria which cause the disease.	Propose homing CRISPR	Wheatley and Yang 2021	1	2	3	4	5	6	7	8	9	Y. Yang Pennsylvania State University	USDA Hatch appropriations
	(CABI 2022)	Population modification or suppression proposed	NA – proposal only												

	Species Geographic range (of target species)	Intended use Intended direct effect (of gene drive)	Type of gene drive (our categories) Developer's name for gene drive system	Publications (where research is described)	How close is strain/system to <i>experimental</i> releases in the wild?									Project leader (corresponding author on publications) Institution	Funders
	COLEOPTERA (Bee	etles and weevils)	ا 🛞 🛞												
43	<i>Tribolium castaneum</i> Red flour beetle	Reduction of spoilage of stored grains caused by this species	Homing CRISPR	Drury et al. 2017	Drury et al. 2017 1		3	4	5	6	7	8	9	M.J. Wade University of Wisconsin	NIH Indiana University start- up funds
	Present on all continents except Antarctica (IRAC 2019)	Population suppression	NA – preliminary theoretical study												
44	<i>Scolytinae</i> subfamily Bark beetles	Reduction of damage to timber crops caused by this species	Homing CRISPR	Liu and Champer 2022 (Note that Li, Aidlin Harari, et al. 2020 also imply these	1	2	3	4	5	6	7	8	9	J. Champer Peking University	Peking University SLS-Qidong Innovation Fund
	NA - No single species named as a target yet	Population suppression	NA – preliminary theoretical study	species could be a target)											
45	<i>Listronotus bonariensis</i> Argentine stem weevil	Reduction of damage to pasture grass caused by this species	Not stated – proposal only	Dearden et al. 2018	1	2	3	4	5	6	7	8	9	P. Dearden University of Otago, NZ	Not stated
	Indigenous to South America, it has spread to Australia and New Zealand	Population suppression	NA – proposal only												
46	<i>Sitona lepidus</i> (synonym - <i>S. obsoletus</i>) clover root weevil	Reduction of damage to clover caused by this species (in agricultural contexts)	Not stated – proposal only	Dearden et al. 2018	1	2	3	4	5	6	7	8	9	P. Dearden University of Otago, NZ	Not stated
	(CABI 2022)	Population suppression	NA – proposal only												

	Species Geographic range (of target species)	Intended use Intended direct effect (of gene drive)	(our categories)PublicationsHow close is strain/system(where research ect effectDeveloper's name for is described)is described)in the wild?									Project leader (corresponding author on publications) Institution	Funders		
47	Anthonomus grandis Mexican cotton boll weevil	Reduction of damage to cotton crops caused by this species	Not stated – proposal only	Goldsmith et al. 2022	1	2	3	4	5	6	7	8	9	C. Goldsmith Texas A&M University	USDA
	Indigenous to Central America, has spread to USA, Caribbean, Brazil and other South American countries (CABI 2022)	Not stated – proposal only	NA – proposal only												
	HYMENOPTERA (s	awflies, bees, wasps	and ants) 🍸	* * *											
48	Vespula vulgaris Common wasp	Reduction of ecological effects of invasive populations of this species in New Zealand and elsewhere (e.g. Australia)	Homing CRISPR	i. Dearden et al. 2018 ii. Lester et al. 2020	1	2	3	4	5	6	7	8	9	P. Dearden University of Otago, NZ + P.J. Lester	New Zealand Ministry of Business Innovation and Employment; Victoria University of Wellington
	Palearctic species native to Eurasia, invasive in parts of South America, Australia, New Zealand and Hawaii	Population suppression	NA – preliminary theoretical study											Victoria University of Wellington, NZ	of wearington
49	Vespula germanica German wasp	Reduction of ecological effects of invasive populations of this species in New Zealand and elsewhere (e.g. Australia)	Homing CRISPR	i. Dearden et al. 2018 ii. Lester et al. 2020	1	2	3	4	5	6	7	8	9		
	Predicted distribution - suitable and marginal areas (de Villiers, Kriticos, and Veldtman 2017)	Population suppression	NA – preliminary theoretical study												

ŗ	Species Geographic range (of target species)	Intended use Intended direct effect (of gene drive)	Type of gene drive (our categories) Developer's name for gene drive system	Publications (where research is described)	How close is strain/system to <i>experimental</i> releases in the wild?									Project leader (corresponding author on publications) Institution	Funders
50	Solenopsis invicta Red imported fire ant Native to South America.	Reduction of impacts on agriculture, biodiversity and infrastructure caused by this invasive species Population suppression	Homing CRISPR	Liu and Champer 1 2022	1	2	3	4	5	6	7	8	9	J. Champer Peking University	Peking University SLS-Qidong Innovation Fund
	Imported populations in United States, China, Australia, New Zealand and some other SE Asian and Carribean countries (Chen et al. 2020)		theoretical study												
	THYSANOPTERA (T	Thrips)													
51	<i>Thysanoptera</i> order Thrips	Reduction of damage to crops caused by thrips	Homing CRISPR	Liu and Champer 2022	1	2	3	4	5	6	7	8	9	J. Champer Peking University	Peking University SLS-Qidong Innovation Fund
	NA - No single species named as a target yet	Population suppression	NA – proposal only												

Abbreviations for funders and other organisations

BBSRC	UK Biotechnology and Biological Sciences Research Council
BARD	United States –Israel Binational Agricultural Research and Development Fund
CDC	Centers for Disease Control and Prevention (Atlanta, US)
COPEG	Panama-United States Commission for the Eradication and Prevention of Screwworm
DAAD	German Academic Exchange Service
DARPA	US Defense Advanced Research Projects Agency
DFiD	UK Department for International Development
FAPESP	São Paulo Research Foundation
Gates	The Bill and Melinda Gates Foundation
IGI UC Berkeley	Innovative Genomics Institute, University of California, Berkeley
NIH	US National Institutes of Health
NCSU	North Carolina State University
PAF	Philanthropy Advisory Fellowship
SDC	Swiss Agency for Development and Cooperation
STRI	Smithsonian Tropical Research Institute
Sida	Swedish International Development Cooperation Agency
TATA	TATA trusts
UC	University of California
USDA	US Department of Agriculture

Key to technology levels

- **1** Gene drive proposed: a proposal has been put forward in the scientific literature or from another academic source (e.g. funding body)
- 2 Gene drive proposed with supporting theoretical work, or preliminary laboratory work funded: a proposal has been made in the scientific literature supported by theoretical or modelling work, or preliminary laboratory work has been funded but has not yet been published
- Preliminary laboratory work: laboratory research relevant to gene drive construction published (e.g. developing molecular biology methods) with possibility or intention to construct gene drive stated
- 4 Active research on gene drive construction: research on gene drive construction has been funded, but no results yet published OR results published showing non-functional gene drives, or similar very limited progress
- **5 Limited proof of concept:** Published results show a gene drive is to some extent functional, however there are outstanding technical issues such as resistance or low efficiency
- **Laboratory proof of concept:** Taking published results at face value, the system works effectively in small cage trials.
- **Large cage trials:** Data published on trials in large cages, offering a more accurate simulation of conditions in natural environment.
- **Potential further contained trials:** After large cage trials, it is not currently clear what further trials may take place prior to experimental releases. One possibility is trials in outdoor cages.
- **Experimental releases in natural environment:** Field trials are underway with releases in the natural environment. This does not indicate that the technology has been shown to be effective or safe.
- Abandoned project: Research to construct a gene drive has been carried out, but has been unsuccessful and to our knowledge is no longer active

References

- Adolfi, A., V. M. Gantz, N. Jasinskiene, H. F. Lee, K. Hwang, G. Terradas, E. A. Bulger, A. Ramaiah, J. B. Bennett, J. J. Emerson, J. M. Marshall, E. Bier, and A. A. James. 2020. "Efficient population modification gene-drive rescue system in the malaria mosquito Anopheles stephensi." *Nat Commun* 11 (1):5553. doi: 10.1038/s41467-020-19426-0.
- Anderson, M. E., J. Mavica, L. Shackleford, I. Flis, S. Fochler, S. Basu, and L. Alphey. 2019. "CRISPR/Cas9 gene editing in the West Nile Virus vector, Culex quinquefasciatus Say." *PLoS One* 14 (11):e0224857. doi: 10.1371/journal.pone.0224857.
- Anderson, Michelle A. E., Jessica Purcell, Sebald A. N. Verkuijl, Victoria C. Norman, Philip T. Leftwich, Tim Harvey-Samuel, and Luke S. Alphey. 2020. "Expanding the CRISPR Toolbox in Culicine Mosquitoes: In Vitro Validation of Pol III Promoters." Acs Synthetic Biology 9 (3):678-681. doi: 10.1021/acssynbio.9b00436.
- Bernardini, F., A. Kriezis, R. Galizi, T. Nolan, and A. Crisanti. 2019. "Introgression of a synthetic sex ratio distortion system from Anopheles gambiae into Anopheles arabiensis." *Sci Rep* 9 (1):5158. doi: 10.1038/s41598-019-41646-8.
- Berni, M., D. Bressan, Y. Simão, A. Julio, P. L. Oliveira, A. Pane, and H. Araujo. 2020. "Pigmentation loci as markers for genome editing in the Chagas disease vector Rhodnius prolixus." *bioRxiv*:2020.04.29.067934. doi: 10.1101/2020.04.29.067934.
- Bier, E. 2022. "Gene drives gaining speed." Nat Rev Genet 23 (1):5-22. doi: 10.1038/s41576-021-00386-0.
- Buchman, A., S. Gamez, M. Li, I. Antoshechkin, H. H. Li, H. W. Wang, C. H. Chen, M. J. Klein, J. B. Duchemin, P. N. Paradkar, and O. S. Akbari. 2019. "Engineered resistance to Zika virus in transgenic Aedes aegypti expressing a polycistronic cluster of synthetic small RNAs." *Proc Natl Acad Sci U S A* 116 (9):3656-3661. doi: 10.1073/pnas.1810771116.
- Buchman, A., J. M. Marshall, D. Ostrovski, T. Yang, and O. S. Akbari. 2018. "Synthetically engineered Medea gene drive system in the worldwide crop pest Drosophila suzukii." *Proc Natl Acad Sci U S A* 115 (18):4725-4730. doi: 10.1073/ pnas.1713139115.
- Buchman, Anna, Stephanie Gamez, Ming Li, Igor Antoshechkin, Hsing-Han Li, Hsin-Wei Wang, Chun-Hong Chen, Melissa J. Klein, Jean-Bernard Duchemin, James E. Crowe, Jr., Prasad N. Paradkar, and Omar S. Akbari. 2020. "Broad dengue neutralization in mosquitoes expressing an engineered antibody." *Plos Pathogens* 16 (1). doi: 10.1371/journal. ppat.1008103; 10.1371/journal.ppat.1008103.r001; 10.1371/journal.ppat.1008103.r002; 10.1371/journal.ppat.1008103.r004.
- CABI. 2022. "CABI, 2022, Invasive Species Compendium. Wallingford, UK: CAB International. ." www.cabi.org/isc.
- Carballar-Lejarazú, R., C. Ogaugwu, T. Tushar, A. Kelsey, T. B. Pham, J. Murphy, H. Schmidt, Y. Lee, G. C. Lanzaro, and A. A. James. 2020. "Next-generation gene drive for population modification of the malaria vector mosquito, Anopheles gambiae." *Proc Natl Acad Sci U S A* 117 (37):22805-22814. doi: 10.1073/pnas.2010214117.
- Carballar-Lejarazú, R., T. Tushar, T. B. Pham, and A. A. James. 2022. "Cas9-mediated maternal-effect and derived resistance alleles in a gene-drive strain of the African malaria vector mosquito, Anopheles gambiae." *Genetics.* doi: 10.1093/genetics/iyac055.
- Chen, Shuai, Fangyu Ding, Mengmeng Hao, and Dong Jiang. 2020. "Mapping the Potential Global Distribution of Red Imported Fire Ant (Solenopsis invicta Buren) Based on a Machine Learning Method." *Sustainability* 12 (23):10182.
- Chen, W., F. Yang, X. Xu, U. Kumar, W. He, and M. You. 2019. "Genetic control of Plutella xylostella in omics era." Arch Insect Biochem Physiol 102 (3):e21621. doi: 10.1002/arch.21621.
- DARPA. 2017. "Building the Safe Genes Toolkit." accessed 08/04/2019. https://www.darpa.mil/news-events/2017-07-19.
- Davis, Rebecca J., Esther J. Belikoff, Allison N. Dickey, Elizabeth H. Scholl, Joshua B. Benoit, and Maxwell J. Scott. 2021. "Genome and transcriptome sequencing of the green bottle fly, Lucilia sericata, reveals underlying factors of sheep flystrike and maggot debridement therapy." *Genomics* 113 (6):3978-3988. doi: <u>https://doi.org/10.1016/j. ygeno.2021.10.003</u>.
- de Villiers, M., D. J. Kriticos, and R. Veldtman. 2017. "Including irrigation in niche modelling of the invasive wasp Vespula germanica (Fabricius) improves model fit to predict potential for further spread." *PLoS One* 12 (7):e0181397. doi: 10.1371/journal.pone.0181397.
- Dearden, P., N. Gemmell, O. R. Mercier, P. Lester, M. J. Scott, R. Newcomb, T. Buckley, J. Jacobs, S. Goldson, and D. R. Penman. 2018. "The potential for the use of gene drives for pest control in New Zealand: a perspective." *J R Soc N Z* 48 (4):225-244. doi: 10.1080/03036758.2017.1385030.
- Drury, D. W., A. L. Dapper, D. J. Siniard, G. E. Zentner, and M. J. Wade. 2017. "CRISPR/Cas9 gene drives in genetically variable and nonrandomly mating wild populations." *Sci Adv* 3 (5):e1601910. doi: 10.1126/sciadv.1601910.
- EPPO 2022. EPPO Global Database is maintained by the Secretariat of the European and Mediterranean Plant Protection Organization (EPPO). <u>https://gd.eppo.int/</u>
- Facchinelli, Luca, Ace R. North, C. Matilda Collins, Miriam Menichelli, Tania Persampieri, Alessandro Bucci, Roberta Spaccapelo, Andrea Crisanti, and Mark Q. Benedict. 2019. "Large-cage assessment of a transgenic sex-ratio distortion strain on populations of an African malaria vector." *Parasit Vectors* 12 (1):70. doi: 10.1186/s13071-019-3289-y.
- FAO/IAEA. 2017. "Updated Mediterranean Fruit Fly Global Distribution Map." accessed 12/04/2019. <u>http://www-naweb.iaea.org/nafa/news/2013-medfly-global-map.html</u>.
- Feng, X., V. López Del Amo, E. Mameli, M. Lee, A. L. Bishop, N. Perrimon, and V. M. Gantz. 2021. "Optimized CRISPR tools and site-directed transgenesis towards gene drive development in Culex quinquefasciatus mosquitoes." *Nat Commun* 12 (1):2960. doi: 10.1038/s41467-021-23239-0.
- Galizi, R., L. A. Doyle, M. Menichelli, F. Bernardini, A. Deredec, A. Burt, B. L. Stoddard, N. Windbichler, and A. Crisanti. 2014. "A synthetic sex ratio distortion system for the control of the human malaria mosquito." Nat Commun 5:3977. doi: 10.1038/ncomms4977.

- Galizi, R., A. Hammond, K. Kyrou, C. Taxiarchi, F. Bernardini, S. M. O'Loughlin, P. A. Papathanos, T. Nolan, N. Windbichler, and A. Crisanti. 2016. "A CRISPR-Cas9 sex-ratio distortion system for genetic control." *Sci Rep* 6:31139. doi: 10.1038/srep31139.
- Gantz, V. M., N. Jasinskiene, O. Tatarenkova, A. Fazekas, V. M. Macias, E. Bier, and A. A. James. 2015. "Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito Anopheles stephensi." *Proc Natl Acad Sci U S A* 112 (49):E6736-43. doi: 10.1073/pnas.1521077112.
- Garrood, W. T., N. Kranjc, K. Petri, D. Y. Kim, J. A. Guo, A. M. Hammond, I. Morianou, V. Pattanayak, J. K. Joung, A. Crisanti, and A. Simoni. 2021. "Analysis of off-target effects in CRISPR-based gene drives in the human malaria mosquito." *Proc Natl Acad Sci U S A* 118 (22). doi: 10.1073/pnas.2004838117.
- Goldsmith, C. L., K. E. Kang, E. Heitman, Z. N. Adelman, L. W. Buchman, D. Kerns, X. Liu, R. F. Medina, and A. Vedlitz. 2022. "Stakeholder Views on Engagement, Trust, Performance, and Risk Considerations About Use of Gene Drive Technology in Agricultural Pest Management." *Health Secur* 20 (1):6-15. doi: 10.1089/hs.2021.0101.
- Grafton-Cardwell, E., K. E Godfrey, M. E. Rogers, C. C. Childers, and P. A. Stansly. 2005. "Asian Citrus Psyllid." accessed 12/04/2019. http://www.cdfa.ca.gov/plant/acp/docs/factsheets/PsyllidbrochureAug05.pdf.
- Hammond, A., X. Karlsson, I. Morianou, K. Kyrou, A. Beaghton, M. Gribble, N. Kranjc, R. Galizi, A. Burt, A. Crisanti, and T. Nolan. 2021. "Regulating the expression of gene drives is key to increasing their invasive potential and the mitigation of resistance." *PLoS Genet* 17 (1):e1009321. doi: 10.1371/journal.pgen.1009321.
- Hammond, A. M., K. Kyrou, M. Bruttini, A. North, R. Galizi, X. Karlsson, N. Kranjc, F. M. Carpi, R. D'Aurizio, A. Crisanti, and T. Nolan. 2017. "The creation and selection of mutations resistant to a gene drive over multiple generations in the malaria mosquito." *PLoS Genet* 13 (10):e1007039. doi: 10.1371/journal.pgen.1007039.
- Hammond, A., P. Pollegioni, T. Persampieri, A. North, R. Minuz, A. Trusso, A. Bucci, K. Kyrou, I. Morianou, A. Simoni, T. Nolan, R. Müller, and A. Crisanti. 2021. "Gene-drive suppression of mosquito populations in large cages as a bridge between lab and field." *Nat Commun* 12 (1):4589. doi: 10.1038/s41467-021-24790-6.
- Hammond, Andrew, Roberto Galizi, Kyros Kyrou, Alekos Simoni, Carla Siniscalchi, Dimitris Katsanos, Matthew Gribble, Dean Baker, Eric Marois, Steven Russell, Austin Burt, Nikolai Windbichler, Andrea Crisanti, and Tony Nolan. 2015. "A CRISPR-Cas9 gene drive system targeting female reproduction in the malaria mosquito vector Anopheles gambiae." *Nature Biotechnology* 34:78. doi: 10.1038/nbt.3439.
- Harvey-Samuel, T., V. C. Norman, R. Carter, E. Lovett, and L. Alphey. 2019. "Identification and characterization of a Masculinizer homologue in the diamondback moth, Plutella xylostella." *Insect Mol Biol.* doi: 10.1111/imb.12628.
- Heu, C. C., R. J. Gross, K. P. Le, D. M. LeRoy, B. Fan, J. J. Hull, C. S. Brent, and J. A. Fabrick. 2022. "CRISPR-mediated knockout of cardinal and cinnabar eye pigmentation genes in the western tarnished plant bug." *Sci Rep* 12 (1):4917. doi: 10.1038/ s41598-022-08908-4.
- Hoermann, A., S. Tapanelli, P. Capriotti, G. Del Corsano, E. K. Masters, T. Habtewold, G. K. Christophides, and N. Windbichler. 2021. "Converting endogenous genes of the malaria mosquito into simple non-autonomous gene drives for population replacement." *Elife* 10. doi: 10.7554/eLife.58791.
- KaramiNejadRanjbar, Mohammad, Kolja N. Eckermann, Hassan M. M. Ahmed, Héctor M. Sánchez C., Stefan Dippel, John M. Marshall, and Ernst A. Wimmer. 2018. "Consequences of resistance evolution in a Cas9-based sex conversionsuppression gene drive for insect pest management." *Proc Natl Acad Sci U S A* 115 (24):6189-6194. doi: 10.1073/ pnas.1713825115.
- Koidou, V., S. Denecke, P. Ioannidis, I. Vlatakis, I. Livadaras, and J. Vontas. 2020. "Efficient genome editing in the olive fruit fly, Bactrocera oleae." *Insect Mol Biol.* doi: 10.1111/imb.12640.
- Kraemer, M. U., M. E. Sinka, K. A. Duda, A. Q. Mylne, F. M. Shearer, C. M. Barker, C. G. Moore, R. G. Carvalho, G. E. Coelho, W. Van Bortel, G. Hendrickx, F. Schaffner, I. R. Elyazar, H. J. Teng, O. J. Brady, J. P. Messina, D. M. Pigott, T. W. Scott, D. L. Smith, G. R. Wint, N. Golding, and S. I. Hay. 2015. "The global distribution of the arbovirus vectors Aedes aegypti and Ae. albopictus." *Elife* 4:e08347. doi: 10.7554/eLife.08347.
- Kriticos, Darren J., Ross E. Darnell, Tania Yonow, Noboru Ota, Robert W. Sutherst, Hazel R. Parry, Habibu Mugerwa, M. N. Maruthi, Susan E. Seal, John Colvin, Sarina Macfadyen, Andrew Kalyebi, Andrew Hulthen, and Paul J. De Barro. 2020.
 "Improving climate suitability for Bemisia tabaci in East Africa is correlated with increased prevalence of whiteflies and cassava diseases." *Sci Rep* 10 (1):22049. doi: 10.1038/s41598-020-79149-6.
- Kyrou, K., A. M. Hammond, R. Galizi, N. Kranjc, A. Burt, A. K. Beaghton, T. Nolan, and A. Crisanti. 2018. "A CRISPR-Cas9 gene drive targeting doublesex causes complete population suppression in caged Anopheles gambiae mosquitoes." *Nat Biotechnol* 36 (11):1062-1066. doi: 10.1038/nbt.4245.
- Lester, P. J., M. Bulgarella, J. W. Baty, P. K. Dearden, J. Guhlin, and J. M. Kean. 2020. "The potential for a CRISPR gene drive to eradicate or suppress globally invasive social wasps." *Sci Rep* 10 (1):12398. doi: 10.1038/s41598-020-69259-6.
- Li, J., O. Aidlin Harari, A. L. Doss, L. L. Walling, P. W. Atkinson, S. Morin, and B. E. Tabashnik. 2020. "Can CRISPR gene drive work in pest and beneficial haplodiploid species?" *Evol Appl* 13 (9):2392-2403. doi: 10.1111/eva.13032.
- Li, M., T. Li, N. Liu, R. R. Raban, X. Wang, and O. S. Akbari. 2020. "Methods for the generation of heritable germline mutations in the disease vector Culex quinquefasciatus using clustered regularly interspaced short palindrome repeats-associated protein 9." *Insect Mol Biol* 29 (2):214-220. doi: 10.1111/imb.12626.
- Li, M., T. Yang, N. P. Kandul, M. Bui, S. Gamez, R. Raban, J. Bennett, H. M. C. Sanchez, G. C. Lanzaro, H. Schmidt, Y. L. Lee, J. M. Marshall, and O. S. Akbari. 2020. "Development of a confinable gene drive system in the human disease vector Aedes aegypti." *Elife* 9. doi: 10.7554/eLife.51701.
- Liu, Y., and J. Champer. 2022. "Modelling homing suppression gene drive in haplodiploid organisms." *Proc Biol Sci* 289 (1972):20220320. doi: 10.1098/rspb.2022.0320.

MAP. 2019. "The Malaria Atlas Project." accessed 11/02/2019. https://map.ox.ac.uk/mosquito-malaria-vectors/.

- Meccariello, Angela, Flavia Krsticevic, Rita Colonna, Giuseppe Del Corsano, Barbara Fasulo, Philippos Aris Papathanos, and Nikolai Windbichler. 2021. "Engineered sex ratio distortion by X-shredding in the global agricultural pest Ceratitis capitata." BMC Biology 19 (1):78. doi: 10.1186/s12915-021-01010-7.
- Ni, X. Y., W. J. Lu, X. Qiao, and J. Huang. 2021. "Genome editing efficiency of four Drosophila suzukii endogenous U6 promoters." Insect Mol Biol 30 (4):420-426. doi: 10.1111/imb.12707.
- Ogola, E. O., J. O. Odero, J. M. Mwangangi, D. K. Masiga, and D. P. Tchouassi. 2019. "Population genetics of Anopheles funestus, the African malaria vector, Kenya." *Parasit Vectors* 12 (1):15. doi: 10.1186/s13071-018-3252-3.
- Paulo, D. F., M. E. Williamson, A. P. Arp, F. Li, A. Sagel, S. R. Skoda, J. Sanchez-Gallego, M. Vasquez, G. Quintero, A. A. Pérez de León, E. J. Belikoff, A. M. L. Azeredo-Espin, W. O. McMillan, C. Concha, and M. J. Scott. 2019. "Specific Gene Disruption in the Major Livestock Pests Cochliomyia hominivorax and Lucilia cuprina Using CRISPR/Cas9." *G3 (Bethesda)* 9 (9):3045-3055. doi: 10.1534/g3.119.400544.
- Peng, Lu, Qing Wang, Ming-Min Zou, Yu-Dong Qin, Liette Vasseur, Li-Na Chu, Yi-Long Zhai, Shi-Jie Dong, Li-Li Liu, Wei-Yi He, Guang Yang, and Min-Sheng You. 2020. "CRISPR/Cas9-Mediated Vitellogenin Receptor Knockout Leads to Functional Deficiency in the Reproductive Development of Plutella xylostella." *Front Physiol* 10. doi: 10.3389/fphys.2019.01585.
- Pham, T. B., C. H. Phong, J. B. Bennett, K. Hwang, N. Jasinskiene, K. Parker, D. Stillinger, J. M. Marshall, R. Carballar-Lejarazu, and A. A. James. 2019. "Experimental population modification of the malaria vector mosquito, Anopheles stephensi." *PLoS Genet* 15 (12):e1008440. doi: 10.1371/journal.pgen.1008440.
- Polo, N., M. Lopes-da-Silva, R Sivori, and S. Dos Santos. 2016. Potential spread and economic impact of invasive Drosophila suzukii in Brazil. Vol. 51.
- Quinn, C., A. Anthousi, C. Wondji, and T. Nolan. 2021. "CRISPR-mediated knock-in of transgenes into the malaria vector Anopheles funestus." *G3 (Bethesda)* 11 (8). doi: 10.1093/g3journal/jkab201.
- Samy, A. M., A. H. Elaagip, M. A. Kenawy, C. F. Ayres, A. T. Peterson, and D. E. Soliman. 2016. "Climate Change Influences on the Global Potential Distribution of the Mosquito Culex quinquefasciatus, Vector of West Nile Virus and Lymphatic Filariasis." *PLoS One* 11 (10):e0163863. doi: 10.1371/journal.pone.0163863.
- Scott, M. J., J. B. Benoit, R. J. Davis, S. T. Bailey, V. Varga, E. O. Martinson, P. V. Hickner, Z. Syed, G. A. Cardoso, T. T. Torres, M. T. Weirauch, E. H. Scholl, A. M. Phillippy, A. Sagel, M. Vasquez, G. Quintero, and S. R. Skoda. 2020. "Genomic analyses of a livestock pest, the New World screwworm, find potential targets for genetic control programs." *Commun Biol* 3 (1):424. doi: 10.1038/s42003-020-01152-4.
- Simoni, A., A. M. Hammond, A. K. Beaghton, R. Galizi, C. Taxiarchi, K. Kyrou, D. Meacci, M. Gribble, G. Morselli, A. Burt, T. Nolan, and A. Crisanti. 2020. "A male-biased sex-distorter gene drive for the human malaria vector *Anopheles gambiae*." *Nat Biotechnol* 38 (9):1054-1060. doi: 10.1038/s41587-020-0508-1.
- Sosa-Estani, S., and E. Leonor Segura. 2015. Integrated control of Chagas disease for its elimination as public health problem -A Review. Vol. 110.
- Taxiarchi, C., A. Beaghton, N. I. Don, K. Kyrou, M. Gribble, D. Shittu, S. P. Collins, C. L. Beisel, R. Galizi, and A. Crisanti. 2021. "A genetically encoded anti-CRISPR protein constrains gene drive spread and prevents population suppression." *Nat Commun* 12 (1):3977. doi: 10.1038/s41467-021-24214-5.
- Terradas, G., A. Hermann, A. A. James, W. McGinnis, and E. Bier. 2022. "High-resolution in situ analysis of Cas9 germline transcript distributions in gene-drive Anopheles mosquitoes." *G3 (Bethesda)* 12 (1). doi: 10.1093/g3journal/jkab369.
- Verkuijl, Sebald A. N., Estela Gonzalez, Ming Li, Joshua Ang, Nikolay P. Kandul, Michelle A. E. Anderson, Omar S. Akbari, Michael B. Bonsall, and Luke Alphey. 2020. "A CRISPR endonuclease gene drive reveals two distinct mechanisms of inheritance bias." *bioRxiv*:2020.12.15.421271. doi: 10.1101/2020.12.15.421271.
- Wellcome. 2017. "A platform for the transgenic modification of sand flies (Lutzomyia longipalpis) and triatomine bugs (Rhodnius prolixus) towards deriving insect vectors refractory to disease agents mediated by CRISPR-Cas9 gene drive." https://wellcome.org/grant-funding/people-and-projects/grants-awarded/a-platform-transgenic-modification-sand-flies.
- Wheatley, M. S., and Y. Yang. 2021. "Versatile Applications of the CRISPR/Cas Toolkit in Plant Pathology and Disease Management." *Phytopathology*:Phyto08200322ia. doi: 10.1094/phyto-08-20-0322-ia.
- Xu, X., T. Harvey-Samuel, H. A. Siddiqui, J. X. Ang, M. E. Anderson, C. M. Reitmayer, E. Lovett, P. T. Leftwich, M. You, and L. Alphey. 2022. "Toward a CRISPR-Cas9-Based Gene Drive in the Diamondback Moth Plutella xylostella." *Crispr J* 5 (2):224-236. doi: 10.1089/crispr.2021.0129.
- Zalucki, Myron P., Asad Shabbir, Rehan Silva, David Adamson, Liu Shu-Sheng, and Michael J. Furlong. 2012. "Estimating the Economic Cost of One of the World's Major Insect Pests, Plutella xylostella (Lepidoptera: Plutellidae): Just How Long Is a Piece of String?" *J Econ Entomoly* 105 (4):1115-1129. doi: 10.1603/ec12107.
- Zhao, S., Z. Xing, Z. Liu, Y. Liu, X. Liu, Z. Chen, J. Li, and R. Yan. 2019. "Efficient somatic and germline genome engineering of Bactrocera dorsalis by the CRISPR/Cas9 system." *Pest Manag Sci* 75 (7):1921-1932. doi: 10.1002/ps.5305.