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PRELIMINARY PUBLICATION

Gene Drive Development:

Current and proposed non-insect targets, including vertebrates, snails, fungi and plants.

A horizon scanning survey

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Summary of findings:

Screening and analysis of the scientific literature for gene drive development in non-insect targets up to 31 December 2022,[1] showed:

- There are 43 current or proposed non-insect targets[2].
- Proposals span a wide range of species and taxonomic groups: from mammals and fish to snails, arachnids, fungi and plants (see Table 1).
- In the vast majority of cases the aim is to suppress or eradicate the target.
- Compared to gene drive systems in insects, the systems in other taxonomic groups are further away from releases into the environment.
- A significant amount of research has focussed on developing gene drives in mice, so far with limited success, though efforts are ongoing.
- Development of gene drives in mice is seen by many as a pathway to applying the technology in other mammals.
- There appear to be significant obstacles in applying homing CRISPR gene drive technology in new species and taxonomic groups.

Context

In 2016, the National Academy of Sciences Engineering and Medicine (NASEM) published their report 'Gene Drives on the Horizon'. This was two years after Esvelt and colleagues first published their conceptual paper on utilising the then new CRISPR/Cas system to build a functional gene drive for the modification or eradication of wild populations. At the same time both publications highlighted the dangers and risks of this approach.

Within a year the first proof of concept was published, at that time in the fruit fly *Drosophila melanogaster*, a major model organism for insects (Gantz & Bier 2015). Other proofs of concept followed.

Where is research and development of gene drives now? What is on the horizon? What are the trends? Where has research advanced and where has it hit obstacles? Which species are being focused on and why? And which gene drive systems are being proposed and for which purposes?

To answer these questions, we have undertaken a survey of the scientific literature up until 31 December 2022. Whilst there was a slow steady stream of publications related to "gene drives" in the 10 years up to 2015, a steep rise occurred in 2016 and 2017 (see Figure 1). This started to plateau by 2018, with an average of 135 publications per year since, covering a wide range of disciplines, also including ethics, social sciences, and regulatory issues.

1 This is an updated version of this survey. The original covered literature up to 31 October 2022.

2 The vast majority of the targets identified in the literature are single species, however some early stage proposals relate to broader taxonomic groups, the *Cervid* family (entry 11), the *Tetranycahidae* (19), snail genera hosting schistosome parasites (21.1 -21.3), the *Schistosoma* genus (23) and the *Myrtaceae* family (31).

This survey focuses on non-insect targets only. A separate horizon scanning survey for insect targets was published in July 2022 (Wells & Steinbrecher 2022)[5].

This survey does 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.

This 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.
- How far developments have progressed and what the next stages of experimentation might be.

KINGDOM	PHYLUM or SUB-PHYLUM	CLASS or SUPERCLASS or INFRAPHYLUM	ORDER		Entry number(s)
Animals					
Vertebrates	Mammals	*Rodentia* (Rodents)		House mice	1.1.1 - 1.9
				Other rodents	2.1 - 6.2
			Carnivora (cats, dogs and related mammals)		7.1 - 9
			Diprotodontia (Possums and related marsupials)		10
			Artiodactyla (Deer and related mammals)		11
			Lagomorpha (Rabbits and hares)		12.1-12.4
		Birds			13
		Amphibians			14.1-15
		Bony fish			16-17
		Jawless fish			18.1-18.2
	Arthropods	Arachnids			19-20
		Insects			See separate table[5]
	Molluscs				21.1-21.3
	Nematodes				22
	Flatworms				23
Fungi					24-27
Plants					28-31

Table 1: Overview of current gene drive targets.
Overview of gene drive survey data in taxonomic order. Entry numbers correspond to rows in the main data table.

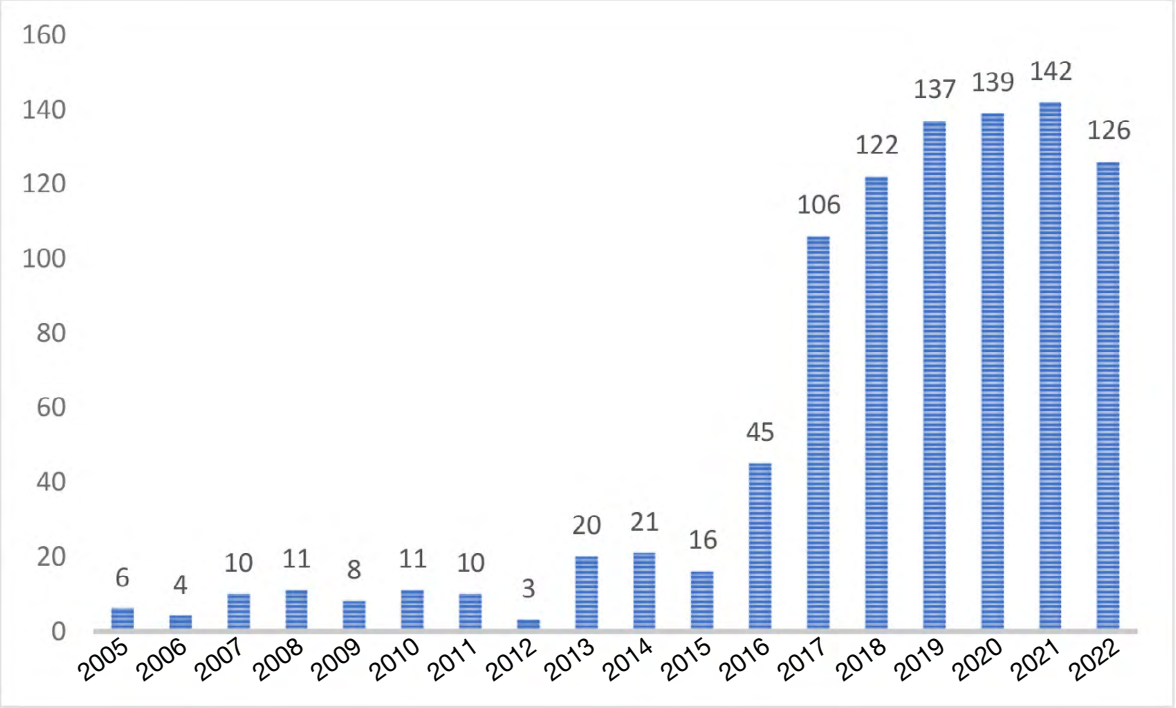


Figure 1: Preliminary number of publications per year related to gene drives

Findings

1. **There are proposals in a wide range of species and taxonomic groups:** showing there is momentum and ambition that goes far beyond mosquitoes and mice.
2. **In the vast majority of cases the aim is to suppress or eradicate the target**[2] (33 out of 37[3]), in some cases by modifying the target to render it susceptible to suppression.[4]
3. **Compared to gene drive systems in insects, the systems in other taxonomic groups are further away from releases in the environment.** The two most advanced systems - where there is an intention to target the organism in the wild - are both being developed in house mice (entries 1.1.1 and 1.7 in table). Neither of these systems have yet reached full proof of concept in the laboratory.
4. **A significant amount of research has focussed on developing gene drives in mice, so far with limited success, though efforts are ongoing.**
5. **Development of gene drives in mice is seen as a pathway to applying the technology in other mammals.** While this intention is often stated in general terms, an example that names a specific eventual target is the study from Castle *et al*. (2022) who use mice as a model organism with the ultimate aim of modifying deer (entries 1.6 and 11 in table).
6. **No functional gene drive system has so far been constructed in plants. A homing CRISPR gene drive was reported in Arabidopsis (28) but the publication was later retracted.** A 'gene drive like' system has been reported in *Nicotiana tabacum* (29), however the functionality of this system is limited, namely to producing point mutations in the mitochondrial genome.

3 Five species that are model organisms where there is no intention to apply the technology in the wild are excluded from this total, these are entries 22, 26-29 in the table

4 Targets where aim is suppression/eradication: 1, 3-10, 12-21, 23, 30 (this entry encompasses 13 invasive plant species).
Targets where aim is modification: 2, 11, 21 (but suppression also proposed for *B. glabrata*), 24, 31
In one case - 25- the intention has not yet been specified.

7. **There appear to be significant obstacles in applying homing CRISPR gene drive technology in new species and taxonomic groups.** While homing CRISPR gene drives appear to be functional in laboratory settings in dipteran insects (i.e. flies and mosquitoes)[5] and some fungi (*S. cerevisiae* and *C. albicans*: 26.1-27), the technology is so far only partially functional in mice (1.1.1 – 1.6). Despite efforts to apply this technology more widely, it is not yet functional in plants (28), nematodes (22), flatworms (23) or in the fungi *Fusarium graminearum* (24.2).

8. **It is possible that gene drive designs not based on homing CRISPR technology may be more effective in some species and taxonomic groups.** Development of designs based on the T-haplotype in mice (1.7) and Spok1 in *F. graminearum* (24.1), appears to have made some progress in the laboratory.

9. **Sixteen of the vertebrate targets relate to controlling or eliminating invasive species for conservation purposes, especially mammals.**

10. **While many proposals relate to eliminating invasive mammals on islands, there is ambition to apply gene drive technology for eradications at continental scale in Australia** (e.g. see Birand, Cassey, Ross, Thomas, et al. (2022)). There is ongoing interest in Australia in a number of mammalian targets including house mice, black rats, rabbits, cats, and foxes, with a body of work published from 2017 through to the present day relating to some or all of these species.

11. **A number of target species are integral and important species within ecosystems in their native range**, for example the red fox, the possum or the rabbit. Other targets are able to cross-breed with endangered species, such as feral house cats with the European wild cat. Significantly Thresher (2022) argues that employing a gene drive that carries the risk of causing complete global extinction of the European rabbit would be justifiable because '….the species seriously threatens agriculture, and native flora and fauna in almost all it's extensive invasive ranges, and its loss, however serious, would still in turn damage only a limited ecosystem and set of economies.'

Please see main table (pp.6-28) for details of findings.

Concluding remarks

Undertaking a broad survey of the research in this field makes the bigger picture clearer, allowing one to perceive trends, as well as obstacles. The wide-ranging ambition for gene drive technology is remarkable, and yet the survey also reveals that homing CRISPR gene drives may not be as broadly applicable across different species and taxonomic groups as originally hoped. A prevalence of proposals to suppress and potentially eradicate species or populations, as opposed to modifying them, is evident. While the reasons for this are not completely clear - it is possible that gene drives are starting to be perceived as a form of species-specific pesticide.

A key outcome of the survey is to raise questions: How might deployment of gene drive technology develop in the medium and long term? Is it going to become the go-to technology to tackle invasive species and 'pests'? From vertebrates to insects to plants, be it for agriculture, conservation, or forestry, will gene drives be used as pesticides have been in the past? If the technology develops on this trajectory – and we observe that many agencies and academics do appear to view it this way – then serious reflection and analysis will be required. Who will model the deployment as a whole and analyse or asses the consequences, especially with regards to cumulative effects? What would this mean for biodiversity, and what for risk assessment, regulation, and governance, especially on an international and global level? And could the technology be used for purposes other than those currently discussed in the literature?

Methodology

Please see end of document.

5 Wells, M. and Steinbrecher, R. Current and proposed insect targets for gene drive development. A horizon scanning survey. EcoNexus, July 2022. https://www.econexus.info/files/gene_drive_insect_table_econexus_2022.pdf. Note this survey is currently being updated.

Key to technology levels

1 **Gene drive proposed**

2 **Gene drive proposed with supporting modelling work, or preliminary laboratory work funded**

3 **Preliminary laboratory work published**

4 **Research on gene drive construction funded**

5 **Limited proof of concept**

6 **Laboratory proof of concept**

7 **Non-insects- scaled up trials**

Insects - large cage trials

8 **Potential further contained trials**

9 **Experimental releases in natural environment**

X **Abandoned project**

Please see page 26 for a complete explanation of the technology levels.

Colouring/symbols for progress of technology

	Evidence shows this approach doesn't work
	System is not intended for release
	No publications in the last three years
? ? ?	Uncertain if research has progressed to this stage
M	Modelling work has been done
G	Genome sequenced (with intention/possibility of constructing gene drive stated)

Key to geographic distribution maps

	Species is not present
	Species native range
	Species invasive range

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
Kingdom: ANIMALS	Phylum: Vertebrates	Class: Mammals	Order: (*Rodentia*) Rodents	Species: House mice			
1.1	***Mus musculus*** **Homing CRISPR – proof of concept only**						
1.1.1	***Mus musculus*** House mouse  After Musser *et al.* 2021	NA – intention is proof of concept homing CRISPR gene drive in mammals Initial aims: 1) using gene drive technology to create lab mouse strains carrying multiple modifications (with otherwise impractical genotypes) for laboratory studies 2) finding a way to eliminate invasive rodent species or addressing rodent-borne diseases	Homing CRISPR CRISPR-Cas9 mediated gene drive	(Grunwald *et al.* 2019, Weitzel *et al.* 2021, and Grunwald, Weitzel Cooper 2022)	1 2 3 4 5 6 7 8 9	K.L. Cooper University of California San Diego, USA	Kinship Pew Packard NIH Allen TATA UCSD
1.1.2		Population suppression Suppressing/eradicating invasive rodents on islands, and reducing impacts of rodents on agriculture	Split homing CRISPR CRISPR-Cas9 based gene drive (test both 'zygotic' and 'germline' forms)	(Pfitzner *et al.* 2020)	1 2 3 4 5 6 7 8 9	P.Q. Thomas University of Adelaide, Australia	DARPA
1.2	***Mus musculus*** **Homing CRISPR – targetting female fertility**						
1.2.1		Population suppression The 2017 press release says the aim is to improve pest control methods	Homing CRISPR (targeting 'haplosufficient female fertility gene') 'Homing gene drive targeting female fertility' (2018 paper) 'CRISPR-Cas9 split gene drive which disrupts an essential female fertility gene' (2019 poster)	(RoslinInstitute 2017) (McFarlane, Whitelaw, and Lillico 2018) - theoretical explanation of proposed GD designs (McFarlane *et al.* 2020) – poster abstract **No results published except poster abstract**	1 2 3 4 5 6 7 8 9	C.B.A. Whitelaw S.G. Lillico Roslin Institute, University of Edinburgh, UK	CSC BBSRC

	Species **Geographic range**	**Intended direct effect** **Intended use** (as stated by authors)	**Type of gene drive** (our categories) **Developer's name for gene drive system**	**Publication(s) where research is described**	**How close is strain/system to experimental releases in the wild?**	**Project leader(s)** **Institution**	**Funders**
1.2.2		Population suppression 'eradicating mice from islands' or at continental scale [presumably Australia] to address their impacts on biodiversity	Homing CRISPR (targeting 'haplosufficient female fertility gene') Homing gene drive	(Brown 2021) - press release (Birand, Cassey, Ross, Russell, *et al.* 2022) (Birand, Cassey, Ross, Thomas, *et al.* 2022)	1 2 **M** 3 4 5 6 7 8 9	T.A.A. Prowse P.Q. Thomas University of Adelaide, Australia	ARC New South Wales Government South Australia Government
1.2.3		Population suppression 'Suppressing' invasive rodents on islands to reduce impacts on biodiversity, agriculture and human health	Homing CRISPR (targeting locally[1] fixed alleles of female fertility genes) Localized synthetic gene drive	(Sudweeks *et al.* 2019, Oh *et al.* 2021)	1 2 **M** 3 **G** 4 5 6 7 8 9	A.L. Lloyd North Carolina State University, USA + A.J. Piaggio USDA APHIS Wildlife Services, USA	DARPA
1.2.4		Population suppression 'eradication of alien rodents on islands' to address impacts on bio-diversity The impacts of rodents on agriculture are also noted as a driver	Homing CRISPR – four[2] designs modelled 'CRISPR gene drive' 'Homozygotic XX sterility'	(Prowse *et al.* 2017) (see also entries 1.3.3 and 1.5)	1 2 **M** 3 4 5 6 7 8 9	T.A.A. Prowse University of Adelaide, Australia	University of Adelaide

1 Locally fixed alleles refers to alleles found in specific geographic locations - sometimes also referred to as 'private alleles'

2 The designs modelled in this publication are covered in entries 1.2.4, 1.3.3 and 1.5

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
1.3	***Mus musculus*** **Homing CRISPR sex ratio distorter – Sox9 cargo**[3]						
1.3.1		Population suppression 'eradicating invasive rodent populations on islands' to address impacts on biodiversity	CRISPR based gene drive involving *Sox9* – probably a homing CRISPR drive with *Sox9* cargo Paper describes development of 'CRISPR/Cas9 and CRISPR/Cpf1[4] gene drives with *Sox9* and Y-shredder'	(Campbell *et al.* 2019) **No results published despite substantial funding** (the work described in entry 1.3.3 may have informed this project)	1 / 2 / 3 / 4 ? / 5 ? / 6 ? / 7 / 8 / 9	Probably P.Q. Thomas University of Adelaide, Australia	DARPA
1.3.2		Population suppression Eradicating invasive mouse populations on islands to address biodiversity impacts - with the Southeast Farallon island used as a case study	Homing CRISPR (with *Sox9* cargo) '*sox9* CRISPR cas9 gene drive'	(Brown, Eikenbary, and Landis 2022)	1 / 2 **M** / 3 / 4 / 5 / 6 / 7 / 8 / 9	W.G. Landis Western Washington University, USA	Funders not stated
1.3.3		Population suppression 'eradication of alien rodents on islands' to address impacts on bio-diversity Aim ultimately is also to address impacts of alien rodents (esp. mice and rabbits) on agricultural production	Homing CRISPR - four designs modelled[2] 'CRISPR gene drive' Variants named: 'Heterozygotic XX sterility' 'Heterozygotic XX sex reversal'	(Prowse *et al.* 2017) (see also entries 1.2.4 and 1.5)	1 / 2 **M** / 3 / 4 / 5 / 6 / 7 / 8 / 9	P.Q. Thomas University of Adelaide, Australia	University of Adelaide

3 *Sox9* is an autosomal gene that codes for a developmental transcription factor crucial for sex determination.

4 Cpf1 is the old term for what is now named Cas12a

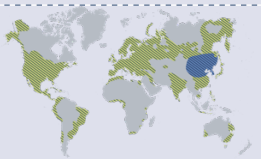
	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
1.4	***Mus musculus*** **Homing CRISPR sex ratio distorter – 'Y-shredder' cargo**						
1.4		Population suppression 'Suppression or eradication' of rodent populations to reduce impacts on biodiversity and agriculture	Homing CRISPR (with 'Y shredder' cargo) Y chromosome shredding gene drive (Campbell *et al*, 2019) 'Y-Chromosome deletion using Orthogonal Programmable Endonucleases (Y-CHOPE)' (Prowse *et al* 2019)	(Prowse *et al.* 2019, Campbell *et al.* 2019) **No results regarding gene drive construction published**	1 2 **M** 3 4 5 6 7 8 9 ? ? ?	J.V. Ross University of Adelaide, Australia	DARPA
1.5	***Mus musculus*** **Homing CRISPR causing recessive emrbyonic lethality**						
1.5		Population suppression 'eradication of alien rodents on islands' to address impacts on bio-diversity The impacts of rodents on agriculture are also noted as a driver	Homing CRISPR – four designs modelled[2] 'CRISPR gene drive' 'Homozygotic embryonic non-viability'	(Prowse *et al.* 2017) (see also entries 1.2.4 and 1.3.3)	1 2 **M** 3 4 5 6 7 8 9	P.Q. Thomas University of Adelaide, Australia	University of Adelaide
1.6	***Mus musculus*** **Feasibility study for homing CRISPR for population modification in deer (see entry number 11)**						
1.6		Population modification To demonstrate feasibility of a gene drive rendering wild deer immune to chronic wasting disease [by spreading *PRNP* null alleles]	Homing CRISPR CRISPR/Cas9 gene drive	(Castle *et al.* 2022)	1 2 3 4 5 6 7 8 9	D. Westaway University of Alberta, Canada	Alberta Prion Research Institute CFI University of Alberta

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
1.7	***Mus musculus*** **T-haplotype[5] targetting female fertility**						
1.7		Population suppression Aim is to explore the potential of an engineered form of the *T*-haplotype for 'mouse population suppression or even eradication on islands'	Split drive: a) *T*-haplotype element with gRNA cargo targeting 'haplosufficient female fertility gene' *(Prl)* b) Cas9 expressed separately (in male germline) tCRISPR split drive	(Gierus *et al*. 2022)	1 **2 M** 3 4 5 6 7 8 9	P.Q. Thomas University of Adelaide, Australia	Funders not stated in pre-print publication
1.8	***Mus musculus*** **T-haplotype sex ratio distorter -Sry[6] cargo (T-Sry)**						
1.8.1		Population suppression Eradicating invasive populations on islands to address biodiversity impacts	*T*-haplotype sex ratio distorter (carrying *Sry* cargo) *T*-complex drive	(Leitschuh *et al*. 2018, Campbell *et al*. 2019) **No results published despite substantial funding**	1 2 3 4 5 6 7 8 9	J. Godwin North Carolina State University, USA	NSF DARPA
1.8.2			*T*-haplotype sex ratio distorter (carrying SRY cargo) *t-Sry*	(Backus and Gross 2016)	1 **2 M** 3 4 5 6 7 8 9	K. Gross North Carolina State University, USA	North Carolina State University NSF

5 *T*-haplotype or t-complex is a selfish genetic element functioning as a meiotic drive and sex-ratio distorter that naturally occurs in mice, though does not spread widely. It is a form of a toxin-antidote system and allows for the insertion of 'cargo' genes into the t-complex, for example female infertility genes such as *Sry*. The *t*-haplotype is linked to the occurrence of taillessness (gene symbol T), which gave it its name.

6 *Sry* is a Y-chromosomal gene responsible for sex determination (**s**ex-determining **r**egion Y) and is required for initiating male development. It is also described as the *male phenotype control gene*. In females it will result in infertility due to partial male development.

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
1.8.3			T-haplotype sex ratio distorter (carrying *Sry* cargo) synthetic sperm-killing gene drive: 't-Sry'	(Manser *et al.* 2019)	1 2 M 3 4 5 6 7 8 9	T.A.R. Price University of Liverpool, UK	SNSF UK NERC
1.9	***Mus musculus*** **Y linked 'X-shredder' gene drive**						
1.9		Population suppression 'eradicating mice from islands' or at continental scale [presumably Australia] to address their impacts on biodiversity	CRISPR based X-shredder gene drive ('driving Y') X chromosome shredding gene drive	(Brown 2021) (Birand, Cassey, Ross, Russell, *et al.* 2022) (Birand, Cassey, Ross, Thomas, *et al.* 2022)	1 2 M 3 4 5 6 7 8 9	T.A.A. Prowse P.Q. Thomas University of Adelaide, Australia	ARC New South Wales Government South Australia Government
Kingdom: ANIMALS	Class: Mammals	Order: (*Rodentia*) Rodents	Species: Other rodents				
2.1	***Peromyscus leucopus*** White footed mouse  After Cassola *et al.* 2016	Population modification To modify wild populations of this species to render them resistant to the bacteria causing Lyme's disease, and thus reduce spread of this disease to humans	Not specified Not specified	(Long *et al.* 2019)	1 2 3 G 4 5 6 7 8 9	A.G. Barbour University of California Irvine	NIH Bay Area Lyme Foundation UCI USC DoD
2.2			CRISPR daisy drive localized 'daisy drive' system	(Buchthal *et al.* 2019)	1 2 3 4 5 6 7 8 9	K.M. Esvelt MIT, USA	Greenwall Rainwater CDMRP - DoD Sloan Burroughs Wellcome Fund NIH MIT Media Lab

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
3.1	***Rattus norvegicus*** Brown rat  After Khlyap 2012, appended after Hulme-Beaman 2021.	Population suppression Eradicating invasive rat populations on islands to address their impacts on biodiversity	Homing CRISPR (targeting 'haplosufficient female fertility gene' or 'haplosufficient zygote viability gene') and 'Y-shredder' (located on X-chromosome) Three drives modelled: 'homing drive' targeting either female fertility or zygote viability; and 'Y-shredder located on the X-chromosome'	(Champer *et al.* 2021)	1 **2 M** 3 4 5 6 7 8 9	P.W. Messer Cornell University, USA	Predator Free NZ NIH Bio-heritage NZ UK NERC
3.2		Population suppression To eradicate invasive populations in New Zealand	Homing CRISPR NA – proposal only	(Dearden *et al.* 2018)	1 2 3 4 5 6 7 8 9	D.R. Penman Lincoln University, New Zealand	Funder not stated
3.3		Population suppression 'to curb pest rodent populations'	Homing CRISPR (targeting 'haplosufficient female fertility gene') Homing gene drive targeting female fertility	(RoslinInstitute 2017) (McFarlane, Whitelaw, and Lillico 2018)	1 2 3 4 5 6 7 8 9	C.B.A. Whitelaw S.G. Lillico Roslin Institute, University of Edinburgh, UK	CSC BBSRC
3.4		Population suppression To control/ eliminate invasive populations on islands	Not specified – t-haplotype and homing CRISPR both mentioned NA – proposal only	(Godwin *et al.* 2019)	1 2 3 4 5 6 7 8 9	P.Q. Thomas University of Adelaide, Australia	DARPA
3.5		Population suppression To eradicate invasive populations on islands	T-haplotype sex ratio distorter (carrying SRY cargo) synthetic sperm-killing gene drive: 't-Sry'	(Manser *et al.* 2019)	1 2 3 4 5 6 7 8 9	T.A.R. Price University of Liverpool, UK	SNSF UK NERC

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
4.1	***Rattus rattus*** Common rat or black rat  Shield & Veitch, 2023 [7]	Population suppression 'eradication of alien rodents on islands' to address impacts on bio-diversity. The impacts of rodents on agriculture are also noted as a driver.	Homing CRISPR – two variants modelled 'CRISPR gene drive' Two variants modelled: 'Homozygotic embryonic non-viability' 'Homozygotic XX sterility'	(Prowse *et al.* 2017)	1 **2 M** 3 4 5 6 7 8 9	P.Q. Thomas University of Adelaide, Australia	University of Adelaide
4.2		Population suppression Eradicating invasive rat populations on islands to address their impacts on biodiversity	Homing CRISPR (targeting 'haplosufficient female fertility gene' or 'haplosufficient zygote viability gene') or 'Y-shredder' located on X-chromosome Three drives modelled: 'homing drive' targeting either female fertility or zygote viability 'Y-shredder located on the X-chromosome'	(Champer *et al.* 2021)	1 **2 M** 3 4 5 6 7 8 9	P.W. Messer Cornell University, USA	Predator Free NZ NIH Bio-heritage NZ UK NERC
4.3		Population suppression Eradication of this species at continental scale, presumably in Australia, to address impacts on biodiversity	Homing CRISPR or 'Y-linked X shredder'- Y-chromosome-linked X-shredder shredding drive ('driving-Y') or 'CRISPR homing drive targeting female fertility'	(Birand, Cassey, Ross, Thomas, *et al.* 2022)	1 **2 M** 3 4 5 6 7 8 9	T.A.A. Prowse University of Adelaide, Australia	ARC New South Wales Government South Australia Government

7 This map shows countries and regions where this species is present, and so does not show the true geographic range. It may be that the species is not present in the whole territory of a country, for example it is probably absent from Arctic areas of Canada.

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
4.4		Population suppression To eradicate invasive populations in New Zealand	Homing CRISPR NA – proposal only	(Dearden *et al.* 2018)	1 2 3 4 5 6 7 8 9	D.R. Penman Lincoln University, New Zealand	Funder not stated
4.5		Population suppression To control or eradicate invasive populations in Australia	Homing CRISPR RNA-guided gene drive	(Moro *et al.* 2018)	1 2 3 4 5 6 7 8 9	M. Tizard Australian Animal Health Laboratory, Australia	No specific funder acknowledged
4.6		Population suppression To control/ eliminate invasive populations on islands	Not specified – t-haplotype and homing CRISPR both mentioned NA – proposal only	(Godwin *et al.* 2019)	1 2 3 4 5 6 7 8 9	P.Q. Thomas University of Adelaide, Australia	DARPA
4.7		Population suppression To eradicate invasive populations on islands	T-haplotype sex ratio distorter (carrying SRY cargo) synthetic sperm-killing gene drive: 't-Sry'	(Manser *et al.* 2019)	1 2 3 4 5 6 7 8 9	T.A.R. Price University of Liverpool, UK	SNSF UK NERC
4.8		Population suppression To eradicate invasive populations in New Zealand	Homing CRISPR 'CRISPR/Cas9 suppression-drive'	(Thresher 2022)	1 2 3 4 5 6 7 8 9	A.C. Thresher University of California San Diego, USA	Not stated

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
5	***Sciurus carolinensis*** Grey squirrel	Population suppression To 'control a targeted grey squirrel population' to reduce impacts on biodiversity and damage to property in the UK (where it is invasive)	Homing CRISPR + Cleave and Rescue [Toxin Antidote] CRISPR combination, with 'daisy-field' HD-ClvR: 'composed of homing (H), daisyfield (D), and cleave-and-rescue (ClvR) gene drives' (a highly speculative and complex drive)	(Faber *et al.* 2021)	1 **2 M** 3 4 5 6 7 8 9	G. Gorjanc Roslin Institute, University of Edinburgh, UK	BBSRC
6.1	***Rattus exulans*** Polynesian rat  After Ruedas *et al.* 2016	Population suppression To eradicate invasive populations in New Zealand to prevent predation of native species	Homing CRISPR NA – proposal only	(Dearden *et al.* 2018)	1 2 3 4 5 6 7 8 9	D.R. Penman Lincoln University, New Zealand	Funder not stated
6.2		Population suppression To control/ eliminate invasive populations on islands	Not specified – t-haplotype and homing CRISPR both mentioned NA – proposal only	(Godwin *et al.* 2019)	1 2 3 4 5 6 7 8 9	P.Q. Thomas University of Adelaide, Australia	DARPA
Kingdom: **ANIMALS** Class: **Mammals** Order: ***Carnivora* (Cats, dogs and related mammals)**							
7.1	***Felis catus*** House cat & feral cat  After Bengsen *et al.* 2015	Population suppression To eradicate or control feral cats in Australia to reduce predation of native species	Not stated Not stated	(Australian Wildlife Conservancy 2022)	1 2 3 4 5 6 7 8 9	Not known	AWC and/or CSIRO

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
7.2	 *Felis silvestris* (wild cat). After Yamaguchi *et al.* 2015 [8]	Population suppression Eradication at continental scale, presumably in Australia, to address impacts on biodiversity	Homing CRISPR or 'Y-linked X shredder'- Y-chromosome-linked X-chromosome shredding drive ('driving-Y') or 'CRISPR homing drive targeting female fertility'	(Birand, Cassey, Ross, Thomas, *et al.* 2022)	1 **2 M** 3 4 5 6 7 8 9	T.A.A. Prowse University of Adelaide, Australia	ARC New South Wales Government South Australia Government
7.3		Population suppression Eradication or control of feral cats in Australia to address their impact on biodiversity, i.e. native fauna.	Homing CRISPR RNA-guided gene drive	(Moro *et al.* 2018)	1 2 3 4 5 6 7 8 9	M. Tizard Australian Animal Health Laboratory, Australia	No specific funder acknowledged All authors appear to be Australian Government employees
8.1	***Vulpes vulpes*** European red fox  After Hoffman & Sillero-Zubri, 2021	Population suppression Eradication at continental scale, presumably in Australia, to address impacts on biodiversity	Homing CRISPR or 'Y-linked X shredder' Y-chromosome-linked X-chromosome-shredding drive 'driving-Y' or 'CRISPR homing drive targeting female fertility'	(Birand, Cassey, Ross, Thomas, *et al.* 2022)	1 **2 M** 3 4 5 6 7 8 9	T.A.A. Prowse University of Adelaide, Australia	ARC New South Wales Government South Australia Government

8 We have included the range of the wild cat, Felis silvestris, which can readily hybridise with the domestic cat, Felis catus.

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
8.2		Population suppression Suppression/eradication to address decline in 'Australia's terrestrial mammal fauna' caused by predation by foxes. The paper also states '...foxes are a serious agricultural pest'.	Homing CRISPR RNA-guided gene drive	(Moro *et al.* 2018)	1 2 3 4 5 6 7 8 9	M. Tizard Australian Animal Health Laboratory, Australia	No specific funder acknowledged All authors appear to be Australian Government employees
9	***Mustela erminea*** Stoats	Population suppression To control or eradicate this invasive species in New Zealand to reduce predation of native birds including kiwis	Homing CRISPR NA – proposal only	(Dearden *et al.* 2018)	1 2 3 4 5 6 7 8 9	D.R. Penman Lincoln University, New Zealand	Funder not stated
Kingdom: ANIMALS Class: Mammals Order: *Diprotodontia* (Possums and related marsupials)							
10	***Trichosurus vulpecula*** Brushtail possum	Population suppression To control or eradicate this invasive species in New Zealand to reduce damage to native trees and the spread of bovine tuberculosis	Homing CRISPR NA – proposal only	(Dearden *et al.* 2018)	1 2 3 4 5 6 7 8 9	D.R. Penman Lincoln University, New Zealand	Funder not stated
Kingdom: ANIMALS Class: Mammals Order: *Artiodactyla* (Deer and related mammals)							
11	***Cervid family*** Deer	Population suppression To render the wild population immune to chronic wasting disease [by spreading *PRNP* null alleles] > see entry 1.6	Homing CRISPR CRISPR/Cas9 gene drive initial work on rabbit and mouse cell lines only	(Castle *et al.* 2022)	1 2 3 4 5 6 7 8 9	D. Westaway University of Alberta, Canada	Alberta Prion Research Institute CFI University of Alberta

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
Kingdom: ANIMALS	Class: Mammals	Order: *Lagomorpha* (Rabbits and hares) 			Theoretical studies only		
12.1	***Oryctolagus cuniculus*** European rabbit  After Tablado *et al.* 2009	Population suppression Eradication of invasive rabbit populations on islands to address biodiversity impacts Impacts of rabbits on agriculture are also noted	Homing CRISPR – two variants modelled CRISPR gene drive Two variants modelled: 'Homozygotic embryonic non-viability' 'Homozygotic XX sterility'	(Prowse *et al.* 2017)	1 **2 M** 3 4 5 6 7 8 9	P.Q. Thomas University of Adelaide, Australia	University of Adelaide
12.2		Population suppression Eradication at continental scale, presumably in Australia, to address impacts on biodiversity	Homing CRISPR or 'Y-linked X shredder'- Y-chromosome-linked X-chromosome shredding drive 'driving-Y' or 'CRISPR homing drive targeting female fertility'	(Birand, Cassey, Ross, Thomas, *et al.* 2022)	1 **2 M** 3 4 5 6 7 8 9	T.A.A. Prowse University of Adelaide, Australia	ARC New South Wales Government South Australia Government
12.3		Population suppression Control or eradication of this invasive species in Australia - to address biodiversity and agricultural impacts	Homing CRISPR RNA-guided gene drive	(Moro *et al.* 2018)	1 2 3 4 5 6 7 8 9	M. Tizard Australian Animal Health Laboratory, Australia	No specific funder acknowledged

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
12.4		Population suppression Eradication of this species where it is invasive, e.g. New Zealand	Homing CRISPR 'CRISPR/Cas9 suppression-drive'	(Thresher 2022)	1 2 3 4 5 6 7 8 9	A.C. Thresher University of California San Diego, USA	Funder not stated
Kingdom: ANIMALS Class: Birds							Theoretical studies only
13	***Sturnus vulgaris*** Common starling	Population suppression Suppression to address 'impacts to biodiversity and agriculture', however this species is noted for the damage it causes to crops so this is likely the primary driver	Homing CRISPR RNA-guided gene drive	(Moro *et al.* 2018)	1 2 3 4 5 6 7 8 9	M. Tizard Australian Animal Health Laboratory, Australia	No specific funder acknowledged All authors appear to be Australian Government employees
Kingdom: ANIMALS Class: Amphibians							
14.1	***Bufo marinus* or *Rhinella marina*** Cane toad  After Solís *et al*, 2009	Population suppression Suppression to address impacts on native species in Australia, which are either predated by toads or poisoned by eating them.	Homing CRISPR RNA-guided gene drive	(Moro *et al.* 2018) (Cooper *et al.* 2020) – conference abstract	1 2 3 4 5 6 7 8 9	M. Tizard Australian Animal Health Laboratory, Australia	No specific funder acknowledged All authors appear to be Australian Government employees
14.2		Population suppression Suppressing 'invasive populations of cane toads'	Z linked W-shredder, with variable parameters *(to control species with ZW sex determination)* Z linked 'W-shredder' (analogue to Y linked X-shredder)	(Holman 2019)	1 2 3 4 5 6 7 8 9	L. Holman University of Melbourne, Australia	ESEB SNSF

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
15	***Eleuthero-dactylus coqui*** Caribbean tree frog	Population suppression Eradication or suppression of this species, (accepting risk of global extinction), to address biodiversity impacts of invasive populations	Homing CRISPR 'CRISPR/Cas suppression-drive'	(Thresher 2022) Feasibility study	1 2 3 4 5 6 7 8 9	A.C. Thresher University of California San Diego, USA	Funder not stated
Kingdom: ANIMALS Super-class: Bony fish							
16	***Cyprinus carpio*** European carp	Population suppression Control of invasive populations of this species	Not specified Not specified	(Minnesota Aquatic Invasive Species Research Centre 2022)	1 2 3 4 ? 5 6 7 8 9 ?	M. Smanski University of Minnesota	ENRTF
17	***Pterois volitans*** Red lionfish	Population suppression To control or eradicate this invasive species to address damaging impacts to native reef communities in Caribbean and Western Atlantic	Homing CRISPR NA -preliminary theoretical study	(Vacura *et al*. 2018)	1 2 3 4 5 6 7 8 9	P. Venturelli Ball State University, USA	Funder not stated

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
Kingdom: ANIMALS	Infraphylum: Jawless fish						Theoretical studies only
18.1	***Petromyzon marinus*** Sea lamprey	Population suppression or population modification to enable suppression	Options proposed include: Split homing CRISPR 'Y-Linked X-shredder' Homing CRISPR Toxin Antidote	(Ferreira-Martins *et al.* 2021)	1 2 3 4 5 6 7 8 9	M.S. Docker University of Manitoba, Canada	Funders not stated
	 After NatureServe, 2013 [9]	Suppression or eradication of the lamprey from the North American Great Lakes to prevent this parasitic species damaging fish stocks	Options proposed include: 'Split gene drive' 'Driving y' 'Homing suppression gene drive' 'Toxin-antidote gene drive'				
18.2		Population suppression	Homing CRISPR	(York, Thresher, and McCauley 2021)	1	D.W. McCauley University of Oklahoma, USA	Funders not stated
		Suppression or eradication of the lamprey from the North American Great Lakes to prevent this parasitic species damaging fish stocks	CRISPR mediated gene drive				
Kingdom: ANIMALS	Phylum: Arthropods	Class: Arachnids					
19	***Tetranychidae family*** Spider mites	Propose population replacement (to render them more susceptible to insecticides)	Homing CRISPR	(Li *et al.* 2020)	1 2 3 4 5 6 7 8 9	B.E. Tabashnik University of Arizona, USA	BARD
		Reduction of damage to agricultural and horticultural crops	NA -preliminary theoretical study				

9 This map shows only the inland range for this species, that is watersheds and freshwater lakes where it is present. The species lives part of its life in saltwater and its native range also 'includes the Atlantic coast of North America from Newfoundland to northern Florida, the Atlantic coast of Europe, and the Baltic, western Mediterranean and Adriatic seas.' (Government of Ontario, 2018). In the great lakes, where it is invasive, it has adapted to live entirely in freshwater conditions (Government of Ontario, 2018).

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
20	***Varroa destructor*** Varroa mite	Population modification to enable suppression Suppression or eradication of varroa mites from honeybee colonies to prevent harm to the colony and honey production	Homing CRISPR (homing) CRISPR Cas9 gene drive	(Faber *et al.* 2021)	1 **2 M** 3 4 5 6 7 8 9	B.A. Harpur Purdue University, USA	BBSRC University of Edinburgh Purdue University Project Apis M.
Kingdom: ANIMALS	Phylum: Arthropods	Class: Insects					
SEE SEPARATE TABLE							
Kingdom: ANIMALS	Phylum: Molluscs	Class: Gastropods					
21.1	***Biomphalaria glabrata***  After Habid *et al* 2020[10]	Population modification The aim is to modify snail populations to increase their immunity to schistosome infection, thereby disrupting the schistosome lifecycle and reducing transmission to humans	Not specified but cites examples of homing CRISPR Not specified	(Hambrook *et al.* 2020)	1 2 **3** 4 5 6 7 8 9	P.C. Hannington University of Alberta, Canada	NSERC

10 This map show countries where this species is present and does not show the exact geographic range.

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
21.2	***Biomphalaria glabrata*** (and other snails of *Biomphalaria, Bulinus, Oncomelania & Neotricul* genera which host schistosome parasites) All *Biomphalaria* species susceptible to *Schistosoma mansoni*. After Habid *et al* 2020 [11] 	Population suppression and/or Population modification 'Modification of natural snail populations' to reduce 'schistosomiasis prevalence and transmission'	Several approaches proposed Several approaches proposed	(Maier *et al.* 2019) - presentation	1 **2** 3 4 5 6 7 8 9	M. Zamanian University of Wisconsin, USA J. Reinhard-Rupp Global Health Institute of Merck, Switzerland	Global Health Institute of Merck
21.3	***Biomphalaria glabrata*** The aim is to modify snail populations to increase their immunity to schistosome infection, thereby disrupting the schistosome lifecycle and reducing transmission to humans	Population modification CRISPR gene drive	Homing CRISPR CRISPR gene drive	(Grewelle *et al.* 2022)	1 **2 M** 3 4 5 6 7 8 9	G.A. De Leo Stanford University, USA	Stanford University NSF
Kingdom: ANIMALS Phylum: Nematodes							
22	***Caenorhabditis brenneri*** to 'test and optimize daisy-chain, daisyfield, and daisy quorum drives—including for daisy restoration—in fast-reproducing laboratory populations of worms… '	Proof of principle experiments – not intended for release to 'test and optimize daisy-chain, daisyfield, and daisy quorum drives—including for daisy restoration—in fast-reproducing laboratory populations of worms… '	daisy-chain drive, daisyfield drive, daisy quorum drive daisy-chain drive, daisyfield drive, daisy quorum drive	(Esvelt 2017b) (Esvelt 2017a) **No results have been published despite substantial funding**	1 2 3 4 5 6 7 8 9	K.M. Esvelt MIT, USA	DARPA This funding has now ended

11 This maps show countries where these species are present, and does not show the exact geographic range.

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
Kingdom: ANIMALS **Phylum: Flatworms**							
23	***Schistosoma genus*** Blood flukes	Population suppression	Z linked W-shredder, with variable parameters (as described by Holman, 2019)	(AAAS 2016) (Holman 2019) **No results have been published**	1 2 3 4 5 6 7 8 9	K.M. Esvelt MIT, USA P. Brindley George Washington University, USA	MaxMind and probably others This funding has likely ended
		To suppress schistosome parasites to thereby reduce human morbidity and mortality from schistomiasis	One proposal would be a Z linked 'W-shredder' (as described by Holman, 2019) 'all of the offspring will be born either female or male.' (AAAS 2016)				
Kingdom: FUNGI							
24	***Fusarium graminearum***	Population modification	Engineered gene drive employing *Spok1* (spore killer meiotic drive from *Podospora* spp.)	(Gardiner et al. 2020, Urquhart and Gardiner, 2022)[12]	1 2 3 4 5 6 ? ? ? 7 8 9	K. Kazan CSIRO, Queensland, Australia D. M. Gardiner CSIRO, Queensland, Australia	CSIRO ARC Australian Goverment
		To modify populations of *F. graminearum* to disrupt virulence factors in this species, and so reduce head blight in wheat and barley	*Spok1*				
24.1		Population modification	Split homing CRISPR	(Gardiner *et al.* 2020)	1 2 3 4 5 6 7 8 9	K. Kazan Agriculture and Food, CSIRO, Australia	CSIRO
		To modify populations of the *F. graminearum* (presumably for same reasons as in 20.1)	Do not use any particular term – but give detailed description of design				
25	***Fusarium verticillioides***	To control this plant pathogen which causes 'ear and stalk rot of maize' and which can 'contaminate maize kernels with fumonisin mycotoxins'	Engineered gene drive employing *Spore Killer Candidate-1 (SKC1) from F. verticillioides*	(Lohmar, Rhoades, Hammond, et al. 2022) (Lohmar, Rhoades, Patel, et al. 2022)	1 2 3 4 5 6 7 8 9	T. M. Hammond University of Illinois, USA Daren W Brown USDA, Agricultural research service, Illinois, USA	NSF USDA
		Not specified	'SKC1 based control practices' [which would 'require modifications to SKC1']				

12 Urquhart and Gardiner (2022) report further experimental work to characterise *Spok1* using the model organisms *S. cerevisiae* and *E. coli.* The 'genetic control of plant-pathogenic fungi' is mentioned as a possible future goal, with *F. graminearum* mentioned specifically.

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
26.1	***Saccharomyces cerevisiae*** brewer's or baker's yeast	Population modification Proof of principle of population modification via a split homing gene drive in this model organism	Split homing CRISPR 'split CRISPR-Cas9 gene drive'	(DiCarlo *et al.* 2015)	1 2 3 4 5 6 ? ? ? 7 8 9	G.M. Church Harvard Medical School, USA	DOE NCI NIDDK Wyss Institute
26.2		Population modification To study gene drives over many generations to understand the emergence of resistance	Probably homing CRISPR (as team had used this technology in other work) NA – no publications	(Aguilera 2017) - press release **No results published**	1 2 3 4 5 6 7 8 9	S. Kryazhimsky J. Meyer University of California San Diego, USA	DARPA
26.3		Population modification To test various methods to modulate gene drive activity, e.g. Cas9 expression level (Roggenkamp *et al.* 2018) and Cas9 nuclear localisation (Goeckel *et al.* 2019)	Split homing CRISPR CRISPR-Cas9 gene drive / CRISPR gene drive	(Roggenkamp *et al.* 2018, Goeckel *et al.* 2019)	1 2 3 4 5 6 ? ? ? 7 8 9	G.C. Finnigan Kansas State University, USA	NIH USDA Kansas State University
26.4		Population modification To test a split gene drive system to simultaneously propagate gene drives at three different loci	Multi-locus split homing CRISPR multi-locus CRISPR gene drive	(Yan and Finnigan 2018)	1 2 3 4 5 6 ? ? ? 7 8 9	G.C. Finnigan Kansas State University, USA	NIH USDA
26.5		Population modification Proof of principle of population modification via a split homing gene drive based on Cas12a	Split homing CRISPR employing Cas12a 'Cas12a-based gene-drive system'	(Lewis, Yan, and Finnigan 2021)	1 2 3 4 5 6 ? ? ? 7 8 9	G.C. Finnigan Kansas State University, USA	Kansas State University USDA

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
26.6		Population modification To generate a library of 'all combinations of 10 missense mutations from across the genome' to study interactions between these mutations (epistasis)	Split homing CRISPR 'hierarchical' CRISPR gene drive	(Bakerlee *et al.* 2022)	1 2 3 4 5 6 ? ? ? 7 8 9	M.M. Desai Harvard University, USA	DoD NSERC Canada NIH NSF
27	***Candida albicans***	Population modification To create single and double deletion mutants in this species for laboratory studies	Split homing CRISPR CRISPR-Cas9 based gene drive	(Shapiro *et al.* 2018, Halder *et al.* 2019)	1 2 3 4 5 6 ? ? ? 7 8 9	J. Collins MIT & Harvard University, USA R.S. Shapiro University of Guelph, Canada	Allen CIHR NIH Wyss Institute NSERC Canada Banting Burroughs Wellcome Fund
Kingdom: PLANTS							
28	***Arabidopsis thaliana*** Thale cress	Population modification The intention was to demonstrate a gene drive system in a plant model species. The authors state this technology could 'accelerate crop breeding'	Homing CRISPR CRISPR/Cas9-based gene drive	(Zhang, Mudgett, *et al.* 2021, Zhang *et al.* 2022) **paper WITHDRAWN after a year**	1 2 3 4 5 6 7 8 9	Y. Zhao University of California San Diego, USA	TIGS UCSD NIH
29	***Nicotiana tabacum*** Tobacco	Population modification The aim is to demonstrate a technology for modifying the plant mitochondrial genome for laboratory experiments and to 'enable the exploitation of mitochondria in biotechnology and synthetic biology'	TALEN gene-drive mutagenesis transcription activator-like effector nuclease (TALEN) gene-drive mutagenesis (GDM), or TALEN-GDM	(Forner *et al.* 2022)	1 2 3 4 5 6 7 8 9	R. Bock Max Planck Institute for Molecular Plant Physiology, Germany	Max Planck Society ERC

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?									Project leader(s) Institution	Funders
PLANTS															
30	**Various weed and invasive species:** ***Alopecurus mysuroides*** Black grass[13] ***Amaranthus palmeri*** Palmer amaranth[13] ***Amaranthus Tuberculatus*** Rough fruited water hemp[13] ***Ambrosia artemisiifolia*** Common ragweed[13] ***Cynodon dactylon*** Bermuda grass[13] ***Cyperus rotundus*** Purple nut sedge[13] ***Eichhornia crassipes*** Water hyacinth ***Kochia scoparia*** Kochia[13] ***Lantana camara*** Common lantana[13] ***Lolium rigidum*** Rigid rye grass[13] ***Lupinus arboreus*** Yellow bush lupin/tree lupin ***Lychnis coronia 'Alba'*** Rose campion ***Setaria glauca*** Yellow foxtail[13]	Population modification to enable suppression To reduce the presence and impact of weed species on agricultural production by modifying them, potentially to render them less competitive, or more sensitive to herbicide. It might also be used to tackle other invasive plant species.	Homing CRISPR is most common proposed technology NA - Proposals only	(Neve 2018) (Kumaran *et al*. 2020) (Perotti *et al*. 2020) (Wong *et al*. 2022) **All the above papers make similar proposals so have been combined into one entry** (Mitchell and Bartsch 2020) suggest common ragweed as a target	1	2	3	4	5	6	7	8	9	Proposals from several funded CSIRO researchers including at the University of Queensland, Australia, and researchers at Rothamsted Research UK	Various funders including BBSRC and CSIRO

13 Agricultural weed

	Species Geographic range	Intended direct effect Intended use (as stated by authors)	Type of gene drive (our categories) Developer's name for gene drive system	Publication(s) where research is described	How close is strain/system to experimental releases in the wild?	Project leader(s) Institution	Funders
31	***Myrtaceae* family** (including ***Eucalyptus spp.***) To modify wild populations in Australia to render them resistant to the fungal pathogen *Puccinia psidii*	Population modification The proposals do not focus on any particular type of gene drive	NA	(Barrett *et al.* 2019)	1 2 3 4 5 6 7 8 9	D.M. Gardiner CSIRO Agriculture and Food, Australia	CSIRO

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 modelling work, or preliminary laboratory work funded:** a proposal has been made in the scientific literature supported by modelling work, or preliminary laboratory work has been funded but has not yet been published

3 **Preliminary laboratory work published**: laboratory research relevant to gene drive construction published (e.g. developing molecular biology methods) with possibility or intention to construct gene drive stated

4 **Research on gene drive construction funded:** 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

6 **Laboratory proof of concept:** Taking published results at face value, the system works effectively in the laboratory

7 **Non-insects- scaled up trials:** Data published from scaled up trials in contained environments, offering a more accurate simulation of conditions in natural environment

Insects - large cage trials: Data published on trials in large cages, offering a more accurate simulation of conditions in natural environment

8 **Potential further contained trials:** After large cage trials (or other scaled up trials), it is not currently clear what further trials may take place prior to experimental releases. One possibility is trials in outdoor cages

9 **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

X **Abandoned project:** Research to construct a gene drive has been carried out, but has been unsuccessful and to our knowledge is no longer active

Abbreviations for funders and other organisations

Allen	Allen Frontiers Group
ARC	Australian Research Council
Banting	Banting Research Foundation
BARD	United States—Israel Binational Agricultural Research and Development Fund
BBSRC	UK Biotechnology and Biological Sciences Research Council
Bioheritage NZ	New Zealand Bio-heritage National Science Challenge
CFI	Canada Foundation for Innovation
CIHR	Canadian Institutes of Health Research
CSC	Commonwealth Scholarship Commission
CSIRO	Commonwealth Scientific and Industrial Research Organisation
DARPA	US Defense Advanced Research Projects Agency
DOE	US Department of Energy
ENTRF	Environment and Natural Resources Trust Fund
ERC	European Research Council
ESEB	European Society for Evolutionary Biology
Greenwall	Greenwall foundation
Kinship	Kinship foundation
NCI	US National Cancer Institute
NIDDK	US National Institute of Diabetes and Digestive and Kidney Diseases
NIH	US National Institutes of Health
NSERC Canada	Natural Sciences and Engineering Research Council of Canada
NSF	US National Science Foundation
Packard	David and Lucile Packard Foundation
Pew	Pew Charitable Trust
Predator Free NZ	New Zealand Predator Free Program
Rainwater	Rainwater Foundation
Sloan	Sloan Foundation
SNSF	Swiss National Science Foundation
TATA	TATA trusts
TIGS UCSD	Tata Institute for Genetics and Society University of California San Diego
UCI	University of California Irvine
USC	University of South Carolina
USDA	US Department of Agriculture
Wyss Institute	Wyss Institute for Biologically Inspired Engineering

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Methodology

Literature searches

Literature searches for 2020 through to the 31 December 2022 were carried out using the Web of Science database and the search term ‘gene drive’. Literature searches for 2019 and previous years were carried out with the PubMed database using the same search term. Relevant journal articles were identified by systematically screening titles and abstracts from the search outputs. Press releases from academic institutions and other relevant materials on the web were identified using appropriate web searches (e.g. searching for the names of group leaders, target species, and the term ‘gene drive’). We recognise that all relevant material on the web may not have been identified.

Criteria for inclusion

Laboratory research and modelling on gene drives in non-insect species as reported in the academic literature and other sources such as press releases from funders and universities, have been included. Proposals for gene drives in non-insect targets as identified from the natural sciences literature are included. Proposals deriving from other academic literature (such as literature relating to policy or ethics) are included at our discretion, for example if such proposals designate novel targets.

Basis for generating entries in table

Broadly, each entry in the table describes development of a particular gene drive concept in a specific target species or group, as described in the relevant literature. In some cases where multiple options are considered in a single publication, multiple proposed gene drives are described in a single entry row (generally these are early-stage proposals or modelling studies). The ‘project leader’ is identified as the last author on the publications describing the research or proposals.

Basis for ordering entries

Entries are grouped taxonomically. Entries for research in house mice are grouped according to the type of gene drive proposed. Entries within other species or taxonomic groups are sorted firstly according to how far research has progressed, and secondly by year of publication.