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Genetic Biocontrol Overview

Great Lakes Panel on Aquatic Nuisance Species

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U.S. Department of the Interior
U.S. Geological Survey

What is genetic biocontrol?

Genetic biocontrol is the exploitation of genetics to get the organism to control *ITSELF*.
(letting nature do the work for us)

- **Numerous technologies or strategies that can be used**

- **Optimal strategy depends on:**
  - **Biology / Life history**
  - **Risk tolerance**
  - **Size of invasion**
  - **Objective**

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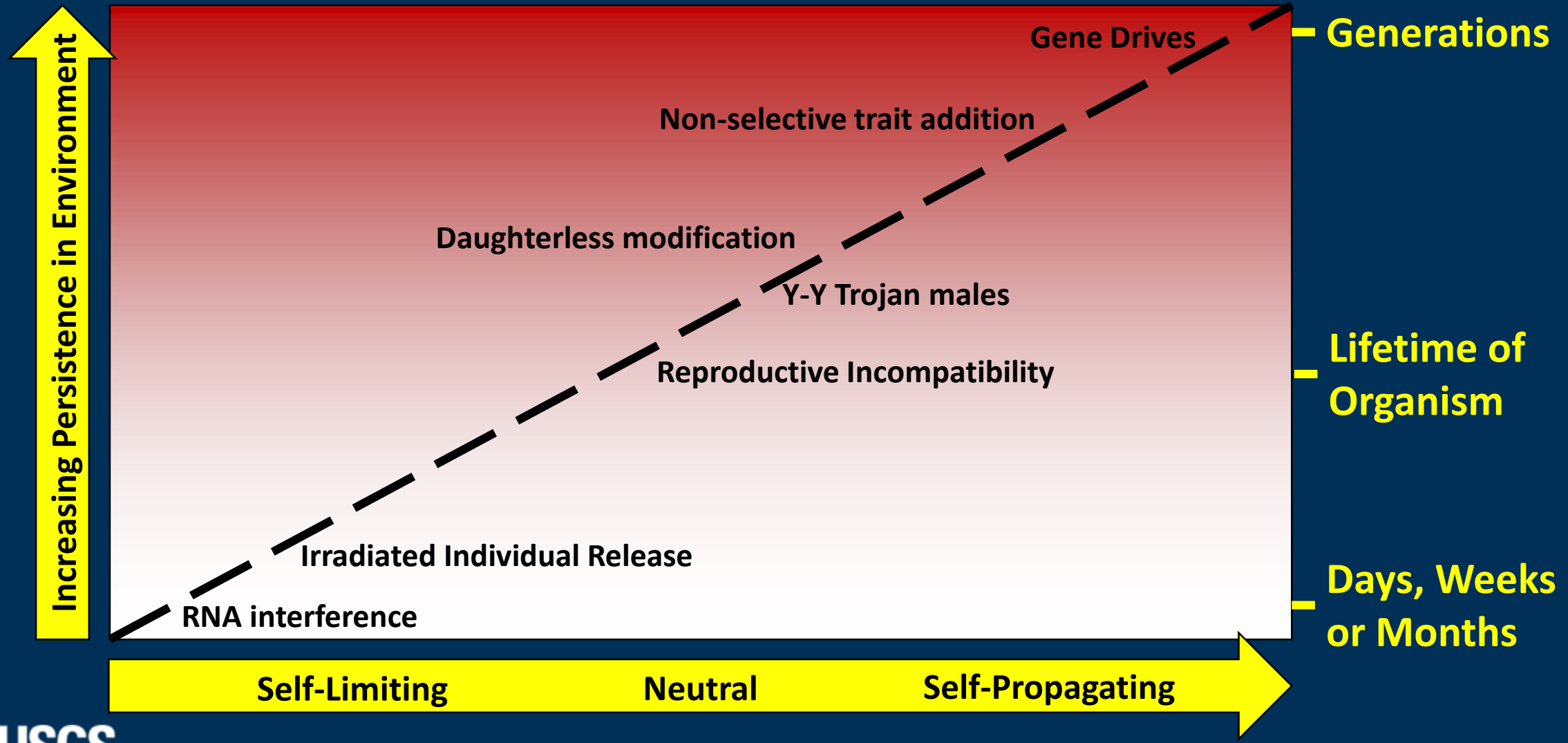
Environmental Persistence



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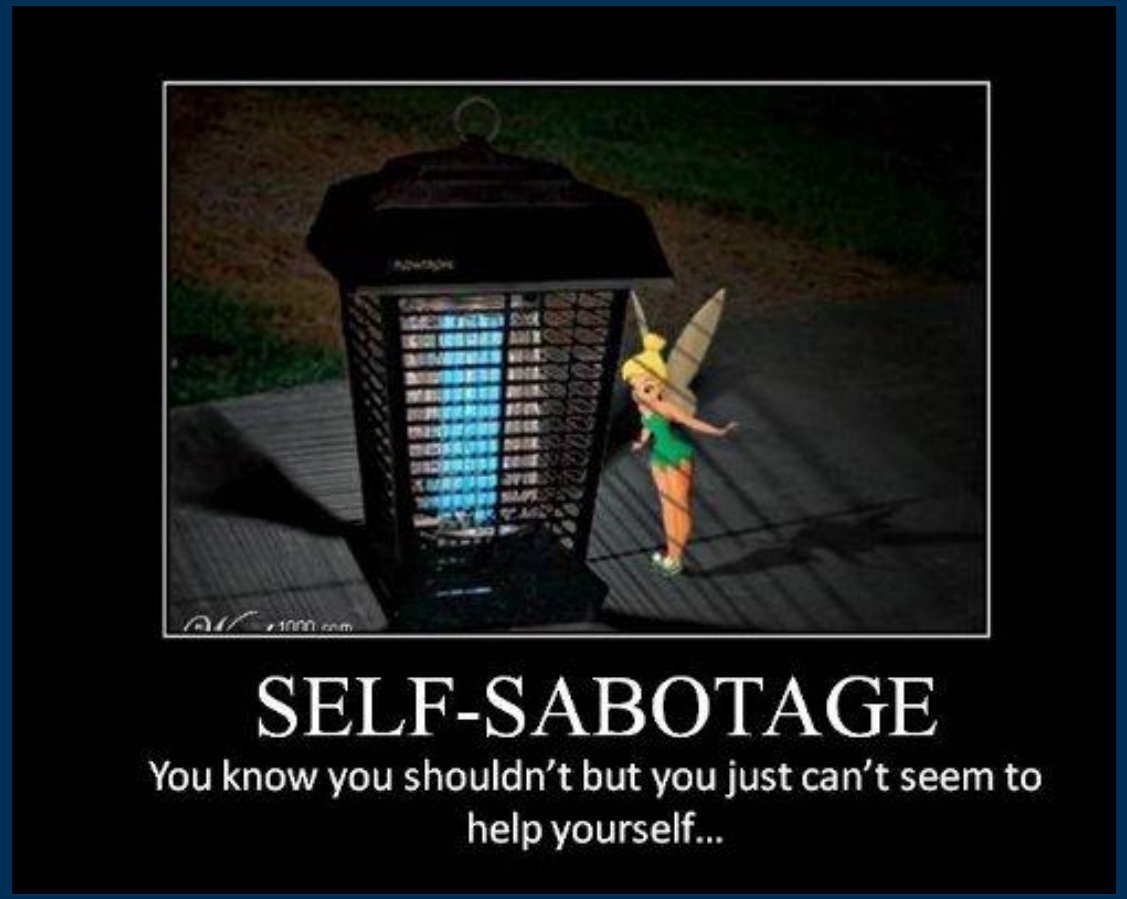
RNA interference (RNAi)

PREMISE: Trick the organism into "thinking" important genes are unimportant on the cellular level.

- **Mello and Fire got Nobel Prize in 2006**
- **Thousands of publications**
- **Use the organism's own molecular machinery to shut down cells.**
- **Specific to DNA sequence beyond just species, but targets genes of that species.**



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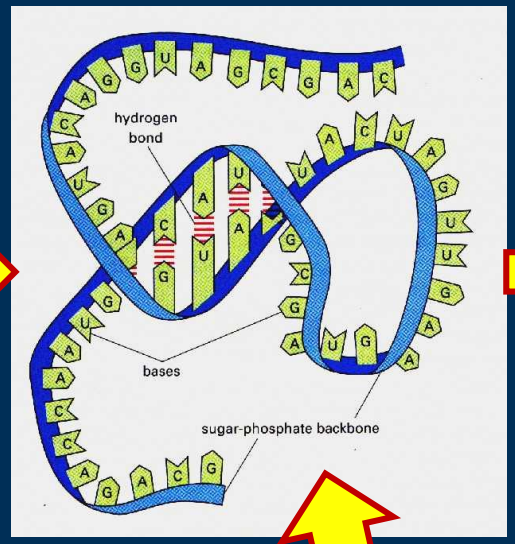
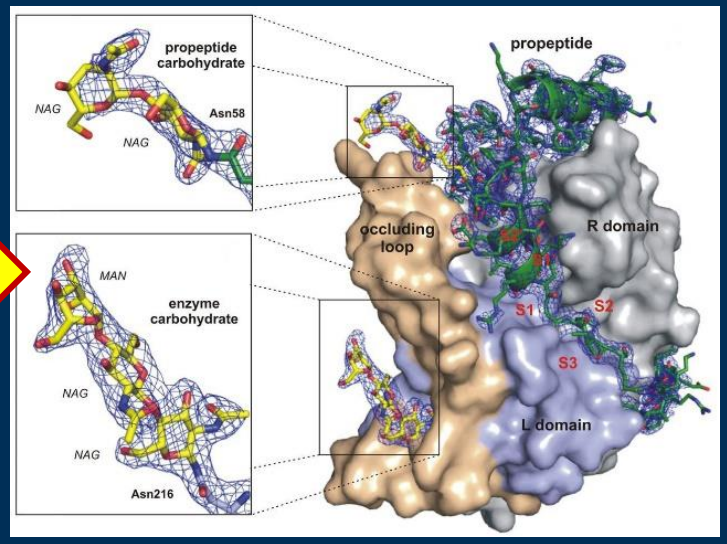
The Central Dogma of Biology

DNA -> RNA -> Protein





RNA interference targets RNA molecules for destruction thus preventing protein from being made

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RNA interference

- RNAi tricks the cell into destroying its own mRNA
- RISC – RNA Induced Silencing Complex
- Small double-stranded RNA molecules guide RISC in what mRNA to cleave

We choose very specifically what genes to turn off
We provide the small dsRNA, and the target individuals do the rest

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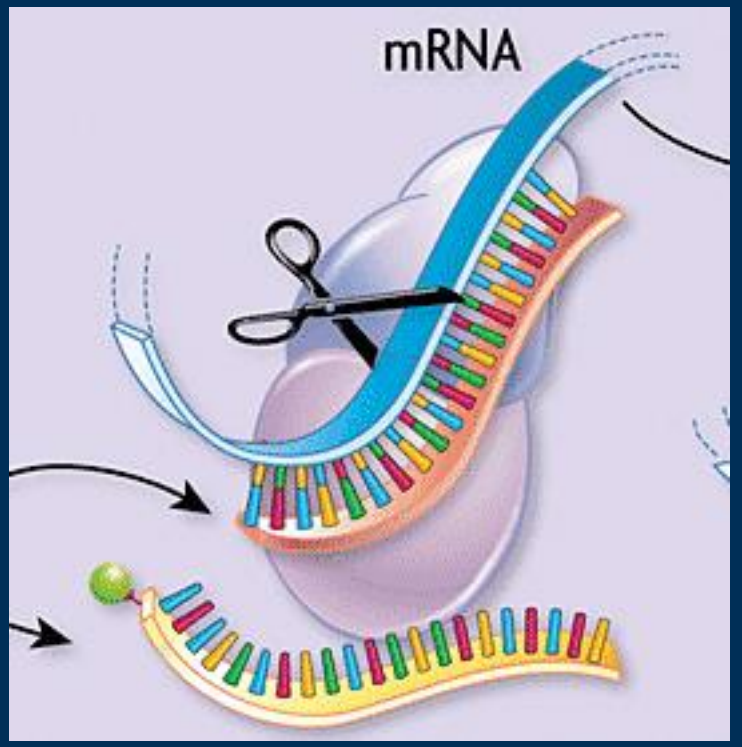
RNA interference

- Potentially cheap to implement
- Total control of deployment
- Does not persist in the environment
- No off-target impacts currently known
- Used in agriculture for pest resistance
- Similar to chemical treatments currently in practice, but much more focused



Insect Genetic Technologies Research Coordination Network

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Sterile Male Release Technique

PREMISE: Suppress reproduction by inducing failed mating

- **Capture wild individuals and sterilize**
  - **Irradiation**
  - **Chemical sterilization**

Aquiloni *et al*.

Great Lakes Fishery Commission

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Sterile Male Release Technique

PREMISE: Suppress reproduction by inducing failed mating

- **Balancing effective sterilization without altering their behavior**
- **Sterilization techniques can be risky to workers**
- **Need to release many individuals**

Kai Kupferschmidt, *Science*

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Engineering Reproductive Incompatibility

PREMISE: Suppress reproduction by inducing failed mating

- **Engineered individuals that offspring are only viable when exposed to particular compound**
- **Make only male offspring viable**
- **Develop species-like barrier**

University of Minnesota, MAISRC

Oxitec

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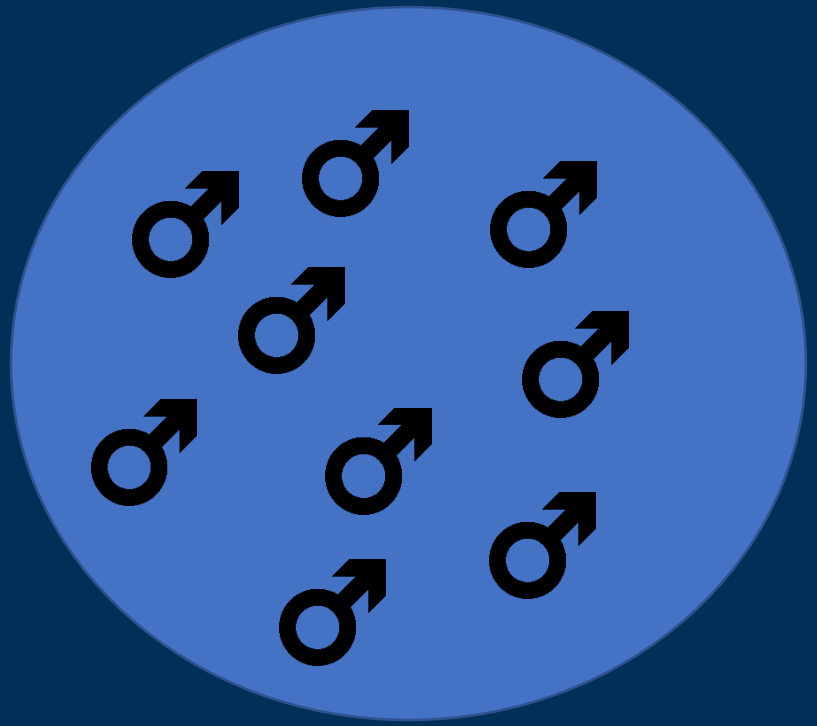
Y-Y male release

PREMISE: Skew sex ratios so that there are only males…
Then the invader cannot reproduce.

- **Won't work for all invasive species…**
- **Depends on XY sex determination, and some other factors.**



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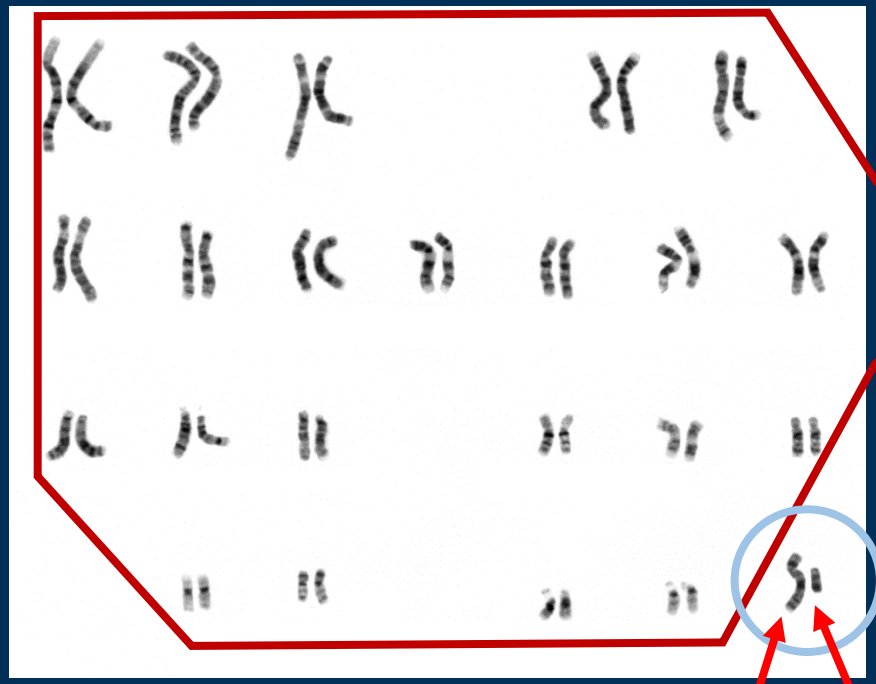
“Normal” Sex Determination



Humans have 22 pairs of “autosomes”…

… and 1 pair of “sex chromosomes”

“X” “Y” – This person is male

“X” “X” – This person is female

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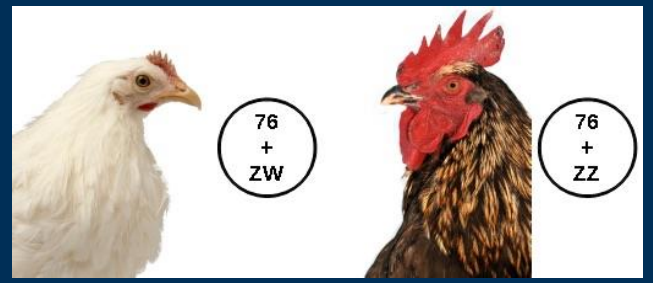
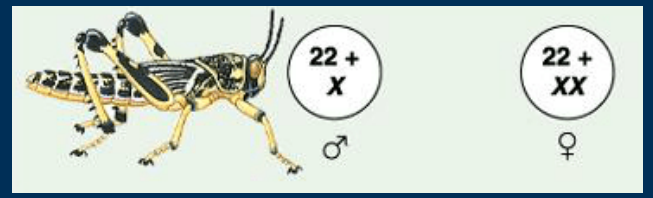
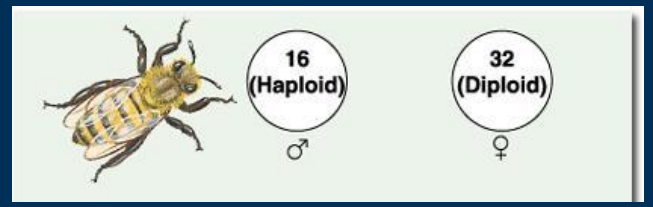
Other types of Sex Determination

- **ZW Sex Determination**
  - Chickens, Komodo Dragons, Giant River Prawn, Moths and Butterflies, Others…
- **X0 Sex Determination**
  - Grasshoppers, Crickets, Cockroaches, Others…
- **Haplodiploid Sex Determination**
  - Bees, Ants, Wasps, Thrips, Others…
- **Temperature-Dependent Sex Determination**
  - Reptiles, Possibly others…







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Y-Y Male Release to control a population: How it works


x


Normal male mated with normal female:

	x	y
x	xx	xy
x	xx	xy

- 50% female
- 50% male


x


Super male mated with normal female:

	y	y
x	xy	xy
x	xy	xy

- 100% male

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Y-Y Male Release to control a population: How it's made

- X-Y genetically male fish will develop into phenotypic female if exposed to estradiol during development
- These X-Y egg producers can then be mated with males

Normal male mated with feminized males:

	x	y
x	xx	xy
y	xy	yy

- 25% female
- 50% normal male
- 25% super male

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Y-Y Male Release to control a population: Considerations

Deal Breakers:

- Sex must be determined genetically with X-Y system with no environmental influence
- Individuals must not be able to spontaneously reverse sexes
- Aquaculture methods must be possible

Deal Makers:

- Low density target populations
- Short-lived species
- Harvestable

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Y-Y Male Release to control a population: Considerations

Other Considerations:

- Reversible
- Must release many super males
- Must continue for years (dependent on species)
- Releasing sex-hormone-treated fish (FDA regulation)

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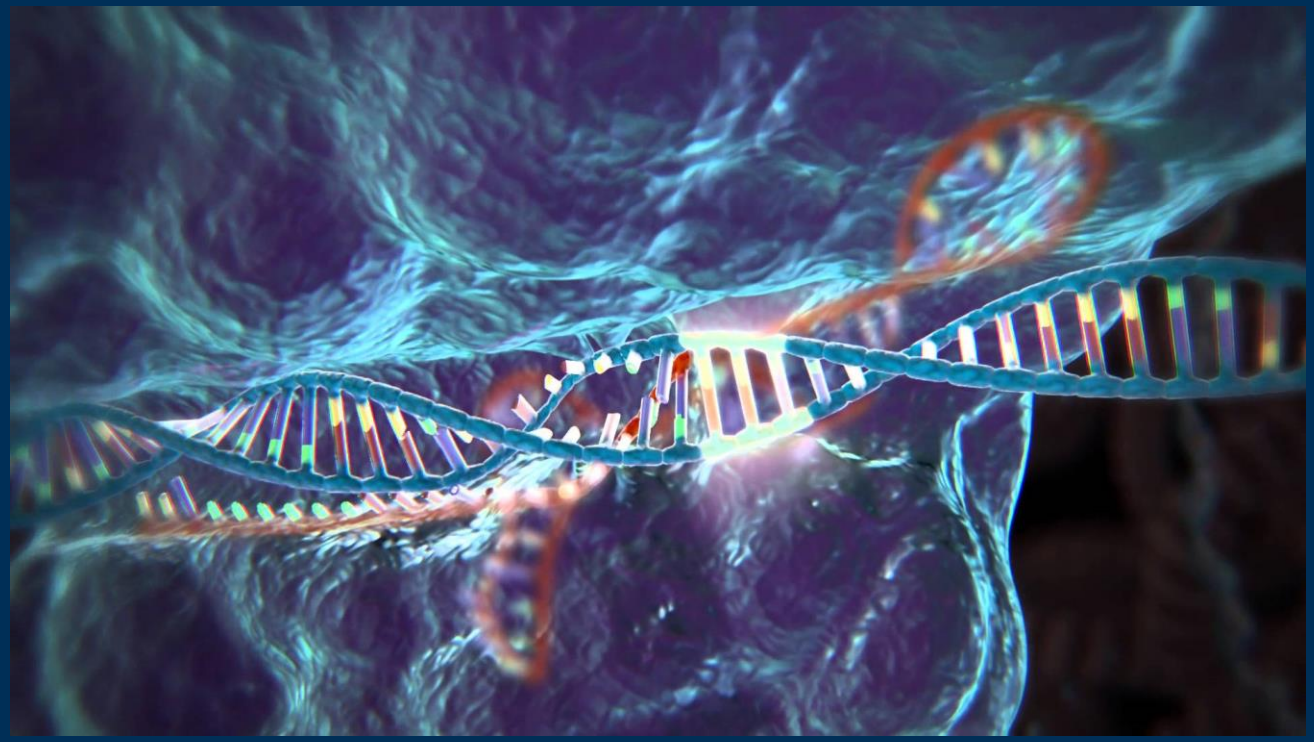
CRISPR gene drives

- **CRISPR: Clustered Regularly Interspaced Short Palindromic Repeats – A method for editing genomes.**



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What's so special about CRISPR?

Compared to previous genome editing methods:

- **Faster, Easier, and Cheaper**
  - Days instead of weeks or months
  - Sequence-based targeting
  - Hundreds instead of Thousands of $$$
- **More reliable targeting**
  - 95-98% fidelity
- **Fewer off-target affects**
  - Less chance of unintended consequences

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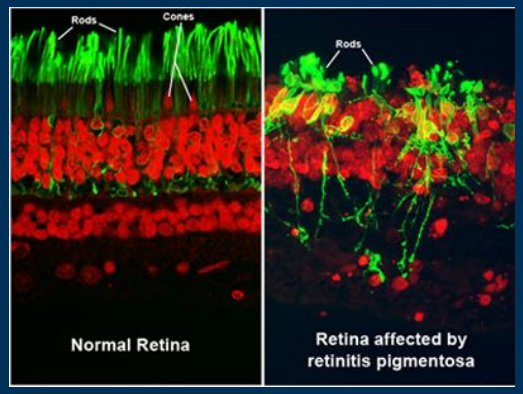
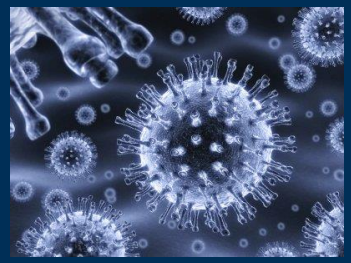
What's so special about CRISPR?

- Originally discovered as a bacterial defense against viruses
  - Chops up viral DNA
- First U.S. human trials approved in 2016 for lung cancer patients
  - Cured Retinitis Pigmentosa
  - Cured Leukemia
  - Aids cure in development
  - Many genetic diseases curable
- Malaria Resistant Mosquitos in development





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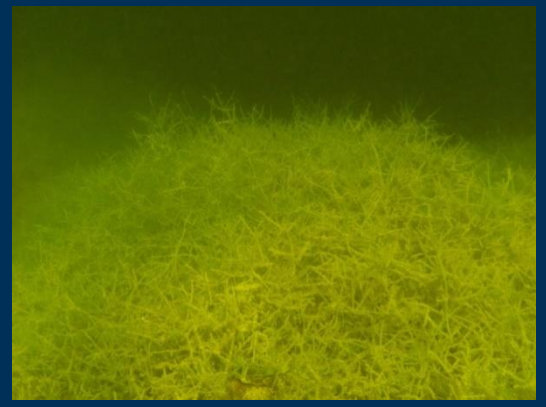
How CRISPR can help with invasive species

- **Gene Drive: A gene that is guaranteed to pass on to all offspring.**

<u>Can be:</u>

- **Lethal alleles**
- **Female sterility alleles**
- **Modified function alleles**



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Ethical Considerations

- Genetic modification has been around a long time
  - Crops, Dogs, Race horses
- Incredibly powerful tool
  - What we “can do” vs. what we “should do”?
- Public engagement
  - Interested parties
  - Scientists
  - Politicians
  - Public at large

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