Possible applications of gene drive research for public health and conservation

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Gene drive properties

- **Introduce new heritable trait into target population**
    - Mating-based
        - exquisitely species-specific
            - direct impact limited to target species only
    - Target-seeking
        - released gene drive individuals will actively seek mates

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Single target species

Can access hard-to-reach / hard-to-find populations

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- **What trait(s)?**

  Most current pest control

  - Population suppression – reduce number of population
    - sterility or similar – if enough pests gain the trait the target population will decline
  - Population modification – reduce harm caused by population
    - pathogen resistance
    - outcome conceptually similar to "vaccinating" pest population

Gene drive applications

Single target species, short generation time

❏ **Population suppression**

   ❏ Rodents (mice, rats) on islands [conservation]

   ❏ Mosquitoes

      ❏ Malaria in sub-Saharan Africa [public health]

      ❏ Dengue and other mosquito-borne viruses [public health]

      ❏ Avian disease [conservation]

   ❏ Agricultural pests

      ❏ Spotted-wing *Drosophila (*one of rather few examples) [agricultural pest]

❏ **Population replacement**

   ❏ Mosquitoes

      ❏ Malaria [public health]

      ❏ Dengue and other mosquito-borne viruses [public health]

❏ NB these all target wild pest populations – no obvious applications for domestic species, e.g. crop plants, livestock where breeding/mating is already under human control

❏ Current developers overwhelmingly universities/institutes; funders are governments and philanthropies

Example – malaria in sub-Saharan Africa

Single target species, short generation time

- **Malaria**
  - ~500,000 deaths per year, most are children <5yrs in sub-Saharan Africa
    - Down from ~1m through use of bednets, enhanced spraying, treatment etc
  - Mosquito-borne
    - Human malaria is exclusively transmitted by *Anopheles* mosquitoes
    - Most important species is *Anopheles gambiae*

- **Gene drive**
  - Spread a reduced-fertility or sex-ratio (male bias) gene through population/species [e.g. http://targetmalaria.org/]
    - Target mosquito population reduced below threshold needed to sustain malaria
  - Spread gene(s) preventing transmission of the malaria parasite [e.g. http://malaria.bio.uci.edu/]
    - Target mosquito population remains, but unable to spread malaria

Aim to spread modification broadly through target mosquito species

Example – rodents on islands

Single target species, short generation time

❑ **Islands**

    ❑ 5.3% of terrestrial area, often evolutionarily distinctive and vulnerable to new introductions

        ❑ 75% of reptile, bird, amphibian and mammal extinctions combined have occurred on islands

        ❑ invasive species implicated in 86% of all recorded extinctions on islands

        ❑ invasive rats, mice, particularly important   https://www.islandconservation.org/

        ❑ successful examples of removal but difficult to achieve with current methods, e.g. mass poisoning

❑ **Gene drive**

    ❑ Spread a reduced-fertility or sex-ratio (male bias) gene through population/species

        ❑ eliminate invasive species from island

        ❑ early stages, but genetics of mice & rats well understood

Aim to spread modification through island population only