Gene drive that results in addiction to a temperature-sensitive version of an essential gene triggers a population collapse in *Drosophila*

Oberhofer G, Ivy T, Hay BA. Proc Natl Acad Sci, 2021 Dec 7;118(49):e2107413118. https://www.pnas.org/content/118/49/e2107413118

Scientific Achievement

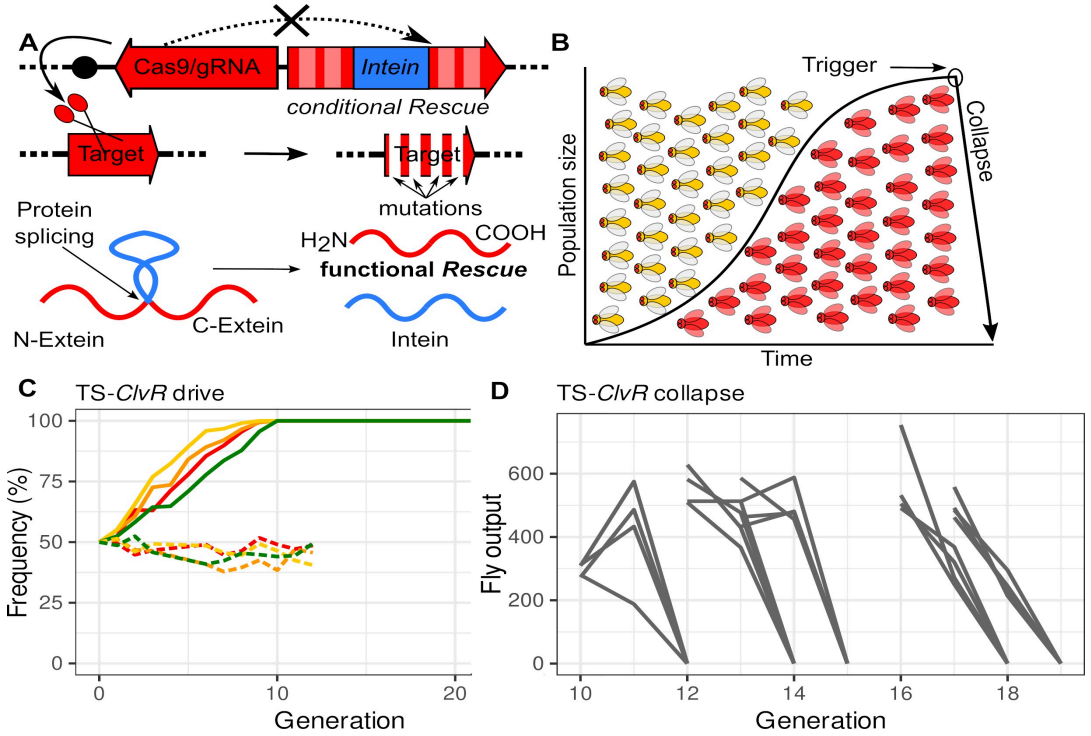
- Replacement of a fly population with a temperature-dependent Cleave and Rescue (*ClvR*) drive element, followed by suppression of the population as the temperature is changed

Significance and Impact

- Shows the use of a gene drive platform for species-specific pest/vector elimination

Technical Details

- *ClvR* uses gene editing tools to disrupt an essential gene, while also including a temperature-dependent Rescue version of the gene. As *ClvR* spreads, the survival of the population becomes temperature-dependent.
- We built a *ClvR* (TS-*ClvR*) in *Drosophila* in which Rescue activity requires removal of a temperature-sensitive intein. TS-*ClvR* spreads to transgene fixation at 23ºC, but when populations now dependent on the Rescue are shifted to 29ºC, the population dies out.



A) *ClvR* mechanism of action: Cas9/gRNAs inactivate an essential gene. Those carrying *ClvR* survive because they also carry an uncleavable Rescue transgene. Here the Rescue is designed to be temperature sensitive through inclusion of an intein that can only be removed at low temperature. **B)** TS-*ClvR* flies (red) are released during a low temperature season, replacing the wildtype population. When the temperature increases in summer, the TS-Rescue becomes non-functional and the population collapses. **C)** Population drive experiment in which TS-*ClvR* (solid lines) but not a control strain (dotted lines) replaces wildtype within 10 generations at 23ºC. **D)** TS-*ClvR* bearing populations from C) rapidly crash when incubated at 29ºC.

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