Ecological Application outline

An Outline of Using Self-Replicating Gene Drives That Can Spread Deleterious Alleles Through Animal Populations on Islands

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A. Problem: Invasive species are populating islands and must be eradicated before they cause the native island species to become extinct

- This is most important for island populations because of their limited resources
- We must make sure that we are not harming the native biodiversity
- Invasive species can become resistant to treatment and become more difficult to control

B. Solution: Using gene drives to spread deleterious alleles and eradicate these species

- How gene drive works: https://wyss.harvard.edu/media-post/crispr-cas9-gene-drives/
- My research involved using CRISPR/Cas12a to cause a Y chromosome deletion in mice. This caused potential male offspring to become females
- This technique causes resistance through NHEJ or may not be effective at all

C. Regulatory Issues: We must determine when gene drive is necessary and how to obtain the best results.

- In Dawson et al., they discuss their recommended procedure to determine "eradication feasibility and distinguish the potential and realistic value of an eradication"
- Because gene drive is such a new technology and must be very specific to a population more research must be done to determine feasibility

D. Proposed Regulation:

- Simply, more research must be done. Since gene drive is a very specific type of modification when it works, we know it will only affect the target populations. We need greater efficiency and minimal mutations that cause resistance. It should not introduce into the wild until it has been refined.
- Use the procedure in Dawson et al. to establish which invasive species to target first and focus gene drive research towards those species.

E. References:

- Prowse, T., Cassey, P., Ross, J. V., Pfitzner, C., Wittmann, T. A., & Thomas, P. (2017). Dodging silver bullets: good CRISPR gene-drive design is critical for eradicating exotic vertebrates. *Proceedings. Biological sciences*, *284*(1860), 20170799. doi:10.1098/rspb.2017.0799 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5563802/#
- Prowse, T. A., Adikusuma, F., Cassey, P., Thomas, P., & Ross, J. V. (2019). A Y-chromosome shredding gene drive for controlling pest vertebrate populations. *eLife*, *8*, e41873. doi:10.7554/eLife.41873 https://www.ncbi.nlm.nih.gov/pubmed/30767891

- Champer, J., Liu, J., Oh, S. Y., Reeves, R., Luthra, A., Oakes, N., … Messer, P. W. (2018). Reducing resistance allele formation in CRISPR gene drive. *Proceedings of the National Academy of Sciences of the United States of America*, *115*(21), 5522–5527. doi:10.1073/pnas.1720354115 https://www.ncbi.nlm.nih.gov/pubmed/29735716
- McCreless, E. E., Huff, D. D., Croll, D. A., Tershy, B. R., Spatz, D. R., Holmes, N. D., … Wilcox, C. (2016). Past and estimated future impact of invasive alien mammals on insular threatened vertebrate populations. *Nature communications*, *7*, 12488. doi:10.1038/ncomms12488 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4992154/
- Oberhofer, G., Ivy, T., & Hay, B. A. (2018). Behavior of homing endonuclease gene drives targeting genes required for viability or female fertility with multiplexed guide RNAs. *Proceedings of the National Academy of Sciences of the United States of America*, *115*(40), E9343–E9352. doi:10.1073/pnas.1805278115 https://www.ncbi.nlm.nih.gov/pubmed/30224454
- Pest demography critically determines the viability of synthetic gene drives for population control. (2018, September 13). Retrieved April 2, 2019, from https://www.sciencedirect.com/science/article/abs/pii/S0025556418301172?via=ihub
- Dawson, J., Oppel, S., Cuthbert, R. J., Holmes, N., Bird, J. P., Butchart, S. H., . . . Tershy, B. (2015, February). Prioritizing islands for the eradication of invasive vertebrates in the United Kingdom overseas territories. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/25163543