UNIVERSITY of TASMANIA

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Darwin and the devil's plight: is natural selection finding a way to combat cancer?

Research into the deadly cancer affecting Tasmanian devils has found the marsupials are mounting their natural defence against the disease.

An international team from Australia, the US, United Kingdom and France has analysed the natural adaptations and evolutionary responses of Tasmanian devils to the devil facial tumour disease (DFTD).

The study, published in the journal *Conservation Biology,* synthesised more than a decade of DFTD research from different devil populations across multiple generations.

The authors found that the evolutionary responses of devils to the cancer epidemic are likely to result in devils coexisting with DFTD, and that future management interventions should integrate the adaptations observed in wild populations.

University of Tasmania disease ecologist Dr Rodrigo Hamede said an increasing amount of evidence demonstrates that wild Tasmanian devils have been evolving defence mechanisms against cancer.

"We have witnessed fast evolution in action and an increasing number of individuals with tumour regressions; that is, devils that can eliminate the cancer on their own," Dr Hamede said.

"At the same time, we have seen signs of selection against DFTD in the devil's genome, more specifically, in genes associated with cancer and immune function.

"Natural selection should favour increases in the frequency of these traits against cancer from generation to generation.

"Therefore, management interventions, both in captivity and in the wild, need to consider these evolutionary processes to ensure adapted genotypes that exhibit resistance to DFTD are represented across populations."

Considerations for management of insurance populations

Co-author Professor Andrew Storfer, from Washington State University, said that reintroducing DFTD-naïve devils from captive breeding populations may result in the introduction of maladapted genetic diversity into the wild.

“Our research has shown that the devils appear to be evolving naturally in response to DFTD. As such, gene frequencies in natural populations are likely to differ from those in captive populations, which are geared toward maximizing overall genetic diversity,” Professor Storfer said.

Dr Hamede said that captive breeding programs had played an important role in providing an insurance population as a safeguard for the species.

The next step is to integrate the evolutionary adaptations observed in the wild into captive breeding programs, balancing the benefits of DFTD-adapted genetic diversity and the costs of losing overall genetic diversity.

“This is a reminder that silver bullets are rarely the answer to complex conservation problems,” he said.

“One of the greatest difficulties we face, in a century characterised by the emergence of infectious diseases, is to acknowledge that human interventions should be undertaken when the benefits of doing so outweigh the benefits of giving species the chance to recover through natural selection.

“Tasmanian devils are reminding us that nature can find its way out of the most complex threats. Facilitating beneficial adaptations and minimising other threatening processes that may act in synergy with DFTD is likely to be the most effective and enduring conservation strategy for the species.”

Learning to coexist with two transmissible cancers

Over the past 25 years, DFTD has reduced devil populations by at least two thirds. The road to recovery may take significant time, with devils now facing another transmissible cancer: Devil Facial Tumour 2 or DFT2.

DFT2 was discovered in 2014 in south-eastern Tasmania, and the effects of this new cancer on devil populations have not been fully evaluated.

“The vital question we need to answer now is whether the adaptations we have seen in response to DFTD are transferable to DFT2, and this may take some time to evaluate,” Dr Hamede said.

“In that sense, the fundamental principle for managing wild devil populations is developing an adaptive and transdisciplinary conservation strategy, allowing us to change directions as new knowledge becomes available.”

Recent studies and epidemiological models have predicted that in the absence of management interventions, such as reintroductions or immunisations, devils and tumours are likely to coexist.

This means that DFTD is unlikely to disappear in the foreseeable future, but it also means that devils can persist as they evolve to live with this cancer. The authors concluded that future interventions should be restricted to controlled experiments until evidence supports their long-term effects as beneficial in light of devil-DFTD evolutionary processes.

“We need to keep finding novel ways to facilitate their recovery through natural selection and protect devils from other threats such as roadkill, habitat fragmentation and invasive species. This highlights the role of the broader community in devil conservation.”

An international research effort

Dr Hamede said that research on Tasmanian devils and DFTD had attracted the attention of oncologists and cancer biologists from around the world.

Co-author Prof Frederic Thomas, from the French National Centre for Scientific Research (CNRS) and Head of the Centre for Research in Cancer Ecology and Evolution, said that the significance of these natural adaptations to cancer transcends Tasmanian devils.

“Bridging evolutionary ecology and cancer biology is proving to be essential for understanding the biological and environmental mechanisms of cancer emergence and the lethality of tumours in both, animals and humans,” Professor Thomas said.

Darwin, the devil and the management of transmissible cancers was authored by a team of leading national and international researchers: Rodrigo Hamede, Thomas Madsen, Hamish McCallum, Andrew Storfer, Paul A. Hohenlohe, Hannah Siddle, Jim Kaufman, Mathieu Giraudeau, Menna Jones, Frederic Thomas and Beata Ujvari.

PHOTOS ATTACHED: **(1)** Dr Rodrigo Hamede Ross releases a Tasmanian devil during a field trip near Cradle Mountain (Credit: Eddie Safarik); **(2)** A female Tasmanian devil with DFTD, and after tumour regression three months later (Credit: Manuel Ruiz Aravena).

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