Life-history change in disease-ravaged Tasmanian devil populations

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Changes in life history are expected when new sources of extrinsic mortality impact on natural populations. We report a new disease, devil facial tumor disease, causing an abrupt transition from iteroparity toward single breeding in the largest extant carnivorous marsupial, the Tasmanian devil (*Sarcophilus harrisii*), in which males can weigh as much as 14 kg and females 9 kg. This change in life history is associated with almost complete mortality of individuals from this infectious cancer past their first year of adult life. Devils have shown their capacity to respond to this disease-induced increased adult mortality with a 16-fold increase in the proportion of individuals exhibiting precocious sexual maturity. These patterns are documented in five populations where there are data from before and after disease arrival and subsequent population impacts. To our knowledge, this is the first known case of infectious disease leading to increased early reproduction in a mammal. The persistence of both this disease and the associated life-history changes pose questions about longer-term evolutionary responses and conservation prospects for this iconic species.

carnivorous marsupial | infectious cancer | wildlife disease | precocious breeding | semelparity

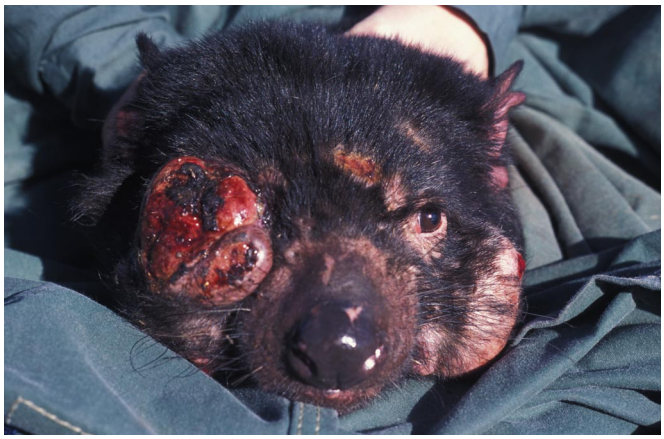

Fig. 1. Tasmanian devil facial tumor disease, a recently emerged infectious cancer, has caused virtual semelparity and a dramatic increase in the proportion of juvenile females breeding.

Changes in life history are expected when new sources of extrinsic mortality impact on natural populations (1, 2). In age-structured populations, juvenile survival and age at first reproduction respond rapidly to changes in density, followed by changes in fecundity (3, 4). Adult survival is influenced by phenotypic effects on juveniles and is the last vital rate to be affected (3, 4). Life-history change has been documented in response to release from culling pressure (4), an increase in fishing pressure (2), and changes in predator assemblage and level of predation (1, 5). Early reproduction as a consequence of parasitism has been predicted theoretically (6), with limited supporting empirical evidence (7, 8). Here, we report a new disease, devil facial tumor disease (DFTD) (Fig. 1), causing an abrupt transition from iteroparity toward single breeding in the largest extant carnivorous marsupial, the Tasmanian devil (*Sarcophilus harrisii*). Endemic to the Australian island of Tasmania, male Tasmanian devils can weigh as much as 14 kg and females 9 kg. To our knowledge, this is the first known case of infectious disease leading to increased early reproduction in a mammal.

Symptoms resembling DFTD were first reported in 1996 and by 2007 had spread over more than half of the species' range on the island of Tasmania (Fig. 2), including the majority of higher-density populations (9, 10). Populations affected by DFTD have suffered declines as great as 89% (9, 10). This consistently fatal disease is an infectious cancer, thought to be transmitted by allograft, with tumor cells spread directly between devils through biting (11, 12). Very low diversity in MHC genes, which play a key role in immune response to tumors and grafts, enables transmission (13). The tumors primarily affect adults (animals $\geq$2 years old) and cause death within months. Evidence that most penetrating biting injuries occur among adult males and females in the mating season (14) and that the disease persists at very low population densities suggests that the disease may be strongly frequency-dependent (10). Frequency-dependent diseases do not burn out at low host density and can cause extinction (15). Indications of frequency dependence and predictions from two different types of population modeling, combined with estimated rates of ongoing spread, have led to concerns that extinction in the wild is a possibility in 20–25 years' time (10). That this novel disease could have catastrophic consequences for the Tasmanian devil is an unfortunate coincidence of loss of genetic diversity at a functional gene region and aggressive mating-season behavior in a carnivore that frequently inflicts penetrating wounds with its canine teeth.

In this article, we investigate changes in life history in Tasmanian devil populations affected by the facial tumor disease. We analyzed data from five study sites where individually marked devil populations have been studied both before and after the arrival of the disease. Changes in precocial sexual maturity are documented in relation to changes in population age structure and consequent lifetime number of breeding events that result from the disease-induced increase in adult mortality.

Results

Disease has had a highly significant effect on the age structure of the devil populations at all five sites ($\chi^2 = -5.52$, df = 1, $P <$

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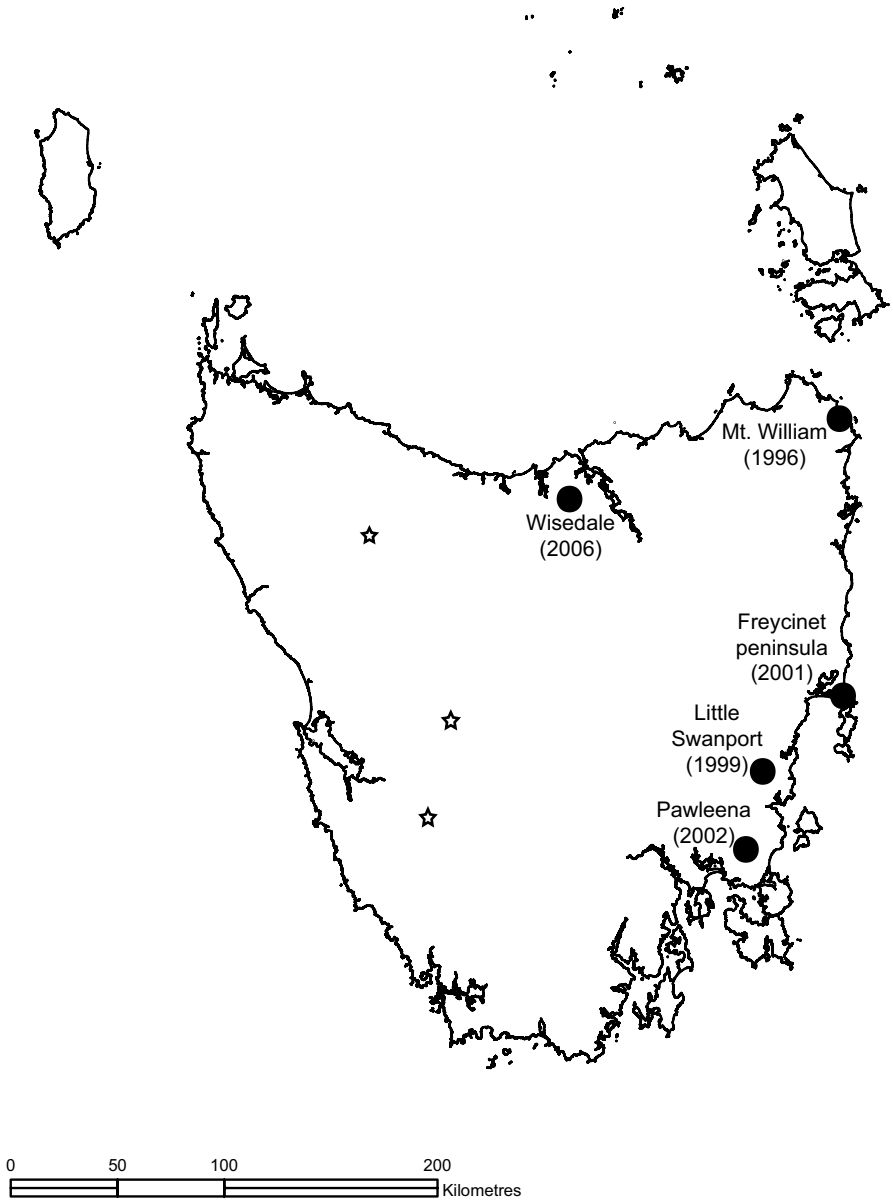

Fig. 2. Study sites in relation to current distribution of DFTD. A year in brackets is the year in which the disease was first detected at each site. Stars represent the known westernmost distribution of the disease in 2007.

0.001), with a much higher proportion of older (3+ years) animals present in the population before the disease (log odds ratio of being old vs. young before and after disease = −1.774, 95% C.I. −2.428 to −1.257; Fig. 3*a*). The final model included only disease (fixed effect) and between-year variation within site (random effect). There were no consistent differences between sexes (removal of sex term from model: $\chi^2 = 2.728$, df = 1, $P = 0.099$) or among sites (removal of site term from model: $\chi^2 = 7.663$, df = 4, $P = 0.105$).

Before the disease emergence at Freycinet, a significantly greater proportion of females (21 of a total of 29) produced more than one litter in their lifetime than after the disease spread across the site (6 of 17; Fisher's exact test, $P = 0.028$; Fig. 4). Precocial breeding by 1-year-old females increased substantially after disease emergence (log odds ratio of 1-year-old breeding vs. not breeding before and after disease = −3.2797, 95% C.I. −5.147 to −1.728; $\chi^2 = -4.057$, df = 1, $P < 0.001$; Fig. 3*b*). Before the disease, between zero (at three sites) and 12.5% (year 2000 at Freycinet) of 1-year-old females bred. After the disease spread, precocial breeding increased on average 16-fold to between 13.3% (Mt. William, 2004) and 83.3% (also Mt. William, 2006), except at Little Swanport, where it remained at zero. The final model included only disease (fixed effect) and between-year variation within site (random effect). There were no statistically significant differences attributable to site (removal of site term from model: $\chi^2 = 7.437$, df = 4, $P = 0.115$).

Discussion

The arrival of DFTD on the Freycinet Peninsula in 2001 triggered an immediate and steady decline in survival rates (16) of at least 60% compared with former levels (10), resulting in a population comprised almost entirely of animals <3 years of age. Before the disease, the modal female began seasonal breeding at age 2 and produced a litter annually for 3 years, with senescence and death occurring in her fifth or sixth year (M.E.J., unpublished work) (17, 18). Females now generally have one breeding

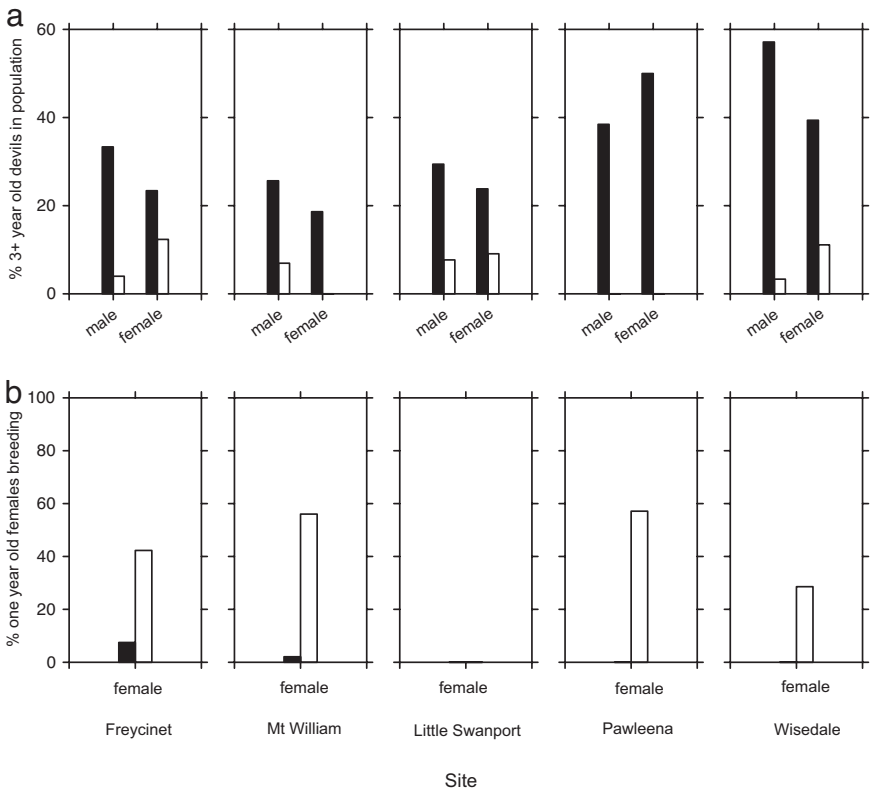

Fig. 3. Changes in life-history traits of Tasmanian devils (*Sarcophilus harrisii*) in response to invasion by DFTD at five sites across eastern Tasmania. Filled bars, before disease; open bars, after disease emergence. Sample sizes are provided in *Methods*. (*a*) Proportions of all males and all females 3 years or older before and after the appearance of the disease. (*b*) Proportion of 1-year-old females breeding in populations before and after arrival of the disease.

opportunity and may not survive long enough to rear that litter. Hence, they are now largely semelparous.

Comparable changes in age structure have occurred at four additional sites where data before and after disease invasion were collected. At Mt. William National Park, where the disease was first recognized 10 years ago, the population has declined by an estimated 89% following arrival of disease (10).

Substantial increases in precocial breeding by 1-year-old females occurred at four of the five sites. A cause for the lack of increase in precocial breeding at the Little Swanport site after disease arrival cannot be determined given the snapshot nature of the data and may be due to chance. Habitat is equivalent to other sites. We lack the data to test whether the disease status of breeding females the previous year affected growth and survival of the 1-year-old cohort of potential precocial breeders.

Tasmanian devils have shown their capacity to respond to this disease-induced increased adult mortality with precocious sexual maturity. A mechanism that might facilitate early breeding is more rapid growth in response to reduced population density and probably reduced food competition (4). A reduction in interference competition from older, more dominant females could also play a role, although it is unlikely to produce such dramatic results. Most adult devils breed in any one year (S.L., H.M., and M.E.J., unpublished work), even small, subordinate 2-year-old females. In addition, before DFTD emergence, records of precocial breeding were rare, and records were restricted to sites with good soil and plentiful prey, suggesting that resource levels may play a role.

Life-history theory predicts that selection for early reproduction will arise when adult survival is reduced to a greater extent than juvenile survival (19). In the specific case of parasitism, provided the prevalence of disease in the population increases with age, selection for early reproduction will occur (6). Demographic responses can, over time, evolve into new, genetically mediated life-history parameters (1). Tasmanian devils are the largest member of a marsupial clade famous for intense investment in early reproduction at the expense of longevity, exemplified by the repeated evolution of semelparity (20). Devils share with semelparous carnivorous marsupials (20) several traits that may predispose them to an emergent shift in breeding toward precociality when semelparity is imposed. They breed few times and reproduction is costly. Over the mating season, males experience 25% weight loss (M.E.J., unpublished work) (18), anemia (M.E.J., unpublished work), and often a reduction in immunocompetence (B. Burton and G. Woods, unpublished work). Devils are thus an excellent model species with an interesting new disease, which behaves like a parasite in that it is a piece of devil that propagates itself to another devil, in which to pursue questions of adaptation.

Rapid evolution on ecological time scales is now widely recognized in natural ecosystems (21), including resistance to parasites (22). There is accumulating evidence that adaptation to strong directional selection can contribute to the persistence of populations (23). Whereas the presence of genetic variation in populations needed for traits such as age at maturation is well established (24–27), of emerging interest is the role of phenotypic plasticity in adaptive responses. If a particular form of phenotypic plasticity enhances an organism's probability of surviving directional selection at the population level, it may lead to an adaptive evolutionary response (28). A pertinent example that demonstrates life-history change under directional selection is increased mortality under harvesting pressure inducing early maturation in cod (2). Although such evolutionary responses are predicted, and demographic responses in age at maturity to

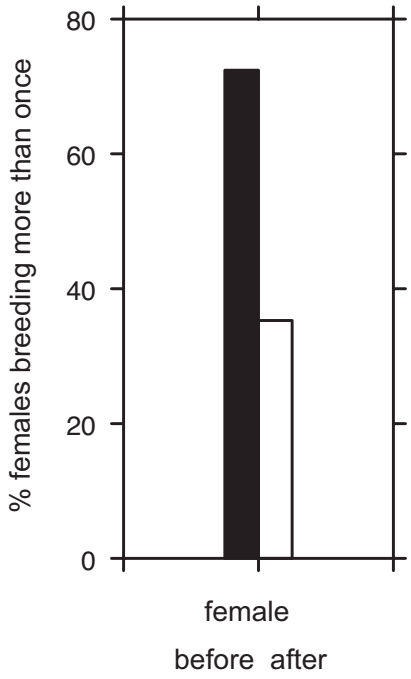

Fig. 4. Change in the proportion of all known adult females producing more than one litter in their lifetime before and after invasion of DFTD at Freycinet in eastern Tasmania.

harvesting pressure are documented (29), there is little empirical evidence for this phenomenon in mammals (27).

Here, we have a persistent situation of almost complete mortality of individuals in their first year of adult life from a new disease that is likely to become a permanent feature of devil biology. Phenotypic plasticity in life-history traits in Tasmanian devils is evident in the variation in precocial breeding among populations and years before the emergence of DFTD. Any ability in devils to increase lifetime reproductive output beyond one litter, or indeed to rear a single litter to independence before death from cancer, should also enhance the fitness of those individuals. Although MHC gene diversity is very low in Tasmanian devils in eastern Tasmania (13), this is not universal across either the genome or the island (e.g., neutral microsatellite loci) (30), and there is some diversity on which selection can operate. At this stage, all we have evidence for is a phenotypic response. We suggest that DFTD is a novel, strong selective agent for life-history change that might lead to rapid adaptation toward a population genetically and demographically more robust to the effects of DFTD.

To our knowledge, this is the first known case of infectious disease leading to increased early reproduction in a mammal. The persistence of this disease and ongoing population decline is of profound conservation concern for a unique endemic carnivore (10). Although the ability to switch to precocious reproduction offers some prospect for persistence and recovery, the prognosis for this iconic species remains uncertain.

Methods

We used data from five study sites that broadly represent the current geographic extent of the disease and where populations were trapped and individually marked both before and after the emergence of DFTD (Fig. 2). A 160-km^2 site on the Freycinet peninsula on the east coast of Tasmania was continually monitored from 1999 to 2007. The disease was first detected at the northern end of the peninsula in July 2001 and progressively spread southwards down the peninsula. Devil populations over the entire geographic area used in these analyses were affected by 2005. We compared ''before disease'' data from 2000 and 2001 (n = 110:129 males:females; n = 65 1-year-old females) only with ''after'' data from 2005 and 2006 (n = 45:48 males:females; n = 33 1-year-old females) because data from the intervening years included parts of the study site that were diseased combined with areas where the disease had not yet spread. At Mt. William National Park in northeast Tasmania, where the disease signs were first detected in 1996 (9), data from 2004 to 2006 (n = 39:35 males:females; n = 28 1-year-old females) was compared with that from an earlier study in 1983–1985 (n = 87:61 males:females; n = 42 1-year-old females) (18). Postdisease trapping data collected in 2006 were compared with 1999 data (30) for two other sites in southeast Tasmania: Little Swanport, which was in the early stages of disease invasion in 1999 (before: n = 17:13 males:females, n = 13 1-year-old females; after: n = 21:11, n = 8), and Pawleena, where the disease was first detected in 2002 (before: n = 13:16 males:females, n = 5 1-year-old females; after: n = 15:7, n = 7). Wisedale in northern Tasmania is near the current disease front and has been monitored to collect epidemiological parameters since the early stages of disease invasion in 2006. Data from 2006 and 2007 are presented (before: n = 21:33 males:females, n = 9 1-year-old females; after: n = 30:18, n = 14).

Populations were monitored by trapping conducted over 7 (Freycinet) or 10 (all other sites) consecutive nights at each study site, using specially designed carnivore traps baited with meat. Wire-cage traps were used until 2004, and PVC-pipe traps were used thereafter. After the disease emerged, biosecurity protocols were used to reduce the chance of the trapping program contributing to the spread of the disease. Devils were gently emptied into sacks, individually marked with ear tattoos (before 2004) or microchips (from 2004 to 2007), weighed and measured, and assessed for age and reproductive condition. Age was estimated by using a combination of molar tooth eruption, molar and canine tooth wear, canine over-eruption, body weight, and general appearance (M.E.J., unpublished work). The reproductive condition of females was assessed upon inspection of the pouch for pouch young or active lactation (enlarged teats and mammary glands). Field trapping of devils was approved by the Animal Ethics Committees of the University of Tasmania, the Australian National University, the University of Queensland, and the Tasmanian Department of Primary Industry and Water. These are established ethics committees which have an undertaking that the provisions of the *Australian Code of Practice for the Care and Use of Animals for Scientific Purposes*, referred to in the *Statement of Animal Experimentation*, will be observed.

Most female devils reach sexual maturity at the age of 2 and few live beyond 5 years of age in the wild (M.E.J., unpublished work). Breeding is seasonal, with the majority of births in March and April (31). The population was thus divided into young animals, defined as independent 1- and 2-year-olds before March of the year they turn 3, and devils older than 2. The aging techniques used are definitive to the age of 2 years, which is beyond the age of precocial breeding (14 months), and reliable to the age of 3, after which individual variance in tooth wear, and consequently over-eruption, reduces precision. To analyze the effect of DFTD on the proportion of females that breed more than once in their lifetime, we used only data from Freycinet, where detailed information on life history, including entire individual lifespans, has been collected since 1999 (before:after n = 29:17). For this analysis, reproductive events over the entire lifespan of individual females were examined for females that were present in 2000, 2001, 2005, and 2006.

All analyses were performed by using R version 2.5.0. The age structure and precocial breeding data were analyzed by using an REML-based generalized linear mixed model (lmer in R package lme4) with binomial error and a logistic link, using disease status and site as fixed effects and year within site as a random effect. The models were simplified by removing terms along lines recommended by Crawley (2005). The effects of removing terms are reported as χ^2 distributed likelihood ratios comparing models, and the effects of the fixed effects on the response variable are reported as Wald statistics (estimate divided by standard error). An mcmc resampling procedure using 1,000 iterations was used to provide confidence intervals for the effect of the disease, the effect of the log odds of being young rather than old, and the effect of breeding at age 1 or not before and after the disease. Mixed models were used because of significant residual variation associated with the year within site term when this term was included as a fixed effect in an entirely fixed-effects model. Lack of any two- or three-way interactions in the fixed-effects models also confirmed that no important interactions had been neglected. The proportion of all known adult females producing more than one litter in their lifetime before and after the disease on the Freycinet peninsula was analyzed by using Fisher's exact test.

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1. Reznick DA, Bryga H, Endler JA (1990) Experimentally induced life-history evolution in a natural population. *Nature* 346:357–359.
2. Olsen EM, *et al.* (2004) Maturation trends indicative of rapid evolution preceded the collapse of northern cod. *Nature* 428:932–935.
3. Eberhardt LL (2002) A paradigm for population analysis of long-lived vertebrates. *Ecology* 83:2841–2854.
4. Coulson T, Guinness F, Pemberton JM, Clutton-Brock T (2004) The demographic consequences of releasing a population of red deer from culling. *Ecology* 85:411–422.
5. Reznick DN, Ghalambor CK (2005) Can commercial fishing cause evolution? Answers from guppies (Poecilia reticulata). *Can J Fish Aquat Sci* 62:791–801.
6. Hochberg ME, Michalakis Y, de Meeus T (1992) Parasitism as a constraint on the rate of life-history evolution. *J Evol Biol* 5:491–504.
7. Agnew P, Koella JC, Michalakis Y (2000) Host life history responses to parasitism. *Microbes Infect* 2:891–896.
8. Michalakis Y, Hochberg ME (1994) Parasitic effects on host life-history traits: A review of recent studies. *Parasite J Soc Fr Parasitol* 1:291–294.
9. Hawkins CE, *et al.* (2006) Emerging disease and population decline of an island endemic, the Tasmanian devil Sarcophilus harrisii. *Biol Conserv* 131:307–324.
10. McCallum H, *et al.* (2007) Distribution and impacts of Tasmanian devil facial tumour disease. *EcoHealth* 4:318–325.
11. Pearse AM, Swift K (2006) Transmission of devil facial-tumour disease. *Nature* 439:549.
12. Pyecroft SB, *et al.* (2007) Towards a case definition for Devil Facial Tumour Disease: What is it? *EcoHealth* 4:346–351.
13. Siddle HV, *et al.* (2007) Transmission of a fatal clonal tumour by biting occurs due to depleted MHC diversity in a threatened carnivorous marsupial. *Pro Natl Acad Sci USA* 104:16221–16226.
14. Hamede R, McCallum HI, Jones ME (2008) Seasonal, demographic and density-related patterns of contact between Tasmanian devils: Implications for transmission of Devil Facial Tumour Disease. *Aust Ecol* 33:614–622.
15. de Castro F, Bolker B (2005) Mechanisms of disease-induced extinction. *Ecol Lett* 8:117–126.
16. Lachish S, Jones M, McCallum H (2007) The impact of devil facial tumour disease on the survival and population growth rate of the Tasmanian devil. *J Anim Ecol* 76:926–936.
17. Guiler ER (1978) Observations on the Tasmanian devil, *Sarcophilus harrisii* (Dasyuridae: Marsupialia) at Granville Harbour, 1966–75. *Pap Proc R Soc Tasmania* 112:161–188.
18. Pemberton D (1990) Social organisation and behaviour of the Tasmanian devil, Sarcophilus harrisii. PhD thesis (Univ of Tasmania, Hobart).
19. Charnov EL, Schaffer WM (1973) Life history consequences of natural selection: Cole's result revisited. *Am Nat* 107:791–793.
20. Oakwood M, Bradley AJ, Cockburn A (2001) Semelparity in a large marsupial. *Proc R Soc London Ser B* 268:407–411.
21. Carroll SP, Hendry AP, Reznick DN, Fox CW (2007) Evolution on ecological time-scales. *Funct Ecol* 21:387–393.
22. Duffy MA, Sivars-Becker L (2007) Rapid evolution and ecological host-parasite dynamics. *Ecol Lett* 10:44–53.
23. Kinnison MT, Hairston NG (2007) Eco-evolutionary conservation biology: Contemporary evolution and the dynamics of persistence. *Funct Ecol* 21:444–454.
24. Reznick DN, Shaw FH, Rodd FH, Shaw RG (1997) Evaluation of the rate of evolution in natural populations of guppies (Poecilia reticulata). *Science* 275:1934–1937.
25. Roff DA (2000) Trade-offs between growth and reproduction: An analysis of the quantitative genetic evidence. *J Evol Biol* 13:434–445.
26. Tenhumberg B, Tyre AJ, Pople AR, Possingham HP (2004) Do harvesting refuges buffer kangaroos against evolutionary responses to selective harvesting? *Ecology* 85:2003–2017.
27. Proaktor G, Coulson T, Milner-Gulland EJ (2007) Evolutionary responses to harvesting in ungulates. *J Anim Ecol* 76:669–678.
28. Ghalambor CK, McKay JK, Carroll SP, Reznick DN (2007) Adaptive versus non-adaptive phenotypic plasticity and the potential for contemporary adaptation in new environments. *Proc Natl Acad Sci USA* 21:394–407.
29. Langvatn R, Albon SD, Burkey T, Clutton-Brock TH (1996) Climate, plant phenology and variation in age of first reproduction in a temperate hervivore. *J Anim Ecol* 65:653–670.
30. Jones ME, Paetkou D, Geffen E, Moritz C (2004) Genetic diversity and population structure of Tasmanian devils, the largest marsupial carnivore. *Mol Ecol* 13:2197–2209.
31. Hesterman H (2007) Reproductive physiology of the Tasmanian devil (Sarcophilus harrisii) and spotted-tailed quoll (Dasyurus maculatus). PhD thesis (Univ of Tasmania, Hobart).